ISSN 0972-1789

Annual Report 2020-21

Celebrating 70 Glorious Years

CSIR-Central Drug Research Institute

Fundamental Science Driven Innovation

csir_cdri | csir.cdri | www.cdri.res.in | director@cdri.res.in

Editorial Board

Acknowledgement

Editorial board sincerely thanks and acknowledges all those who have extended their generous support, advice and help, in the preparation of the Annual Report 2020-21. We are grateful to all the Area Coordinators and Heads/ In Charge of Divisions/ Units, Administration for timely submission of data and for the support.

Published by Scientific Directorate on behalf of the Director, CSIR-Central Drug Research Institute, Lucknow

Printed at : APP Press, 33 Nehru Road, Sadar Cantt., Lucknow, Ph.: 522-481164

With best compliments from

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ANNUAL REPORT
2020 - 21

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Organizational Structure

Shri Narendra Modi
Hon'ble Prime Minister of India
& President, CSIR

Dr. Harsh Vardhan
Hon'ble Union Minister for Health & Family Welfare,
Science & Technology and Earth Sciences
& Vice-President, CSIR

Dr. Shekhar C. Mande
Secretary, DSIR & Director General, CSIR

Prof. Tapas K. Kundu
Director, CSIR-CDRI

Research Council — Management Council

R&D Divisions
- Biochemistry
- Botany
- Cancer Biology
- Endocrinology
- Medicinal and Process Chemistry
- Microbiology
- Molecular & Structural Biology
- Molecular Parasitology and Immunology
- Neuroscience and Ageing Biology
- Pharmaceutics & Pharmacokinetics
- Pharmacology
- Toxicology & Experimental Medicine

Unique R&D Facilities and Services Group
- GLP Test Facility
- *Common Research and Technology Development Hub*
- Sophisticated Analytical Instrument Facility
- Laboratory Animal Facility
- Tissue & Cell Culture
- National Repository of Organic Compounds
- Knowledge Resource Centre
- Herbarium and Horticulture

Knowledge Management Group
- Scientific Directorate
- Business Development & Intellectual Property Group
- Academic Affairs
- Human Resource Development

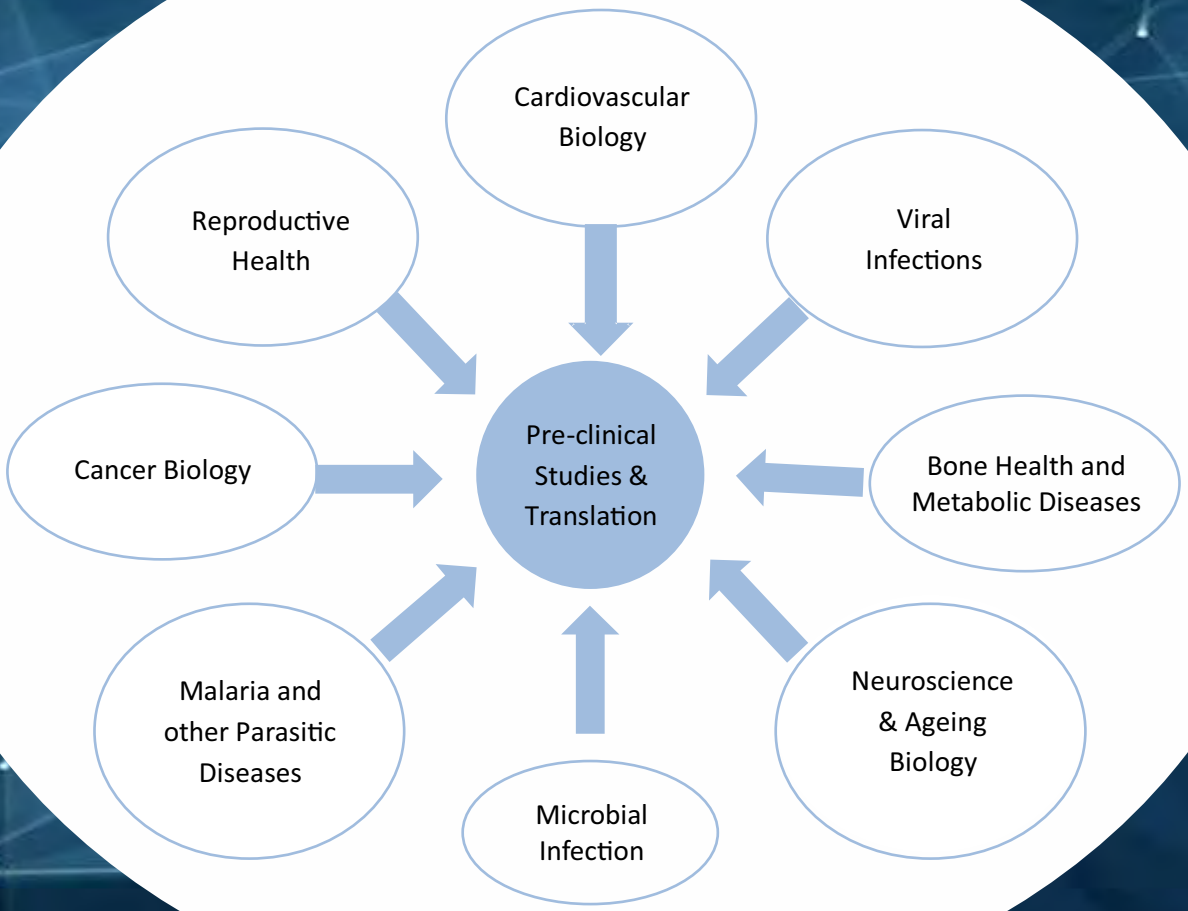
Infrastructure Management Group
- IT and Networking
- Centralized Utility Services and House Keeping
- Auditorium
- Instrumentation
- Engineering Services

Field Stations
- CDRI Clinical Pharmacology Unit, Seth G.S. Medical College, Mumbai
- KGMU, Lucknow
- PGIMER, Chandigarh

General Administration and Facilities
- Administration
- Finance & Accounts
- Stores & Purchase
- CSIR Dispensary
- Canteen

Contents

Thrust Areas of Research



From the Director's Desk

I am delighted to present the Annual Report 2020-21 of our Institute, a premier drug research centre of India engaged in globally significant fundamental research-driven innovations in the area of biomedical and pharmaceutical sector. This year, we are celebrating 70 glorious years of the foundation of our Institute. When I look back at the contributions of this premier Institute over the last 70 years, it makes me proud and also a sense of huge responsibility.

Our Institute was conceptualized well before the Independence of our Nation and was formally dedicated to the Nation on 17 February 1951. The founding mission of our Institute was to revamp the pharmaceutical sector of India, which was almost non-existent then. Over the last seven decades, the Institute has grown into an epicentre of new drug discovery and development in India. Out of 21 new drugs discovered and developed in India, 13 are from our Institute. Globally accepted antimalarial drug alpha-beta Arteether; and the world's first non-steroidal oral contraceptive – Centchroman (INN: Ormeloxifene) are the proud contributions of CSIR-CDRI. More than 80 indigenized process technologies for the drugs and pharmaceuticals, the highest quality human resource, and consultancy to pharma industries have paved the way for the transformation of the Indian Pharmaceutical sector. For the last several years, India is popularly known as "Pharmacy of World." The direct and indirect contributions of CSIR-CDRI are critical in this transformation.

Fundamental disease biology and medicinal chemistry are the innate strength of our Institute. Now, aligned with the vision, mission, and policy of the Government, the Institute is focussing on immediate national priorities with a futuristic vision. While collaborating with biopharma industries and premier academic organizations, research emphasis is in the area of Parasitic & Microbial Infections, Ageing & Neuroscience, Cancer Biology, Lifestyle disorders and Reproductive Health. Considering the immediate as well as futuristic needs, the Institute is strengthening its capabilities in the areas of Ageing & Neuroscience and viral infections. In the area of Cancer Biology, the Institute is leading a PAN CSIR Cancer Research Program focussing on women empowerment. We are also networking with multiple prominent Medical Colleges across India to achieve the objectives of the PAN CSIR Cancer Research Program. Similarly, in the area of Viral Infections, in collaboration with APJAKTU, Lucknow and KGMU, Lucknow, the Institute is working to establish a Centre Unit of Excellence for Viral Research and Therapeutics. In this program, emphasis will be on Corona, Japanese Encephalitis and Dengue viruses that are posing renewed threats to our Nation. Our ambitious proposal to establish a centre for drug discovery and development using natural products at Hengbung village, Manipur is also at an advanced

stage of consideration. This centre shall be created in about 100 Acre strategically chosen hilly terrain to exploit the natural treasure of medicinal plants and the traditional knowledge therapy of the region.

The year 2020, dominated by the COVID-19 pandemic, was a challenging year for life and science globally. During the first half of 2020, the work-life of researchers was severely affected. Despite the odds, I find that 2020 was one of the productive years for our Institute, albeit with a slight change in the pace and the emphasis of the research activities of the Institute.

Soon after the declaration of the COVID-19 pandemic by WHO, CSIR-CDRI, with ample experience of new drug discovery, development, process chemistry, and molecular & structural biology, advantageously positioned itself to contribute to the Nation's fight against COVID-19 with vigour. Within one month of nationwide lockdown, our Institute scientists developed a process technology for Umifenovir, an antiviral drug with the potential to be a COVID-19 therapeutic. Subsequently, the technology was transferred to industry, IND filed, DCGI permission obtained and Phase III clinical trials were initiated in a record time. Clinical trials of the Umifenovir is currently at an advanced stage and we are anticipating to conclude it very soon. Efforts were also initiated for the development of technology for four more drugs with the potential to be a COVID-19 therapeutic. Considering the national emergency, in a month's time, the Institute set-up the COVID-19 testing facility, approved by the Indian Council for Medical Research, and initiated testing of samples from Uttar Pradesh. Till date, more than 1.3 lakh samples have been tested in the facility. In collaboration with King George's Medical University & SGPGI, Lucknow, the Institute initiated Genome sequencing studies of the SARS-CoV-2 samples from Uttar Pradesh. Genomic studies of SARS-CoV-2 samples have given vital clues of genomic variation in the symptomatic and asymptomatic cases, including lethal strains. Another team of researchers from CSIR-CDRI, collaborated with an industry partner for the development of the fluorescent dye and quencher for the indigenous qRT-PCR kit. We anticipate that this product will reach the market very soon. Team CSIR-CDRI is proud of its contributions to the Nation's fight against COVID-19.

I am happy to report that in the year bygone, in a span of twelve months' period, Institute has filed 3 INDs and received permission for clinical trials from the Drug Controller General of India. This accomplishment is unique for any organization in India involved in drug discovery and development. In January 2020, we received DCGI permission for Phase I Clinical Trial of S007-867 (antithrombotic) candidate drug discovered and developed by the Institute. In June 2020, DCGI permission was received for the Phase III clinical trials of Umifenovir on COVID-19 patients. Again on 8th January 2021, our Institute received DCGI approval for the Phase I clinical trial of S007-1500, a promising oral fracture healing agent discovered and developed by the Institute.

In terms of measurable performance, the Institute has made significant accomplishments in the year 2020. As per the provisional data, a total of 218 research papers have been published by the Institute researchers with an average impact factor of 3.66. The Institute has filed 8 patents in India and has been granted 5 foreign patents and 8 Indian patents. A total of 42 Ph.D. scholars submitted their thesis and 15 aspirants have received post-graduate training. During the year, Institute has also initiated a total of 22 externally funded projects, including 2 industry-sponsored projects and 2 consultancy projects. Total approved budget of the projects is Rs. 8.53 Crore. I am happy to report that during the year, the Institute scientists received several major honours and awards including fellowship of Science Academies of India, awards from significant agencies and societies. The ensuing pages of this report showcase the accomplishments of the Institute and its researchers during the year.

The recruitment drive for the first batch of 13 Scientists is at the concluding stage. We expect the joining of the new recruits to CSIR-CDRI very soon. The second batch of 17 scientist posts has received a huge response from aspiring candidates. Similarly, for the advertisement for recruitment of 57 positions of Technical Gr. III and Gr. II positions, a large number of applications have been received. We are hopeful of recruiting excellent human power soon who will serve the Institute and the Nation for the coming several years.

I am hopeful that the Institute will continue to reap even more fruitful achievements in the coming year through the relentless efforts of its dedicated team of researchers and support staff in collaboration with industries, research Institutes and academic organizations. CSIR-CDRI will continue to advance innovations in biomedical and pharmaceutical research. The focus of the Institute will remain on national priorities with global significance.

I thank all my colleagues at each level for their constant support and wish them the very best for many more recognitions and accolades.

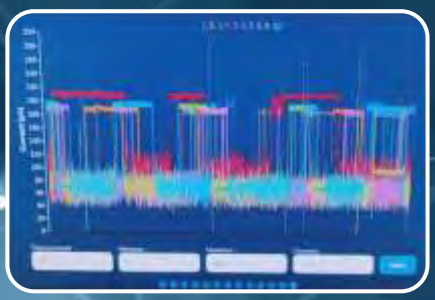
(Tapas K. Kundu)

17 February 2021

Executive Summary and R & D Highlights








Genome Sequencing
so far, 200 SARS-CoV-2 genomes have been sequenced.

Drug repurposing
Phase III clinical trial of Umifenovir ongoing

CDRI's efforts in Nation's fight against covid-19 pandemic

COVID-19 Testing Facility
So far, more than 1,30,000 samples have been tested.

Novel Diagnostic Tools
CSIR-CDRI has designed dual labelled probe for RT-PCR.






Highlights of Achievements 2020-21

CSIR-CDRI

Products & Technologies		
IND filed and DCGI Permission received	:	• Umifenovir (Antiviral) – Phase III Clinical Trial • S007-1500 (Fracture Healing) – Phase I Clinical Trial
Technologies Developed, Licensed & Transferred	:	• Umifenovir (Antiviral) transferred to M/s Medizest Pharmaceuticals Pvt. Ltd., Goa • Fluorescent dye and quencher for indigenous qRT-PCR transferred to Biotech Desk Pvt. Ltd. Hyderabad
Technologies Developed (Lab scale)	:	• Niclosamide (Antihelminthic) • Centhaquin (For management of hypovolemic shock)
Facility Creation and Accreditation	:	• COVID-19 Testing Laboratory approved by ICMR • Medical testing laboratory accredited by NABL • GLP Test Facility for Pharmaceuticals (Human) accredited by NGCMA
Publications in SCI Journals		
Total Number	:	218
Average Impact Factor	:	3.66
Publications with >5 Impact Factor	:	36
Patents		
Filed in India	:	8
Granted Abroad	:	5
Granted in India	:	8
Human Resource Development		
Ph.D. Thesis Submitted	:	42
Post Graduate / Skill Trainings	:	15
New Projects Initiated		
Externally funded projects (Grant-in-Aid & Sponsored)	:	22
Total approved cost of the externally funded projects (Grant-in-Aid & Sponsored)	:	Rs. 8.53 Crore

Breakthrough Achievement in 2020-21

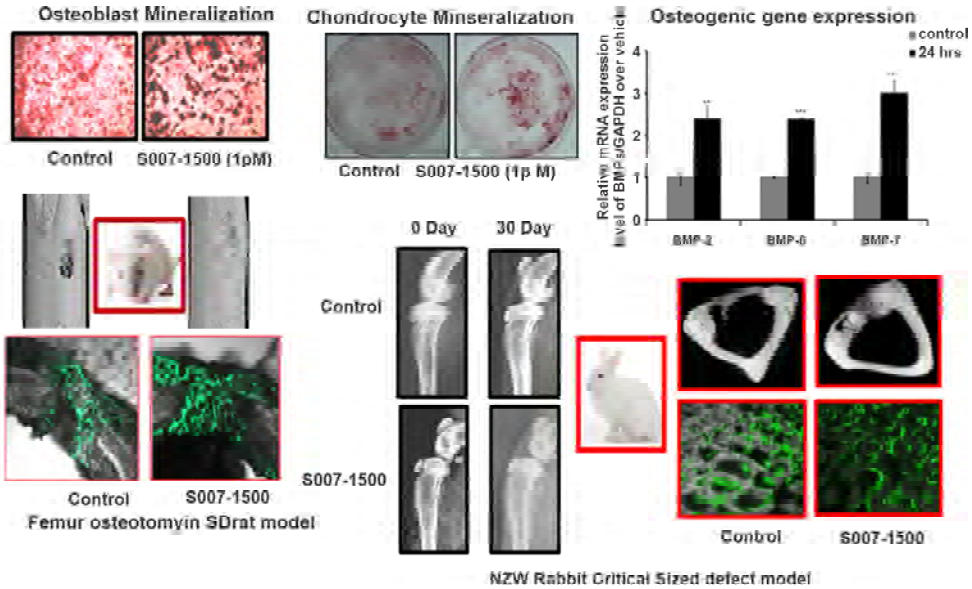
Investigational New Drug S007-1500:
A Novel Orally Active Fracture Healing Drug Candidate

DCGI Approval Received on 08 January 2021 for Phase I Clinical Trial

Fatalities and injuries resulting from road traffic accidents are a major and growing public health problem in India. Fractures resulting in this injuries are mainly of delayed union or non-union type which take very long time to heal. Currently there is no FDA approved orally active fracture healing drug available nationally or internationally. Recombinant human BMP2 (INFUSE® Bone Graft) has been approved for open tibial fractures by FDA. However, the use of BMP2 is hampered by numerous clinical complications such as postoperative inflammation, cyst-like bone formation and life-threatening cervical swelling. Moreover, bone grafts are very costly. Packages of Infuse can range from $2,500 to $5,000. Thus, there is an unmet need for new fracture healing agents which are cost effective and devoid of any side effects. CSIR-CDRI studies have led to the identification of a novel orally active fracture healing agent S007-1500. The salient features of the molecule are as below:

S007-1500 Salient features

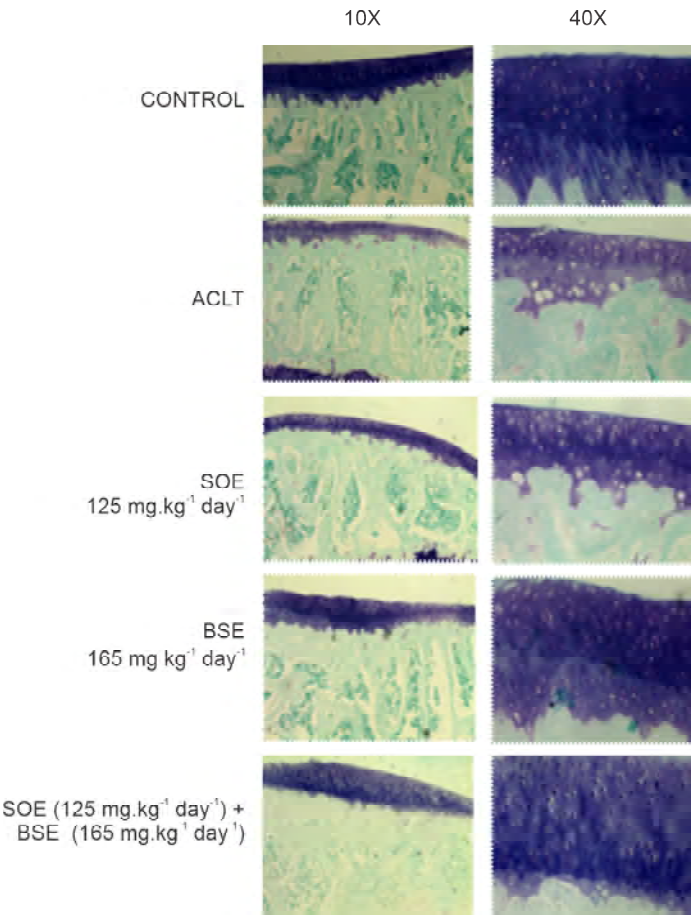
- Novel orally active fracture repairing drug candidate.
- Enhances osteoblast differentiation and mineralization at concentration as low as 1pM (EC_{50}= 3.125 nM).
- Enhances new bone formation and restores bone microarchitecture in adult osteopenic rats.
- Enhances bone regeneration at fracture site at only 1.0 mg $kg^{-1}.day^{-1}$ dose by stimulation of BMP/Smad signaling pathway.
- New bone formation at the fracture site is increased by ~40% in rats treated with S007-1500.
- S007-1500 enhances bone mineral density, new bone formation and bone biomechanical strength in ovariectomized osteopenic rat model.
- S007-1500 restores ovariectomized (Ovx) induced deterioration in bone microarchitecture.
- S007-1500 prevents Ovx induced increase in bone resorptive marker, CTx (a collagen breakdown product).
- S007-1500 prevents Ovx induced increase in bone turnover marker like serum OCN.
- Oral administration of S007-1500 at 1 mg/kg in rabbit critical size defect model led to almost complete bone healing at defect site as analyzed by radiography.
- S007-1500 is found safe in regulatory toxicity and safety pharmacology in GLP (rodents and non-rodents) as per Schedule “Y” and FDA guidelines.



Breakthrough Achievement In 2020-21

Synergistic combination of *Spinacea oleracea* and *Boswellia serrata* for improved response in osteoarthritis

After launching JOINT FRESH a nano-formulation for osteoarthritis in the market, further experiments, were carried *Spinacea oleracea* which has been reported for its chondroprotective potential was further explored the possibility of combining its chondrogenic efficacy along with a strong anti-inflammatory agent *Boswellia serrata*. Studies showed increase in the ratio of hyaline cartilage to calcified cartilage, histologically, in the rat model after the inductuction of OA in the group treated with a combined dose of *Spinacea oleracea* (SOE) and *oswellia serrata (*BSE) *(Please refer to figure).* Furthermore, performed the rotarod experiment in order to evaluate the synergistic potency of the combination of SOE and BS extract in improving the latency to fall, which manifests its role in alleviating the pathogenesis of osteoarthritis in the human mimic rat model of ACLT induced osteoarthritis. RT-PCR analysis show increased fold activity in the expression of Sox9 and Col 2 which are key chondrogenic markers, in the chondrocytes treated with the combination of two extracts and the combination of individual purified compounds respectively as compared to the cells treated alone. Also assessed its synergy in scavenging reactive oxygen species (ROS) and reactive nitrogen species (RNS) generated in the *in-vitro* system by DCFDA and Griess reagent respectively.



Clinical trial: A randomized parallel group placebo Phase-II clinical trial was done with Ayurved Seva Sanghs Ayurved Mahavidyalaya, Nashik with formulation of *Spinacea oleracea* extract (500mg) and *Boswellia serrata* extract (400 mg) in 148 patients for 6 months. Both markers of cartilage formation and regeneration were studied. Osteo-arthritis was assessed on basis of W Score In all groups, mean scores show significant difference between before and after treatment for VAS scale and WOMAC Score. For these parameters it can be said that treatment is effective in knee osteoarthritis.

The reduction in knee pain observed was statistically significant. Findings confirmed the effect of spinach in improving the symptoms of osteo-arthritis. The product by the name ***On toes*** in tablet form to be lunched soon.

Breakthrough Achievement in 2020-21

Licensing and demonstration of know-how process technology for the preparation of the Umifenovir for COVID-19 and Phase III Clinical Trial

Umifenovir is an antiviral drug, which have been used for the treatment of influenza infection in Russia and China. This drug is presently unavailable to Indian patients. Umifenovir is being investigated as a potential treatment and prophylactic agent for COVID 19 caused by SARS-CoV2 infections in combination with both currently available and investigational HIV therapies. At CSIR-CDRI we developed the improved and scalable process of Umifenovir on a multi-gram scale and this technology was transferred to our industrial partner Medizest Pharmaceuticals Pvt. Ltd., Goa.

Phase III, Randomized, Double-blind, Placebo Controlled trial of Efficacy, Safety and Tolerability of Antiviral Drug Umifenovir vs Standard Care of Therapy in non-severe COVID-19 patients is ongoing at multiple clinical trial sites in Uttar Pradesh, including King George's Medical University, Lucknow; Ram Manohar Lohia Institute of Medical Sciences, Lucknow; and Eras Lucknow Medical College and Hospital, Lucknow.

CDRI's efforts in Nation's Fight Against COVID-19 Pandemic

COVID Testing Facility Approved by ICMR

Since the COVID-19 outbreak in Seafood market of Wuhan city, China, in November 2019, in a span of about 4 months, the disease spread to 213 countries and territories around the world and infected millions of people. On 30 January 2020, considering the severity and the territory that COVID-19 covered, WHO declared it as Public Health Emergency of International Concern. Subsequently, on 11 March, WHO declared this disease as Pandemic.

In the first week of February, only 14 laboratories in India were testing for COVID-19. There was emergent need to increase the number of testing facilities across India to meet the requirement. Considering the national need, Institute established RT-PCR based SARS CoV-2 screening laboratory with BSL2+ facility within one month of announcing the Nationwide lockdown and initiated testing of samples received from State Government of Uttar Pradesh. About 800-1000 samples are being tested daily. More than 1,30,000 patient samples have been tested in the facility till date.

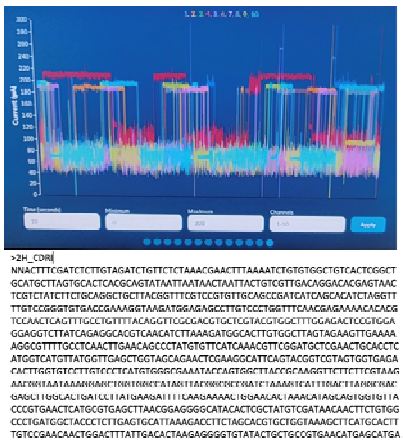
CDRI's efforts in Nation's Fight Against COVID-19 Pandemic

Development of drug-target based assay platforms and screening against COVID 19

Considering the pandemic situation due to COVID-19, enormous efforts are being made to identify lead drug candidates either through drug repurposing or by identification of new chemical entities. This important activity requires the establishment of Drug-target based Assay platforms and screening against COVID 19. This project on development of drug target based assay platforms and screening against COVID-19 was implemented in CSIR laboratories with CSIR-CDRI as a nodal laboratory. Purification of proteins and assays for targets like m-pro, PL-pro, RNA-dependent RNA polymerase and Spike-ACE2 have been standardized across the laboratories. The FDA approved library of drugs and isolated natural product compounds from important plants like *Andrographis paniculata*, were screened against them computationally and the best hits were evaluated against them through *in vitro* inhibition assays and virus culture inhibition assays. The results are being exploited in drug-repurposing strategies as well as in new lead development.

Sequencing of viral strains from patient samples to identify mutations and their implications for therapeutics

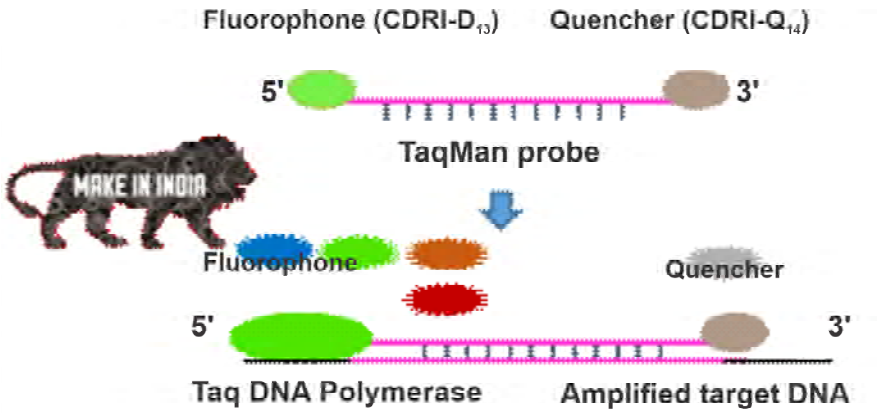
Coronaviruses possess the largest genomes (26.4–31.7 kb) among all known RNA viruses, with G+C contents varying from 32% to 43%. Variable numbers of small ORFs are present between the various conserved genes (ORF1ab, spike, envelope, membrane and nucleocapsid) and, downstream to the nucleocapsid gene in different coronavirus lineages. Given the high rate of human to human transmission of this virus, it is important to identify the basis of its replication, structure, and pathogenicity for discovering a way to its treatment or the prevention. Sequencing of the viral genome Uttar Pradesh was first undertaken by the Central Drug Research Institute, Lucknow. So far sequenced about 200 viral isolates and found significant differences in the viral genome sequence across patient categories based on the level of symptoms (unpublished data). Sequencing study on samples from Uttar Pradesh, suggested a lot of similarities and differences with viral genomes from other parts of the country, signifying the importance of sequencing the regional samples.



CDRI's efforts in Nation's Fight Against COVID-19 Pandemic

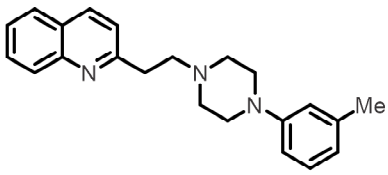
CDRI Designed Dual labeled probe for RT-PCR

The cornerstone of COVID-19 containment is testing of the SARS-CoV-2 infection, followed by quarantine or treatment of the infected individuals. Currently, RT-PCR is the most robust and accurate method of testing for the SARS-CoV-2. Several fluorescent dyes and quenchers with a variety of excitation and emission characteristics were prepared for TAQMAN probes, which are used in qRT-PCR diagnostics of COVID-19. With goal of capacity building for India on the path to make India self-reliant without depending on the supply of key materials from foreign manufacturers. Institute developed dual labeled probe for RT-PCR. The technology of fluorescent dyes and quenchers has been transformed to a company for further development and commercialization.

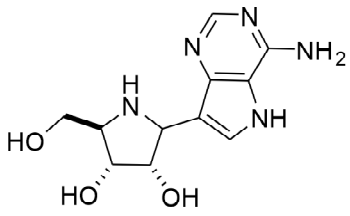


Indigenized Process Technologies of Drugs

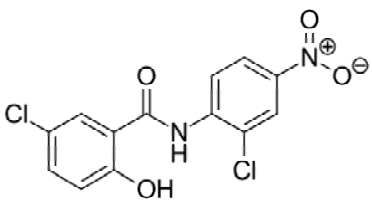
Considering the pandemic situation due to COVID-19, Institute efforts have been focused towards providing solution through repurposing route that would be the fastest way to find a cure. Apart from ongoing work on the repurposing of Umifenovir, in the mission mode project from CSIR, Institute is working on Niclosamide, Galidesivir, PB-28, and Centhaquine. For Centhaquin and Niclosamide, reaction conditions on 10g scale has been optimized.



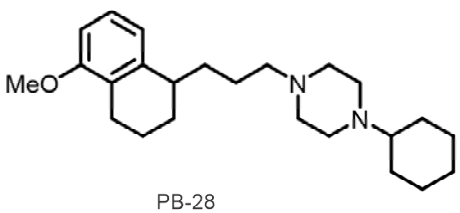
Centhaquin



Galidesivir



Niclosamide



PB-28

Advances in Drug Discovery & Developmental Studies

Nature & Name	Indication	Current Developmental Stage
Synthetic Compounds		
S007-0867	Antithrombotic	DCGI Permission Received for Phase I Clinical Trial
S007-1500	Fracture healing	DCGI Permission Received for Phase I Clinical Trial
S011-1793	Antimalarial	Pre-clinical regulatory studies ongoing
96-261	Antileishmanial	Pre-clinical regulatory studies ongoing
GS/IICT5-6	Antiangiogenic	Pre-clinical studies ongoing
SB-CDRI4-105	Neuropathic pain	Pre-clinical studies ongoing
Phytopharmaceuticals		
CDR219C002	Glucocorticoid induced osteoporosis	IND enabling studies ongoing
CDR267F018	Antidyslipidemic / Cardioprotective	IND enabling studies ongoing
NMITLI-118R(T+)	Anti-stroke	Toxicity studies in primates is being planned.
CDRI1703F003	Anti-PCOS	*In vivo* efficacy in rodent model
Mucuna pruriens extract	Male pro-fertility	Efficacy established in rodent model. Open for licensing
Picroliv	NAFLD	IND enabling studies
CDRI4655	Dyslipidemia	Formulation development for IND enabling studies
CDRI 0135C002	Cognitive impairments	*In vivo* efficacy in rodent model
Peptides		
S016-1348	Anticancer Smac mimetic	*In vivo* efficacy in rodent model
S016-1271	Antimicrobial and anti-endotoxin peptide	*In vivo* efficacy in rodent model
Formulations		
SMEDD formulation of Arteether and Fansidar	Antimalarial	Efficacy studies in Monkey model is to be done
Dry powder inhalation for pulmonary TB	Antituberculosis	Clinical Testing Plan for Phase-1 trial submitted to Institutional Ethics Committees at KGMU and CSIR-CDRI for approval.
Repurposing of Known drugs		
L-Ormeloxifene	Breast cancer	*In vivo* efficacy studies in rodent models
Pentoxifylline	Post-menopausal osteoporosis	Phase II clinical trial preparation ongoing
A depot formulation D-368 of an antimicrobial drug with osteogenic effect.	Long bone non-unions/delayed unions	Pre-clinical studies

Industry / Academia Partnership

Number of Agreements executed

Agreement	Nos
Licensing and Technology Demonstration	2
Collaborative Research	4
Sponsored Agreement	2
Consultancy Agreement	2
Memorandum of Understanding	10
Testing Services Agreement	3
Secrecy Agreement	15
Material Transfer Agreement	11
Memorandum of Agreement	5
Total	**54**

Our Collaborators and Industry Partners

Some Important Publications-2020

Biological Sciences

Author	Title	Journal vol. (Iss), PP	IF
Khanam T, Afsar M, Shukla A, Alam F, Kumar S, Soyar H, Dolma K, Ashish, Pasupuleti M, Srivastava KK, Ampapathi RS and Ramachandran R	*M. tuberculosis* class II apurinic/ apyrimidinic-endonuclease/3'-5' exonuclease (XthA) engages with NAD(+)-dependent DNA ligase A (LigA) to counter futile cleavage and ligation cycles in base excision repair	**Nucleic Acids Research** 48(8), 4325–4343	11.501
Urandur S, Banala VT, Shukla RP, Gautam S, Marwaha D, Rai N, Sharma M, Sharma S, Ramarao P and Mishra PR	Theranostic lyotropic liquid crystalline nanostructures for selective breast cancer imaging and therapy	**Acta Biomaterialia** 113, 522-540	7.242
Kumar H, Chattopadhyay S, Das N, Shree S, Patel D, …. …. … … ….. …. …. ….. …. …. … Tripathi AK, Trivedi AK, Chattopadhyay N, Ramachandran R and Sanyal S	Leprosy drug clofazimine activates peroxisome proliferator-activated receptor-gamma and synergizes with imatinib to inhibit chronic myeloid leukemia cells	**Haematologica** 105(4), 971-986	7.116
Bharti R, Srivastava A, Roy T, Verma K, Reddy DVS, Shafi H, Verma S, Raman SK, Singh AK, Singh J, Ray L and Misra A	Transient transfection of the respiratory epithelium with gamma interferon for host-directed therapy in pulmonary tuberculosis	**Molecular Therapy — Nucleic Acids** 22, 1121-1128	7.032
Haldar AK, Nigam U, Yamamoto M, Coers J and Goyal N	Guanylate binding proteins restrict *Leishmania donovani* growth in nonphagocytic cells independent of parasitophorous vacuolar targeting	**MBIO** 11(4), e01464-20	6.784
Shukla RP, Dewangan J, Urandur S, Banala VT, Diwedi M, Sharma S, Agrawal S, Rath SK, Trivedi R and Mishra PR	Multifunctional hybrid nanoconstructs facilitate intracellular localization of doxorubicin and genistein to enhance apoptotic and anti-angiogenic efficacy in breast adenocarcinoma	**Biomaterials Science** 8(5), 1298-1315	6.183
Sharma A, Singh S, Ahmad S, Gulzar F, Schertzer JD and Tamrakar AK	NOD1 activation induces oxidative stress via NOX1/4 in adipocytes	**Free Radical Biology And Medicine** 162, 118-128	6.171
Mishra S, Divakar A, Srivastava S, Dewangan J, Sharma D, Asthana S, Chaturvedi S, Wahajuddin M, Kumar S and Rath SK	N-acetyl-cysteine in combination with celecoxib inhibits Deoxynivalenol induced skin tumor initiation via induction of autophagic pathways in swiss mice	**Free Radical Biology And Medicine** 156, 70-82	6.171
Gurjar AA, Kushwaha S, Chattopadhyay S, Das N, Pal S, China S Pal, Kumar H, Trivedi AK, Guha R, Chattopadhyay N and Sanyal S	Long acting GLP-1 analog liraglutide ameliorates skeletal muscle atrophy in rodents	**Metabolism-Clinical and Experimental** 103, 154044-154058	6.159
Hasanain M, Sahai R, Pandey P, Maheshwari M, Choyal K, Gandhi D, Singh A, Singh K, Mitra K, Datta D and Sarkar J	Microtubule disrupting agent-mediated inhibition of cancer cell growth is associated with blockade of autophagic flux and simultaneous induction of apoptosis	**Cell Proliferation** 53(4), e12749	5.753

Some Important Publications-2020

Chemical Sciences

Author	Title	Journal vol. (Iss), PP	IF
Husen S, Chauhan A and Kumar R	Site-selective 1,3-double functionalization of arenes using para-quinol, C-N, and C-C/C-P three-component coupling	**Green Chemistry** 22(4), 1119-1124	9.480
Jamali MF, Vaishanv NK and Mohanan K	The Bestmann-Ohira reagent and related diazo compounds for the synthesis of azaheterocycles	**Chemical Record** 20(11), 1394-1408	6.163
Barak DS, Dahatonde DJ, Dighe SU, Kant R and Batra S	Decarboxylative/oxidative amidation of aryl α-Ketocarboxylic acids with nitroarenes and nitroso compounds in aqueous medium	**Organic Letters** 23, 9381-9385	6.092
Kumar H, Prajapati G, Dubey A, Ampapathi RS and Mandal PK	Intramolecular 6-exo-dig Post-Ugi cyclization of N-Substituted 2-Alkynamides: Direct access to functionalized morpholinone glycoconjugates	**Organic Letters** 22, 9258-9262	6.092
Chauhan A, Patel RK, Grellier M and Kumar R	Hydrogen-Bond-Guided reaction of Cyclohexadienone-aldehydes with amines: synthesis of an aminal group containing a fused tetracyclic framework	**Organic Letters** 22(15), 6177-6181	6.092
Ahmad A, Dutta HS, Kumar M, Khan AA, Raziullah and Koley D.	Pd-Catalyzed C-H halogenation of indolines and tetrahydroquinolines with removable directing group	**Organic Letters** 22(15), 5870-5875	6.092
Kumar M, Sharma R, Raziullah, Khan AA, Ahmad A, Dutta HS and Koley D	Cu(II)-Catalyzed Ortho C(sp(2))-H diarylamination of arylamines to synthesize triarylamines	**Organic Letters** 22(6), 2152-2156	6.092
Vaishanv NK, Chandrasekharan SP, Zaheer MK, Kant R and Mohanan K	Substrate-controlled, PBu3-catalyzed annulation of phenacylmalononitriles with allenoates enables tunable access to cyclopentenes	**Chemical Communications** 56(75), 11054-11057	5.999
Singh SP, Tripathi S, Yadav A, Kant R, Srivastava HK and Srivastava AK	Synthesis of β-and γ-lactam fused dihydropyrazinones from Ugi adducts via a sequential ring construction strategy	**Chemical Communications** 56(84), 12789-12792	5.999
Zaheer MK, Gupta E, Kant R and Mohanan K	Metal-free alpha-arylation of alpha-fluoro-alpha-nitroacetamides employing diaryliodonium salts	**Chemical Communications** 56(1), 153-156	5.999
Ansari MY, Swarnkar S and Kumar A	Stereoselective aminosulfonylation of alkynes: An approach to access (Z)-beta-amino vinylsulfones	**Chemical Communications** 56(66), 9561-9564	5.999
Kumar A, Kant R and Tadigoppula N.	Ruthenium(II)-Catalyzed synthesis of Indolo[2,1-a]isoquinolines through double oxidative annulation reaction of phenyl isocyanates with Di(hetero)aryl Alkynes	**Advanced Synthesis & Catalysis** 362(24), 5627-5631	5.851
Ganesher A, Chaturvedi P, Sahai R, Meena S, Mitra K, Datta D and Panda G	New spisulosine derivative promotes robust autophagic response to cancer cells	**European Journal of Medicinal Chemistry** 188, 112011	5.572

Research Highlights

M. tuberculosis class II apurinic/apyrimidinic-endonuclease/ 3'-5' exonuclease (XthA) engages with NAD(+)-dependent DNA ligase A (LigA) to counter futile cleavage and ligation cycles in base excision repair

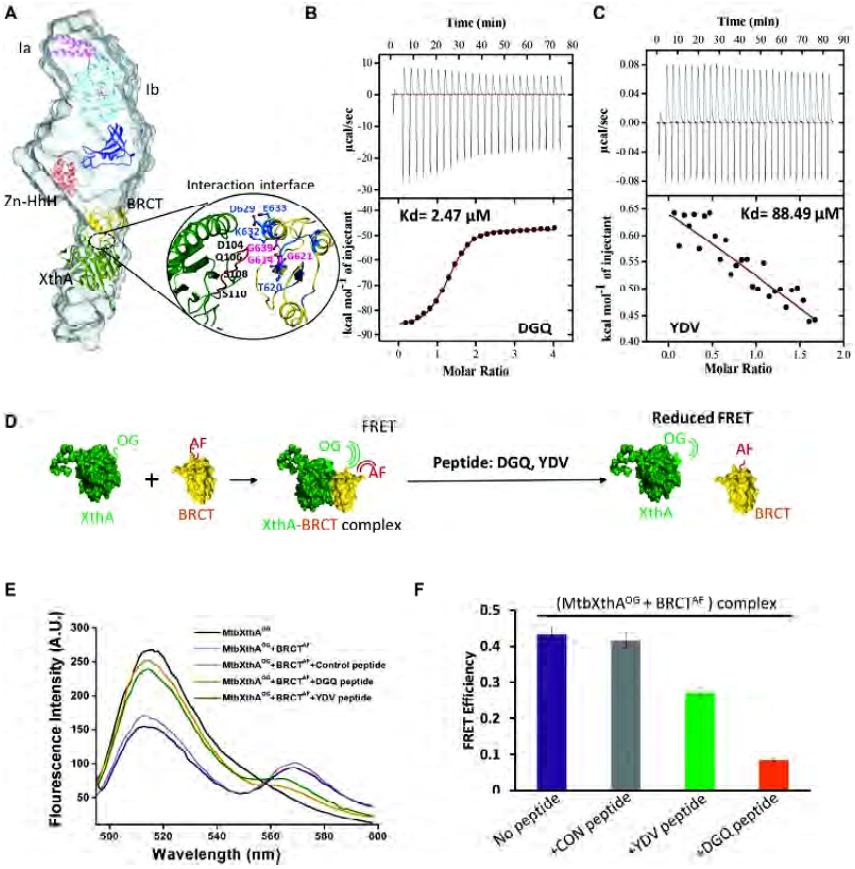
Dr. Ravishankar R.

Khanam T, Afsar M, Shukla A, Alam F, Kumar S, Soyar H, Dolma K, Ashish, Pasupuleti M, Srivastava KK, Ampapathi RS and Ramachandran R

Nucleic Acids Research, 2020, 48(8), 4325–4343

Dr. Taran Khanam

Class-II AP-endonuclease (XthA) and NAD+-dependent DNA ligase (LigA) are involved in initialand terminal stages of bacterial DNA base excision repair (BER), respectively. XthA acts on abasic sites of damaged DNA to create nicks with 32 OH and 52 -deoxyribose phosphate (52 -dRP) moieties. Co-immunoprecipitation using mycobacterial cell-lysate, identified MtbLigA-MtbXthA complex formation. Pull-down experiments using purified wild-type, and domain-deleted MtbLigA mutants show that LigA-XthA interactions are mediated by the BRCT-domain of LigA. Small-Angle-X-ray scattering, 15N/1H-HSQC chemical shift perturbation experiments and mutational analysis identified the BRCT-domain region that interacts with a novel 104DGQPSWSGKP113 motif on XthA for complex-formation. Isothermal-titration calorimetry experiments show that a synthetic peptide with this sequence interacts with MtbLigA and disrupts XthA–LigA interactions. In vitro assays involving DNA substrate and product analogs show that LigA can efficiently reseal 32 OH and 52 dRP DNA termini created by XthA at abasic sites. Assays and SAXS experiments performed in the presence and absence of DNA, show that XthA inhibits LigA by specifically engaging with the latter's BRCT-domain to prevent it from encircling substrate DNA. Overall, the study suggests a coordinating function for XthA whereby it engages initially with LigA to prevent the undesirable consequences of futile cleavage and ligation cycles that might derail bacterial BER.



Research Highlights

Site-selective 1,3-double functionalization of arenes using para-quinol, C-N, and C-C/C-P three-component coupling

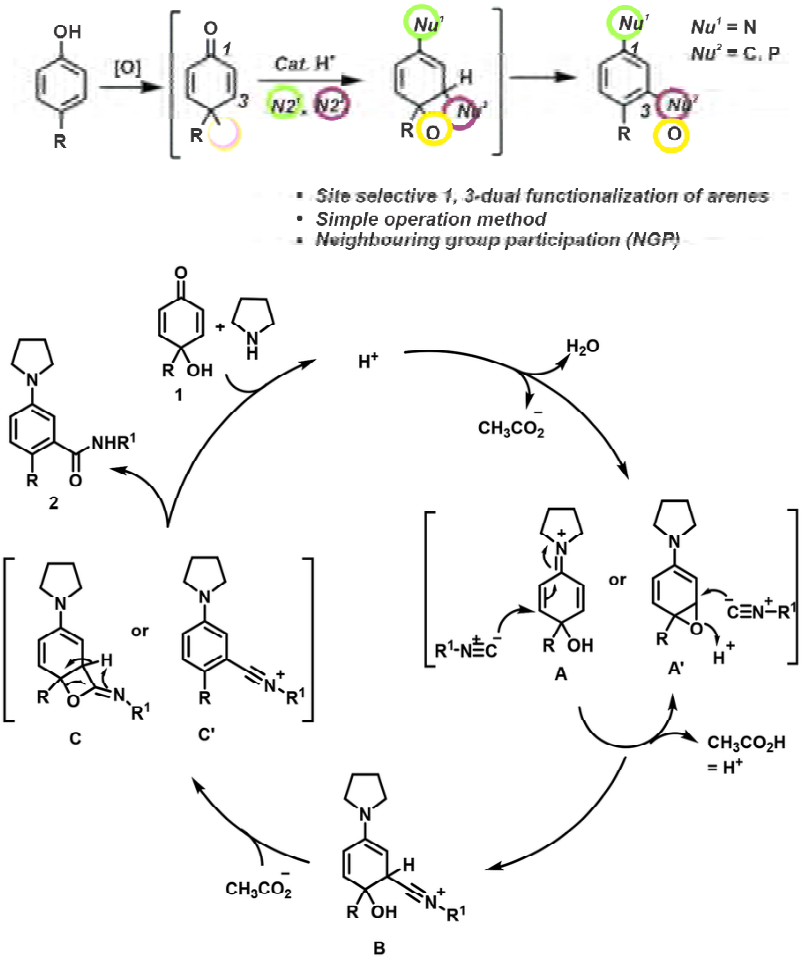
Dr. Ravindra Kumar

Mr. Saddam Husen

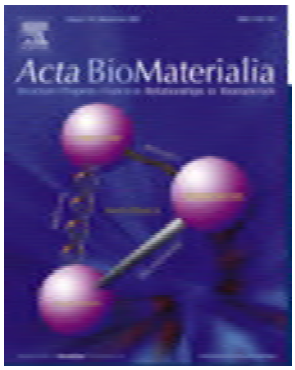
Saddam Husen, Anil Chauhana and Ravindra Kumar

Green Chem., 2020, **22,** 1119-1124,
https://doi.org/10.1039/C9GC04103F

In this research work, a catalytic and site-selective approach has been demonstrated for dual functionalization of arenes *via* cross-coupling reactions of *p*-quinols with amines and isocyanides/phosphites. The strategy enables the production of a series of 3-amino-benzamides and 3-amino-arylphosphonates in good to excellent yields with complete control of regio- and chemo-selectivity. The reaction is highly viable in terms of its environmental benignity, simple operation method, and scalability. Initial mechanistic studies were also carried out to unveil the reaction pathways.



Research Highlights



Theranostic lyotropic liquid crystalline nanostructures for selective breast cancer imaging and therapy

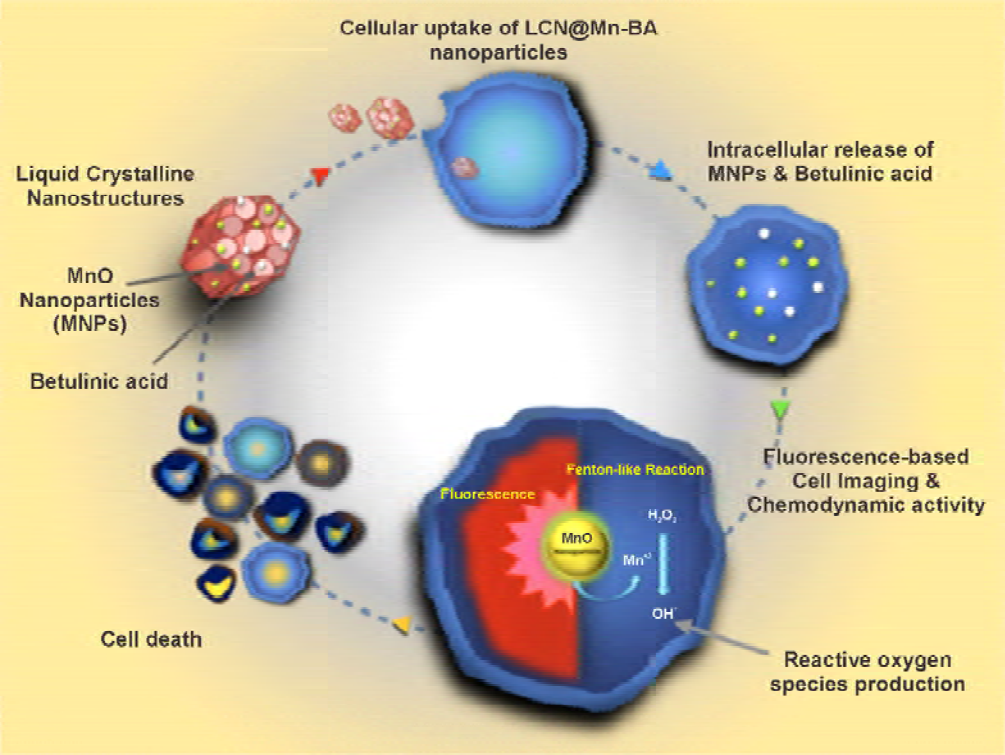

Dr. Prabhat Ranjan Mishra

Sandeep Urandur, Venkatesh Teja Banala, Ravi Prakash Shukla, Shalini Gautam, Disha Marwaha, Nikhil Rai, Madhu Sharma, Shweta Sharma, Pratibha Ramarao, Prabhat Ranjan Mishra

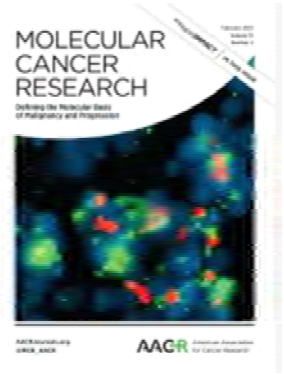
Acta Biomaterialia, 2020, 113, 522-540


Mr. Sandeep Urandur

This work reports the development of theranostic lyotropic liquid crystalline nanostructures (LCN's) loaded with unique MnO nanoparticles (MNPs) for selective cancer imaging and therapy. MNPs serves as a fluorescent agent as well as a source of manganese (Mn^{2+}) and enables localized oxidative stress under the hallmarks of cancer (acidosis, high H_2O_2 level). In pursuit of synergistic amplification of Mn^{2+} antitumor activity, betulinic acid (BA) is loaded in LCN's. In this investigation, nano-architecture of LCN's phase interface is established via SAXS, Cryo-TEM and Cryo-FESEM. Intriguing *in vitro* studies showed that the LCN's triggered hydroxyl radical production and exhibited greater selective cytotoxicity in cancer cells, ensuring the safety of normal cells. Significant tumor ablation is realized by the 96.5 % of tumor growth inhibition index of LCN's as compared to control group. Key insights into on-site drug release, local anti-cancer response, and tumor location are gained through precise guidance of fluorescent MNPs. In addition, comprehensive assessment of the safety, pharmacokinetics and tumor distribution behavior of LCN's is performed *in vivo* or *ex vivo*. This work emphasizes the promise of modulating tumor microenvironment with smart endogenous stimuli sensitive nano systems to achieve advanced comprehensive cancer nano-theranostics without any external stimulus.



Research Highlights



FBW7 Inhibits Myeloid Differentiation in Acute Myeloid Leukemia via GSK3-Dependent Ubiquitination of PU.1

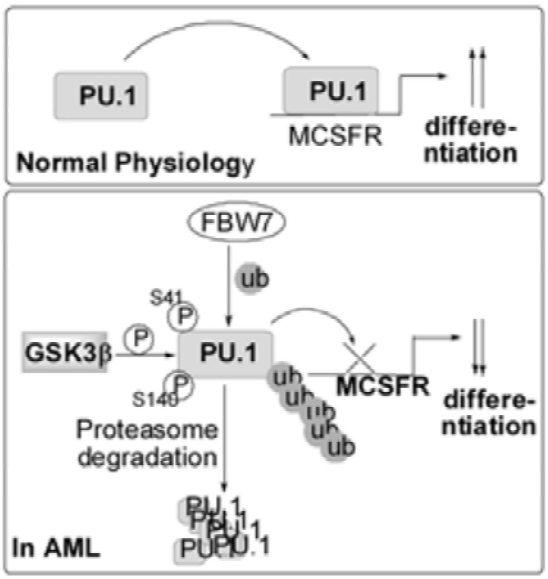
Dr. Arun Kumar Trivedi

Mr. Mukul Mishra

Mukul Mishra, Gatha Thacker, Akshay Sharma, Anil Kumar Singh, Vishal Upadhyay, Sabyasachi Sanyal, Shailendra Prasad Verma, Anil Kumar Tripathi, Madan Lal Brahma Bhatt and Arun Kumar Trivedi

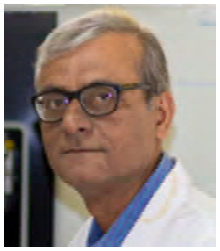
Mol Cancer Res. 2020 Nov 13. doi: 10.1158/1541-7786.MCR-20-0268.

GSK3β, an ubiquitously expressed serine/threonine kinase is reported to be overexpressed and hyperactivated in cancers including Acute Myeloid Leukemia where it promotes self-renewal, growth and survival of Acute myeloid leukemia (AML) cells. Therefore, GSK3β inhibition results in AML cell growth inhibition and myeloid differentiation. Here we identified master transcription factor PU.1 of monocyte-macrophage differentiation pathway as potential GSK3β target. We demonstrate that GSK3β phosphorylates PU.1 at Ser41 and Ser140 leading to its recognition and subsequent ubiquitin-mediated degradation by E3 ubiquitin ligase FBW7. This GSK3-dependent degradation of PU.1 by FBW7 inhibited monocyte-macrophage differentiation. We further showed that a phospho-deficient PU.1 mutant (PU.1-S41,S140A) neither bound to FBW7 nor was degraded by it. Consequently, PU.1-S41, S140A retained its transactivation, DNA binding ability and promoted monocyte-macrophage differentiation of U937 cells even without PMA treatment. We further showed that FBW7 overexpression inhibited both PMA as well as MCSF-induced macrophage differentiation of myeloid cell lines and PBMCs from healthy volunteers respectively. Contrarily, FBW7 depletion promoted differentiation of these cells even without any inducer suggesting for a robust role of GSK3β-FBW7 axis in negatively regulating myeloid differentiation. Furthermore, we also recapitulated these findings in PBMCs isolated from leukemia patients where FBW7 over expression markedly inhibited endogenous PU.1 protein levels. In addition, PBMCs also showed enhanced differentiation when treated with M-CSF and GSK3 inhibitor (SB216763) together compared to M-CSF treatment alone. Taken together, this data demonstrates a plausible mechanism behind PU.1 restoration and induction of myeloid differentiation upon GSK3β inhibition and further substantiates potential of GSK3β as a therapeutic target in AML.



Research Highlights

Transient transfection of the respiratory epithelium with gamma interferon for host-directed therapy in pulmonary tuberculosis

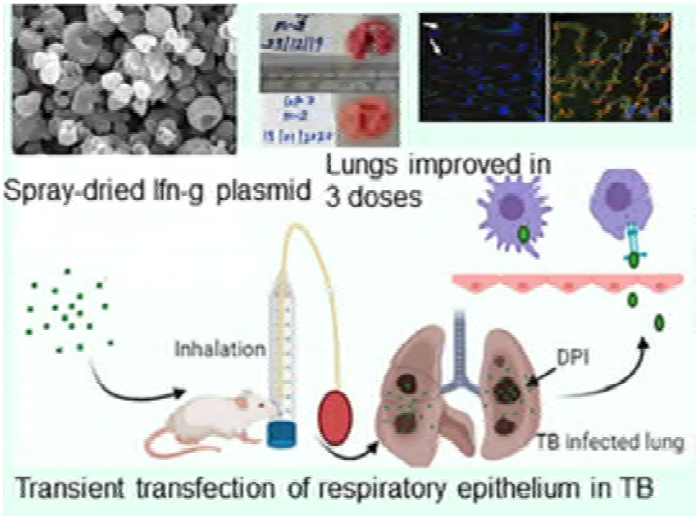

Dr. Amit Misra


Ms. Reena Bharti

Bharti R, Srivastava A, Roy T, Verma K, Reddy DVS, Shafi H, Verma S, Raman SK, Singh AK, Singh J, Ray L and Misra A

Molecular Therapy — Nucleic Acids, 2020, 22, 1121-1128

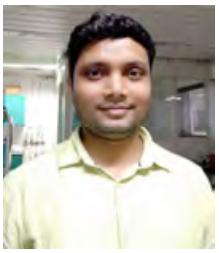
Nebulized gamma interferon (IFN-γ) protein has been studied for clinical safety and efficacy against pulmonary tuberculosis (TB). The protein is expensive, requires a cold chain, and is difficult to deploy in limited-resource, high-incidence settings. We generated a preclinical proof of concept (PoC) for a dry powder inhalation (DPI) containing DNA constructs to transiently transfect the lung and airway epithelium of mice with murine IFN-γ. Bacterial colony-forming units (CFU) in the lungs of mice infected with *Mycobacterium tuberculosis* (Mtb) reduced from about 10^6/g of tissue to ~10^4 after four doses given once a week. Nodular inflammatory lesions in the lungs reduced significantly in number. Immunohistochemistry of infected lung sections for LC3-1 and LAMP-1 indicated autophagy induction between 18 and 48 h after inhalation. ELISA on bronchoalveolar lavage (BAL) fluid showed differences in kinetics of IFN-γ concentrations in the epithelial lining fluid of healthy versus infected mice. Uninfected mice receiving DNA constructs expressing a fluorescent protein were live-imaged. The fluorescence signals from the intracellular protein peaked at about 36 h after inhalation and declined by 48 h. These results establish preclinical PoC of the efficacy of a DPI and dosing regimen as a host-directed and transient gene therapy of experimental pulmonary TB in mice, justifying preclinical development. To our knowledge, this is the world's first report of transient transfection for gene therapy.



Research Highlights

Multifunctional hybrid nanoconstructs facilitate intracellular localization of doxorubicin and genistein to enhance apoptotic and anti-angiogenic efficacy in breast adenocarcinoma

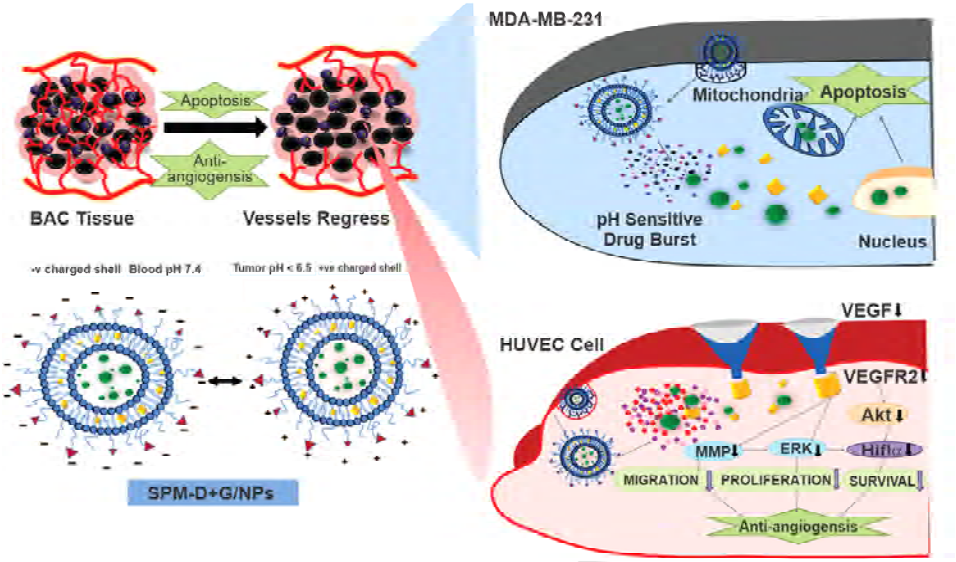

Dr Prabhat Ranjan Mishra


Mr. R P Shukla

Shukla RP, Dewangan J, Urandur S, Banala VT, Diwedi M, Sharma S, Agrawal S, Rath SK, Trivedi R and Mishra PR

Biomaterials Science, 2020, 8(5), 1298-1315

The progressive development of tumors leading to angiogenesis marks the advancement of cancer which requires specific targeted treatment preferably with combination chemotherapy. However, there is still a long way to go to develop an efficient delivery system that could overcome the tumor microenvironment to achieve efficient delivery. Therefore, we have developed spermine (SPM) tethered lipo-polymeric hybrid nanoconstructs with cell surface heparan sulfate proteoglycan (HSPG) specificity for higher intracellular localization and pH dependent charge reversal in the tumor microenvironment (below pH 5.8) to facilitate Doxorubicin (Dox) and Genistein (Gen) release in a synergistic combination. We have observed the specific uptake of SPM anchored hybrid nanoconstructs by receptor-mediated endocytosis in human breast cancer cells (MDA-MB-231) through the HSPG receptor. The SPM-D + G/NPs induced a higher rate of apoptosis in MDA-MB-231 cells *via* disruption of the mitochondrial membrane potential and also exhibited a stronger anti-angiogenic effect governing the inhibition of VEGF pathway modulation, proliferation, invasion and migration of HUVECs in *in vitro* and *in vivo* Balb/c mouse models. The involvement of Akt/Hif1α/VEGF dependent signal cascading and its down-regulation with a pro-apoptotic drug Dox and an anti-angiogenic agent Gen was evident as demonstrated by an *in silico* docking study and subsequently proven by RT-PCR and western blotting. Altogether this study highlights the potential role of SPM in targeting HSPG receptors and synergistic delivery of Dox and Gen as a promising strategy to effectively inhibit BAC progression and these findings could open a new window to deliver combinations of chemotherapeutic agents along with anti-angiogenic ligands using hybrid nanoparticles.



Research Highlights

N-acetyl-cysteine in combination with celecoxib inhibits Deoxynivalenol induced skin tumor initiation via induction of autophagic pathways in swiss mice


Dr. Rath SK

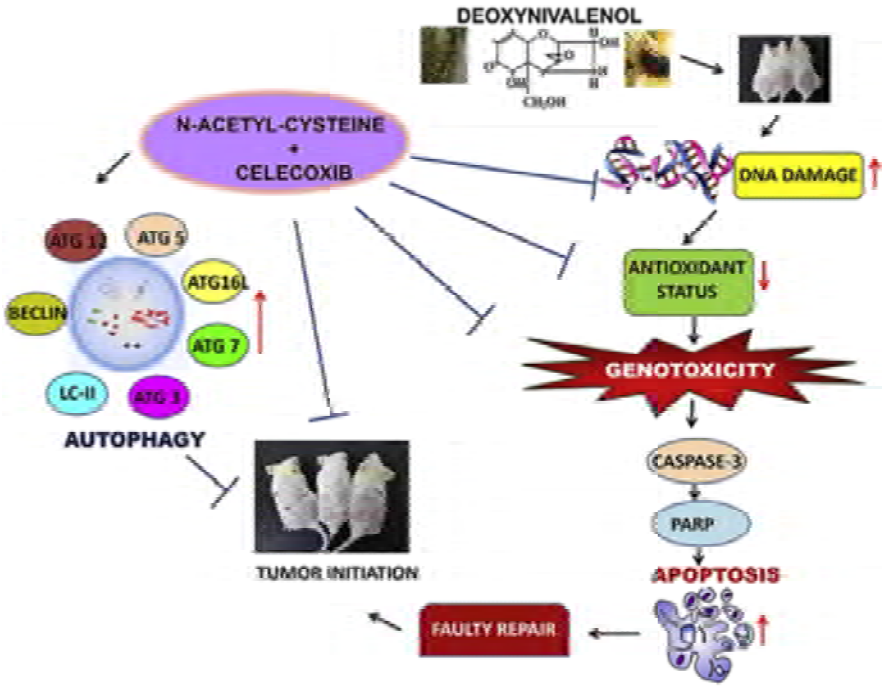

Dr. Sakshi Mishra

Mishra S, Divakar A, Srivastava S, Dewangan J, Sharma D, Asthana S, Chaturvedi S, Wahajuddin M, Kumar S and Rath SK

Free Radical Biology and Medicine, 2020, 156, 70-82

Deoxynivalenol is a trichothecene mycotoxin which naturally contaminates small grain, cereals intended for human and animal consumption. Investigations for dermal toxicity of DON has been needed and highlighted by WHO. Previous studies on dermal toxicity suggest that DON has DNA damaging potential leading to skin tumor initiation in mice skin. However, considering its toxicological manifestations arising after dermal exposure, strategies for its prevention/protection are barely available in literature. Collectively, our study demonstrated that N-acetylcysteine (NAC), precursor of glutathione, significantly alters the genotoxic potential of DON. Further NAC in combination with Celecoxib (CXB) inhibits tumor growth by altering antioxidant status and increasing autophagy in DON initiated *Swiss* mice. Despite the broad spectrum use of CXB, its use is limited by the concerns about its adverse effects on the cardiovascular system. Serum parameters and histology analysis revealed that CXB (2 mg) when applied topically for 24 weeks did not impart any cardiovascular toxicity which could be because skin permeation potential of CXB was quite low when analyzed through HPLC analysis.

Although the anticancer effects of CXB and NAC have been studied, however, the combination of NAC and CXB has yet not been explored for any cancer treatment. Therefore, our observations provide additional insights into the therapeutic effects of combinatorial treatment of CXB and NAC against skin tumor prevention. This approach might form a novel alternative strategy for skin cancer treatment as well as skin associated toxicities caused by mycotoxins such as DON. This combinatorial approach can overcome the limitations associated with the use of CXB for long term as topical application of the same seems to be safe in comparison to the oral mode of administration.



Research Highlights

The Bestmann-Ohira reagent and related diazo compounds for the synthesis of azaheterocycles

Dr. Kishor Mohanan

Mr. MFJamali

Jamali MF, Vaishanv NK and Mohanan K

Chemical Record, 2020, 20(11), 1394-1408

This account summarizes our investigations on the development of novel strategies for the rapid construction of azaheterocycles employing the Bestmann Ohira reagent and other diazo compounds. In addition to the synthesis of pyrazoles, the reactivity of BOR has been successfully tapped in three component domino reactions, creating convenient routes to important heterocycles such as triazolines, triazoles, and isoxazolidines. Besides, this reagent was also found useful in conjugate addition and nucleophilic substitution reactions. Importantly, most of the reactions described in this account do not require harsh reaction conditions, catalysts, or pre activated substrates, providing a broader scope for the synthesis of heterocycles. Although significant progress has been made in this field, there are challenges and demands for more applications of this versatile reagent in the construction of other classes of heterocycles. Given the importance of azaheterocyclic phosphonates in medicinal chemistry and agrochemicals, the continued research in this area may open up new avenues for the synthesis of novel classes of azaheterocycles with potential biological applications.

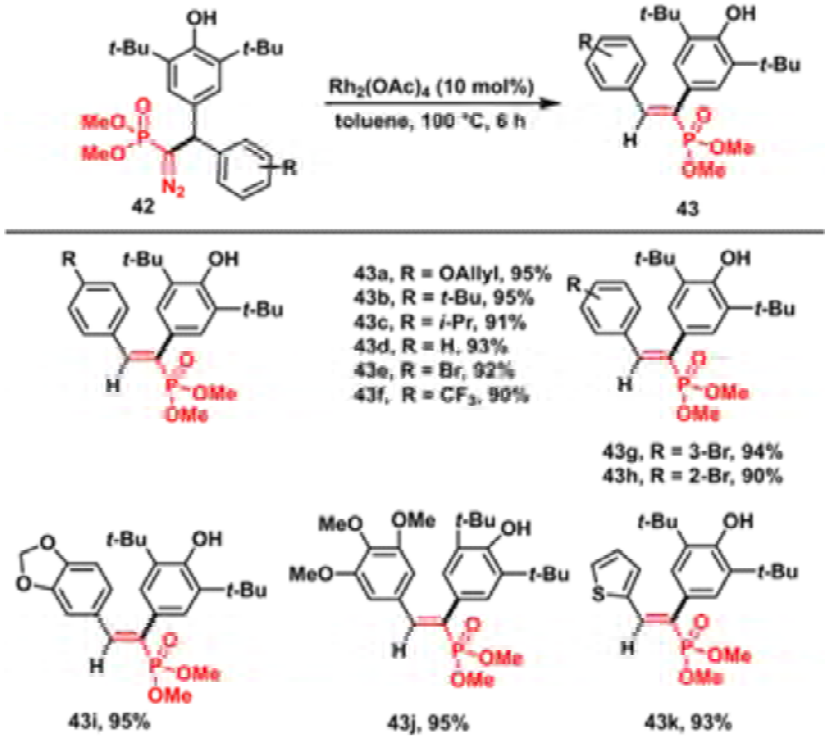
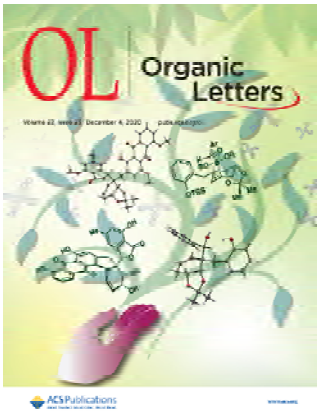


Fig. Scheme for formation of alkenylphosphonates.

Research Highlights



Decarboxylative/oxidative amidation of aryl α-Ketocarboxylic acids with nitroarenes and nitroso compounds in aqueous medium

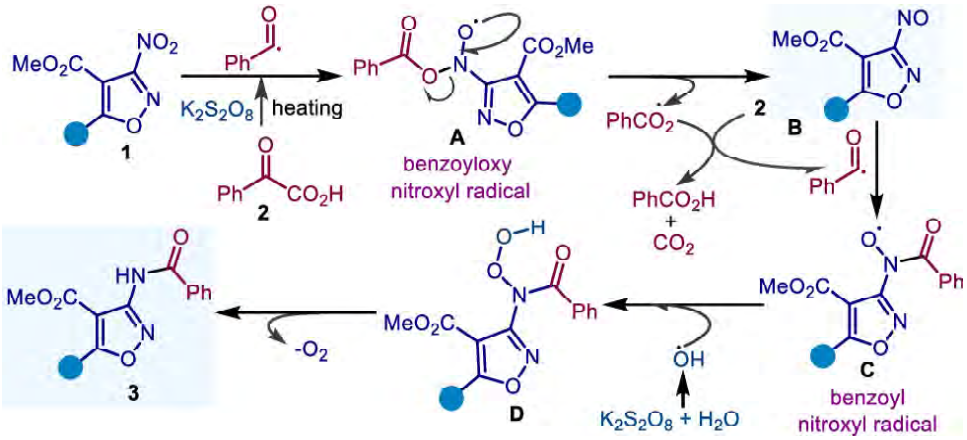

Dr. Sanjay Batra


Mr. DS Barak

Barak DS, Dahatonde DJ, Dighe SU, Kant R and Batra S

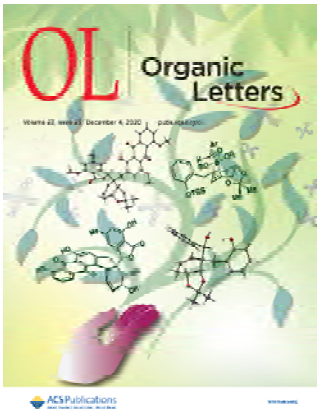
Organic Letters, 2020, 23, 9381-9385

The decarboxylative/oxidative amidation of aryl a-ketocarboxylic acids with 5-aryl-3-nitroisoxazole-4-carboxylates and substituted dinitrobenzenes under oxidative aqueous conditions to afford N-aryl amides is described. The reaction is suggested to proceed via a radical pathway in which a benzoyl nitroxyl radical, the key intermediate formed from reaction between nitroarene and benzoyl radical from glyoxalic acid, couples with hydroxyl radical from water to produce amide. Mechanistic insight allowed the scope of the strategy to be expanded to the synthesis of amides via reaction between aryl a-ketocarboxylic acids and nitroso compounds.



Scheme 1. Proposed mechanism for the formation amide

Research Highlights



Intramolecular 6-*exo-dig* Post-Ugi cyclization of *N* Substituted 2 Alkynamides: Direct access to functionalized morpholinone glycoconjugates

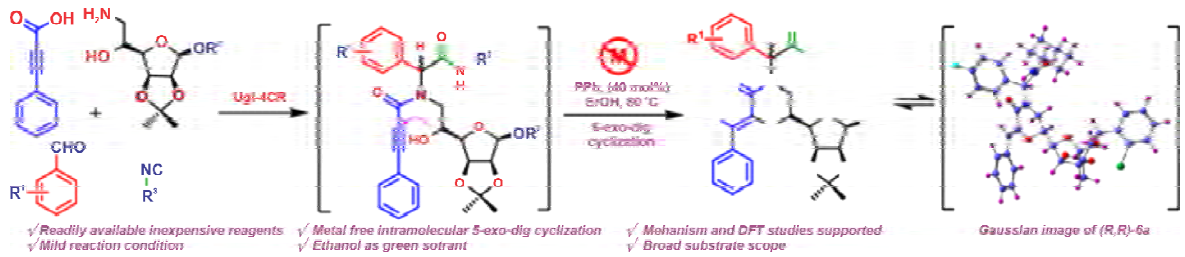
Dr. Mandal PK

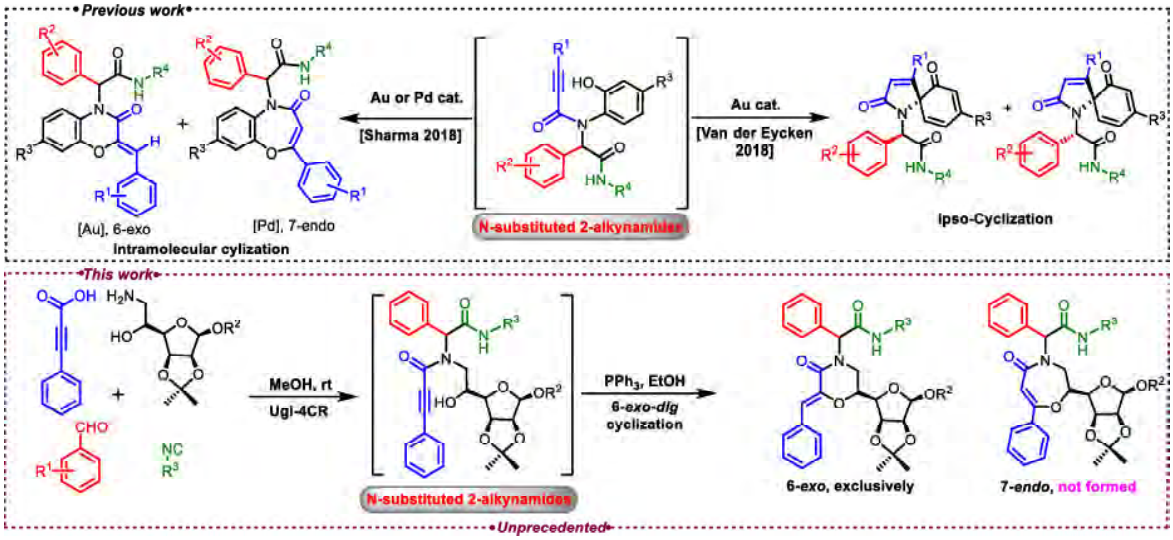
Mr. Kumar H

Kumar H, Prajapati G, Dubey A, Ampapathi RS and Mandal PK

Organic Letters, 2020, 22, 9258-9262

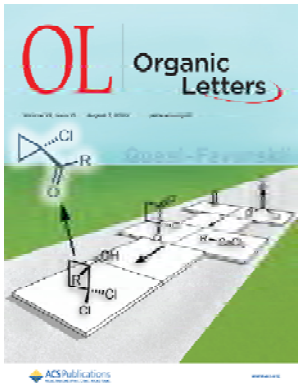
This work report a chemo- and regioselective 6-*exo-dig* catalytic cyclization of Ugi adducts *N*-substituted 2-alkynamides to access functionalized morpholinone glycoconjugates in the presence of triphenylphosphine. This array allows an interesting multicomponent access to a library of functionalized morpholinone glycoconjugates under mild reaction conditions with regeneration of catalyst triphenylphosphine, supported by ^{31}P nuclear magnetic resonance studies. Density functional theory shows the 6-*exo-dig* oxocyclization pathway is preferred, which supports our experimental observation.





Scheme 1. Divergent Post-ugi cyclization pathways of Ugi Aducts containing Alkynoc acid

Research Highlights



Pd-Catalyzed C-H halogenation of indolines and tetrahydroquinolines with removable directing group

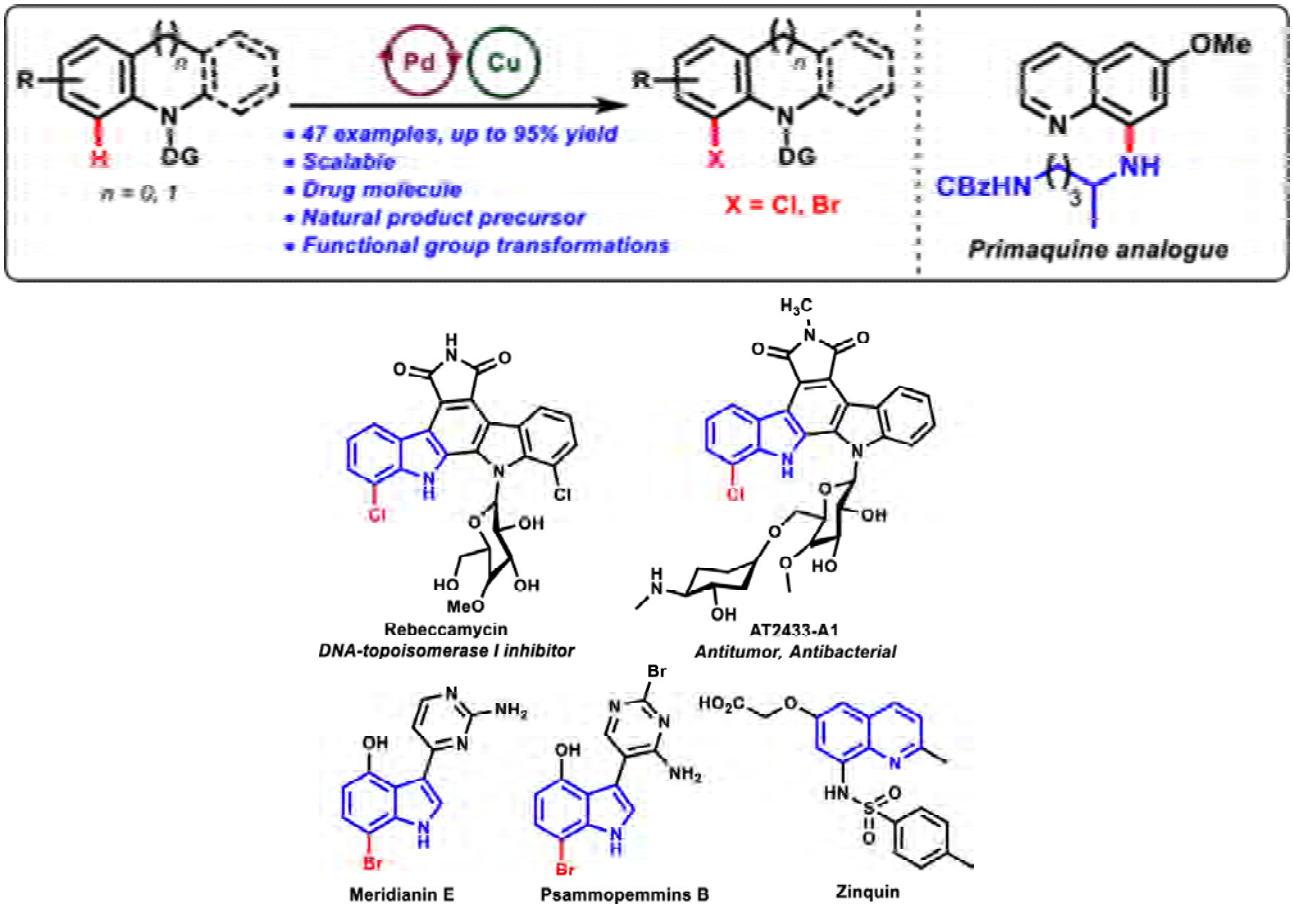

Dr. Dipankar Koley


Mr. Ahmad A

Ahmad A, Dutta HS, Kumar M, Khan AA, Raziullah and Koley D.

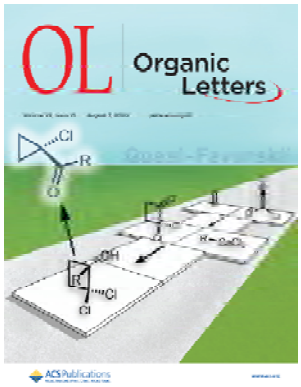
Organic Letters, 2020, 22(15), 5870-5875

Pd-catalyzed directing-group-assisted regioselective halogenations to C7 of indolines and C8 of tetrahydroquinolines were achieved in good to excellent yields. The practicality and utility of the developed method have been illustrated by various functional group transformations such as arylation, alkenylation, cyanation, and silylation utilizing the installed synthetic handle. The concise synthesis of primaquine, an antimalarial drug, and formal syntheses of two bioactive natural products, hippadine and pratosine, have also been demonstrated.



Scheme 1. C7 Halogenated bioactive indole and C8 substituted quinoline derivatives

Research Highlights



Hydrogen-Bond-Guided Reaction of Cyclohexadienone-aldehydes with Amines: Synthesis of an Aminal Group Containing a Fused Tetracyclic Framework

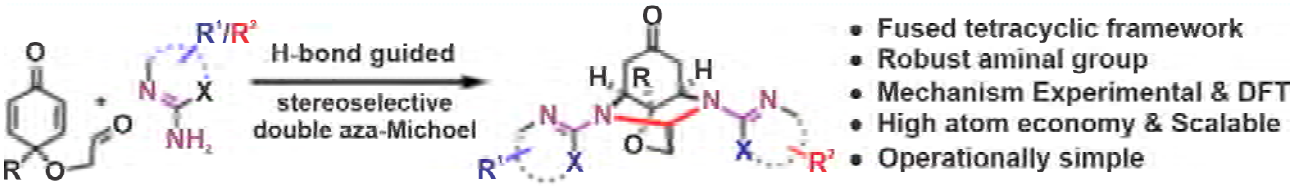

Dr. Ravindra Kumar

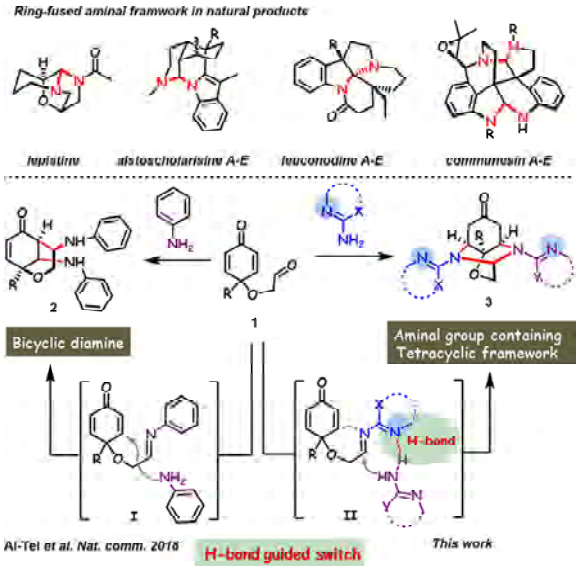

Mr. Anil Chauhan

Anil Chauhan, Raj Kumar Patel, M. Grellier, and Ravindra Kumar

Organic Letters, 2020, 22(15), 6177–6181

In this research work, A modular approach has been developed for an efficient synthesis of an aminal group containing a new tetracyclic framework. The strategy has been devised based on selective hydrogen-bond-guided aza-Michael addition of heteroaromatic amines to cyclohexadienone-aldehydes. The reaction is highly atom economic and practical and involves stereoselective construction of four new C–N bonds and four rings. The synthetic utility of the tetracyclic product was explored. The role of a H-bond was explained with the help of experimental and density functional theory (DFT) computation studies.





Scheme 1. Ring-Fused Aminal (N-C-N) Group containing natural products and stereoselective reaction of cyclo hexadienone-aldehyde with aromatic amines

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Budget

Rs. in lakh

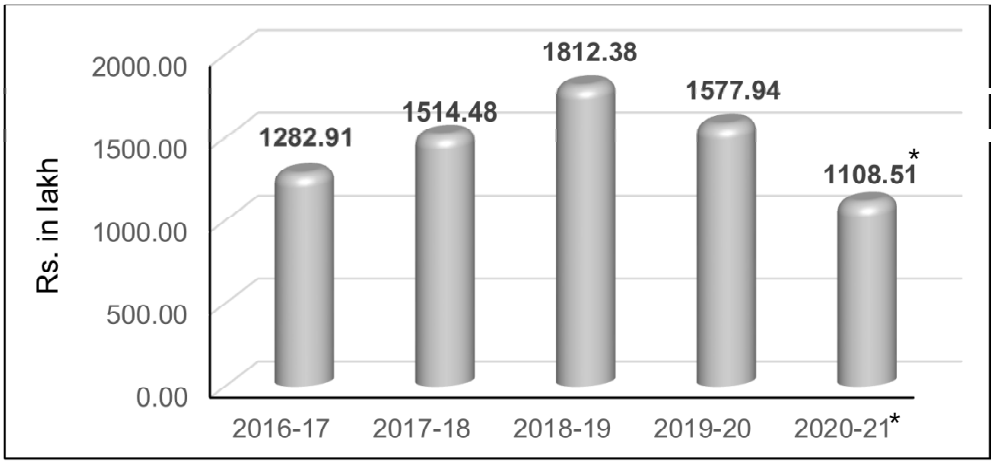
	Heads	2016-17	2017-18	2018-19	2019-20	2020-21* (Allocation)
(A)	**Recurring**					
1	Pay and Allowances	4920.500	5462.718	5619.670	5946.572	6342.000
2	Contingencies	1018.000	1529.995	1162.348	1328.010	1309.600
3	HRD	0.800	-	-		
4	Maintenance	718.000	925.800	1139.564	1155.410	833.300
5	Chemical and Consumables	1323.000	1329.000	854.501	1054.491	1109.000
	Sub-Total	**7980.300**	**9247.513**	**8776.083**	**9484.483**	**9593.900**
(B)	**Capital**					
1	Works and Services / Electrical Installation	200.000	80.060	112.246	71.429	77.000
2	Apparatus and Equipment/ Computer Equipment	1203.000	1084.000	271.000	235.321	844.500
3	Office Equipment, Furniture and Fittings	-	-	-	5.426	-
4	Library Books and Journals	75.000	330.186	338.107	336.680	168.340
	Sub-Total	**1478.000**	**1494.246**	**721.353**	**648.856**	**1089.840**
	Total (A+B)	**9458.300**	**10741.759**	**9497.436**	**10133.339**	**10683.740**
(C)	**Special Projects HCP/ BSC / CSC / ISC / PSC / NCP / FTT / FBR, etc.**	**2060.318**	**218.895**	**625.294**	**944.118**	**379.020**
(D)	**CSIR-800 (Societal Activities)**	**100.00**	**-**	**-**	**-**	**-**
	Grand Total (A+B+C+D)	**11618.618**	**10960.654**	**10122.730**	**11077.457**	**11062.760**

*Data as on 31-01-2021

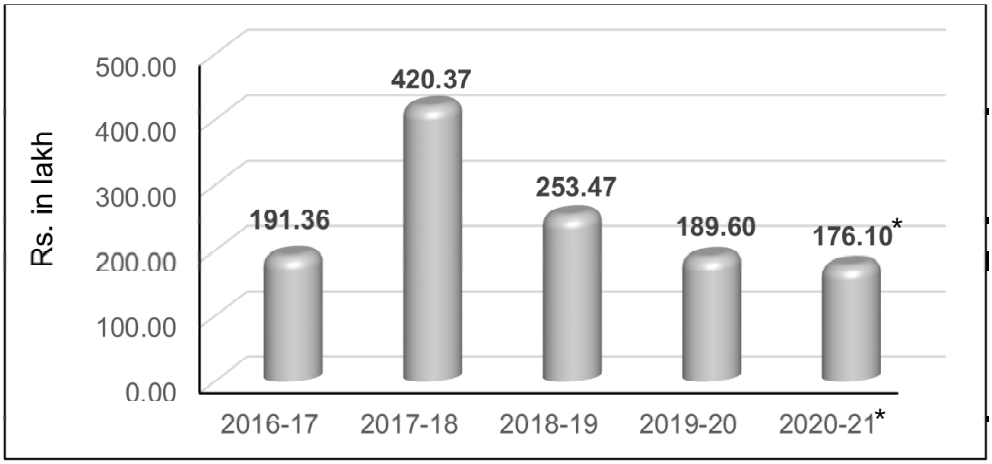
External Budgetary Resources

Rs. in lakh

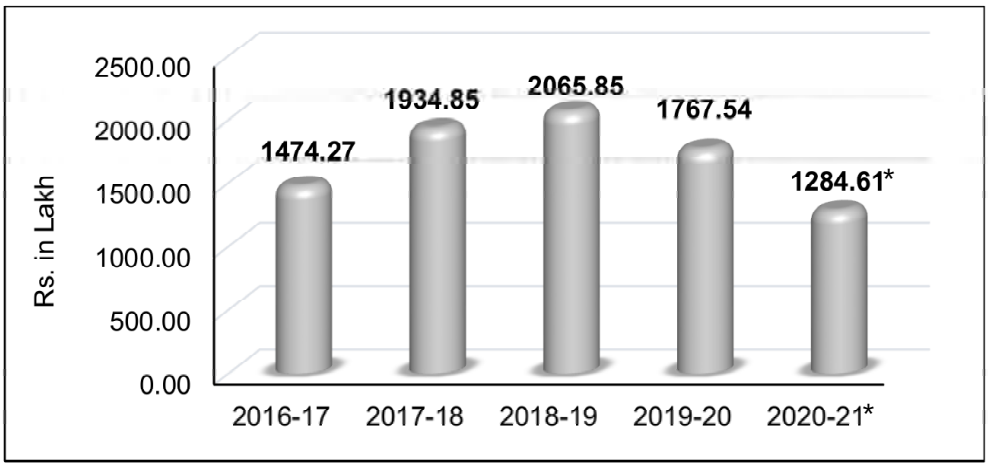
External Cash Flow from Government Agencies & Industries



Lab Reserve Fund Generated



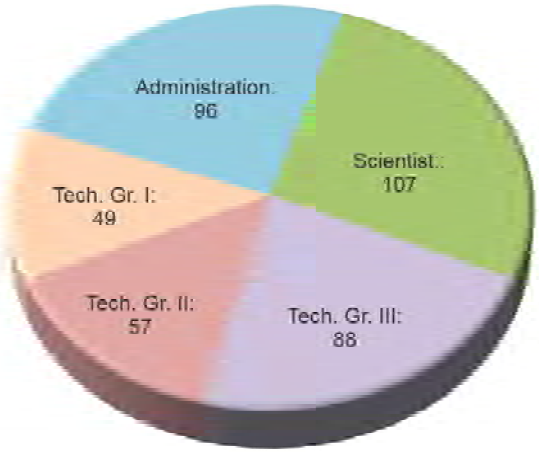
Total External Budgetary Resources (ECF + LRF)



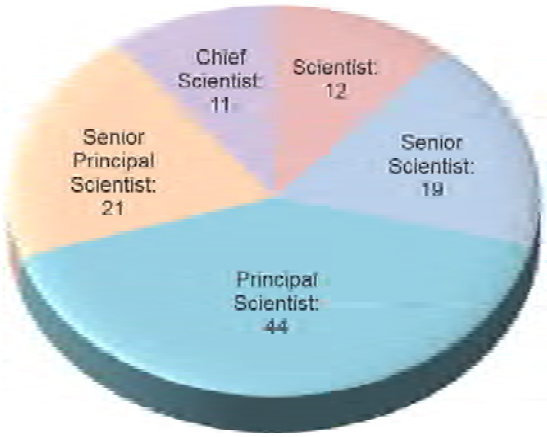
*Data as on 31-01-2021

Manpower

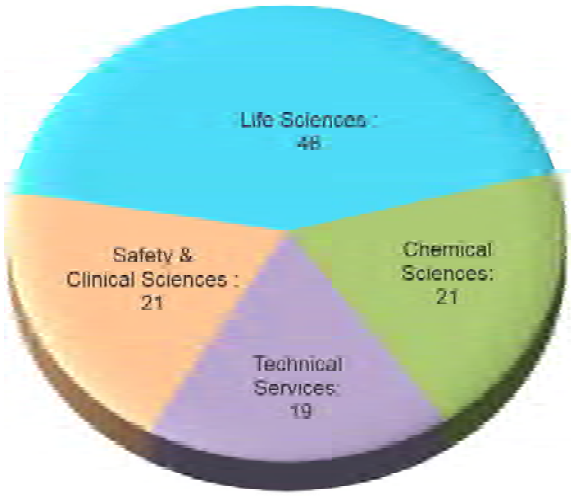
Total Staff (397)



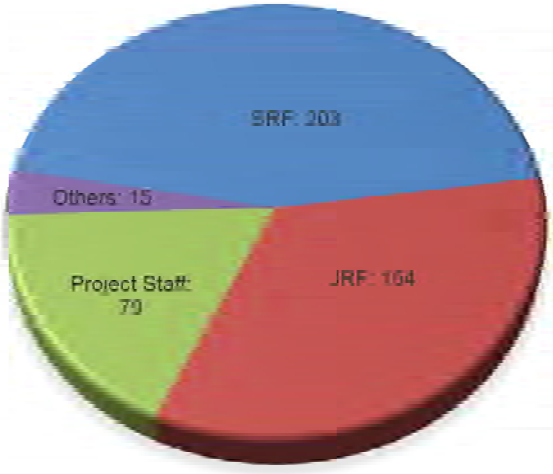
Designation-wise strength of Scientists



Area-wise strength of Scientists



Research Fellows & Project Staff Strength



*Data as on 01-01-2021

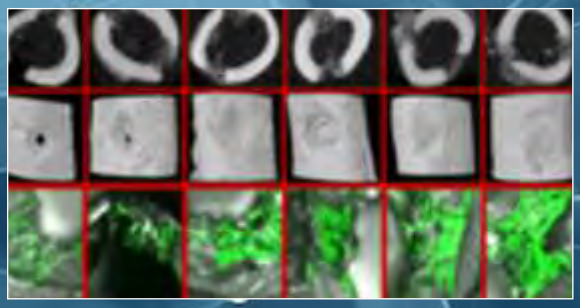
Announcement

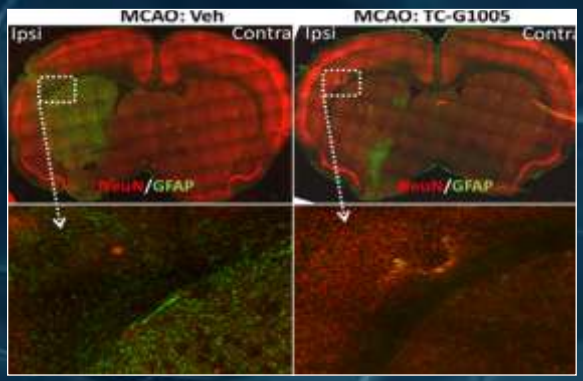
CDRI Awards 2021 for Excellence in Drug Research

The prestigious CDRI Awards 2021 for Excellence in Drug Research in **Chemical Sciences** category has been awarded to **Dr. Vishal Rai,** Associate Professor, IISER, Bhopal.
In **Life Sciences** category, **Dr. Siddhesh Shashikant Kamat,** Associate Professor, IISER, Pune and **Dr. Chandrima Das,** Associate Professor, Saha Institute of Nuclear Physics, Kolkata have been selected of the CDRI Awards 2021.

Our heartiest congratulations to the awardees!
The felicitation ceremony will be held on 26th September 2021 during CSIR Foundation Day Celebrations

Section I:
Progress in Thrust Areas of Research






Acta Biomaterialia
Volume 113, 1 September 2020, Pages 522-540
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Volume 156, 20 August 2020, Pages 70-82
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Cell Prolif. 2020 Apr; 53(4): e12749.
Published online 2020 Mar 13. doi: 10.1111/cpr.12749
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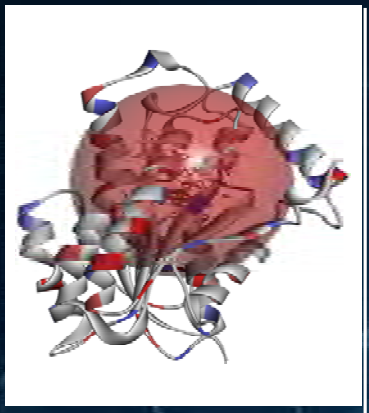


MICROBIAL INFECTION

Area Coordinators: Dr. Gautam Panda & Dr. Bhupendra N. Singh

1

Vision and Goal:

The World Health Organization (WHO) has defined Antimicrobial resistance (AMR) as the ability of a microorganism to stop an antimicrobial from working against it. As a result, standard treatments become ineffective, infections persist and may spread to others. It has further stated "AMR is of particular concern in developing nations, including India, where the burden of infectious disease is high and healthcare spending is low. The country has among the highest bacterial disease burden in the world. Antibiotics, therefore, have a critical role in limiting morbidity and mortality in the country." WHO in its 2017 report categorically stated that tuberculosis and some gram-negative infections caused by ESKAPE (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter* species) pathogens fall in the highest critical priority category and have to be treated with utmost urgency.

The global objectives of CSIR-CDRI program:

i) Drug Discovery studies against drug-resistant mycobacterial infections and ESKAPE pathogens

ii) Discovery of new therapeutic strategies/interventions/diagnostics by Advancing Knowledge Frontiers

Core Competencies and Activities:

The AMR team uses several cutting edge drug discovery platform technologies involving screening, molecular & structural biology, chemistry, computational biology and allied areas. The team has characterized several novel targets and has identified several new scaffolds through early target discovery and research that feeds into the drug discovery pipeline of the institute.

Research Group

Front row (L to R): Dr. Mohammed Imran Siddiqi, Dr. Atul Kumar, Dr. B.N. Singh (Area Coordinator), Dr. Gautam Panda (Area Coordinator) & Dr. Vinita Chaturvedi.
Middle row (L to R): Dr. Mukesh Pasupuleti, Dr. Nayan Ghosh, Dr. Sanjay Batra, Dr. Ajay Kumar Srivastava, Dr. Y. K. Manju, Ms. Neha Topno & Dr. Malleswara Rao Kuram
Back row (L to R): Dr. Damodara Reddy N., Dr. C. B. Tripathi, Dr. Sidharth Chopra, Dr. Sudheer Kumar Singh, Dr. Arunava Dasgupta, Dr. Tejender S. Thakur & Dr. Ravindra Kumar

1.1 New Drug Discovery

1.1.1 Design and Synthesis

1.1.1.1 Discovery, optimization, and characterization of novel benzhydryl amines for the treatment of antibacterial infection

A small library of benzhydryl amines were synthesized through the base mediated 1,6-addition of heterocyclic amines and amides with *p*-Quinone methides. All of the benzhydryl amines having imidazole ring and unsubstituted benzene ring in their structure have been evaluated for antibacterial activity including selected ESKAPE pathogens. Initially promising leads are being investigated further.

1.1.1.2 Design, synthesis and biological evaluation of first amino acids derived Q203 analogs as antimycobacterial agents

Q203 is the newly reported imidazopyridine amide series of compound, which showed MIC_{50} of 2.7 and 0.28 nM against *Mycobacterium tuberculosis* H37Rv (*Mtb*-Rv) under *in vitro* and *ex vivo* (in macrophages) conditions, respectively. It has gone through intensive phase 1 testing and demonstrated excellent results in all studies and now is undergoing phase 2 clinical trials from July 2018 in South Africa. It has robust activity against latent *Mycobacterium tuberculosis* (*Mtb*) and is a promising option for addition to MDR-TB treatment regimens. The binding pocket of Q203 is separated into three parts: the linker region, the core binding region, and the tail binding region. In the core region, Leu174, Pro306, Ser304, and Leu180 amino acid residues are present around the imidazopyridine ring, which is an active pharmacophore. In the linker region, Glu314 amino acid residue is present which have hydroxyl oxygen in the side chain so helps in the hydrogen bonding with amide bond of Q203. In the tail region, aromatic side chains are present which make hydrophobic interactions with residues, Met342, Thr313, Leu180, Met310, Phe158, Phe162, and Tyr161.

In the light of above considerations, undertaken a research program aimed at the design, synthesis and biological evaluation of some analogs of imidazopyridine related amino acids derived Q203 by using multicomponent reaction. In this endeavor several new compounds were designed, synthesized and 19 compounds were evaluated for antimycobacterial activity and their cytotoxicity is currently underway.

1.1.1.3 Corannulene derived unnatural α-Amino acids and peptides: Synthesis, conformational studies and discovery of their antibacterial activities having synergistic effects with rifampicin

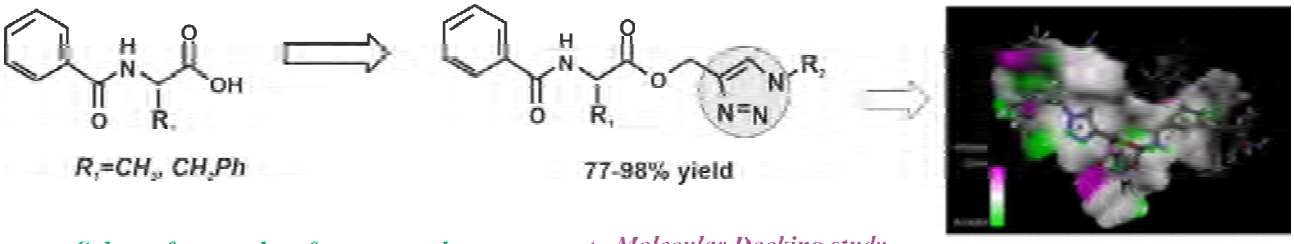
Although corannulene has a great impact in the field of producing soft functional materials, but its concurrent use in the field of biomedical research is yet to be established. We report the preparation of unique corannulene containing four unnatural α-Amino Acids (CAAs) using metal catalyzed cross-coupling protocol and some of these CAAs were converted into peptides with use of lysine and arginine moiety. In addition, bowl-to-bowl inversion energy of corannulene was investigated in synthesized CAAs. *In-vitro* antimicrobial study of CAA containing dipeptide reveals the appreciable antibacterial activity against a broad range of Gram-positive, Gram-negative and multi-drug resistant bacteria. Further it was observed that, dipeptides show unexpected synergistic efficacy against *Staphylococcus aureus* in combination with antibiotic rifampicin. Molecular interaction between dipeptide with rifampicin was further investigated by solution NMR spectroscopy in CD_3OD. This work, therefore, introduces the concept of utilizing Bucky-bowl corannulene containing unnatural α-Amino Acids and their peptides for biomedical applications.

1.1.1.4 TFA-catalysed one-pot, metal-free routes for novel indolo-imidazo [1, 2-a] pyridine derivatives as antimycobacterial agents

A transition-metal free, one-pot tandem synthetic routes for novel indole and imidazo [1,2-a]pyridine derivative hybrids have been established through two sequential Groebke–Blackburn–Bienayme (GBB) and cyclization reaction. Molecular prospective libraries of 14 compounds were synthesized and are being evaluated.

1.1.1.5 Synthesis and biological studies of tetrahydrofuran amino acids containing dodecameric cationic antimicrobial peptides

Various stereoisomers of tetrahydrofuran amino acids (TAAs) and TAA-containing linear cationic dodecapeptides were synthesised by a concise route. Some of these linear peptides show slightly better antimicrobial activities than their tetra- and octameric congeners, but no activity against *Mtb*, for which octapeptides exhibited by far the best results; this implies that antibacterial activity is dependent on the length of these linear peptides. All the dodecapeptides described here were found to be toxic in nature against Vero cells. The study helps us to delineate the optimal length of linear peptides and select potential leads in the development



- *Solvent-free, workup free approach*
- *Low copper loading*
- *Combinatorlal synthesis*
- *Non-cytotoxic antimycobacterial agents*

- *Molecular Docking study*
- *Cytotoxicity study*
- *ADME study*
- *Gram scale synthesis*

of novel cationic peptide-based antibiotics ***(ChemBioChem, 2020, 21, 2518–26).***

1.1.1.6 Potent antitubercular novel amino acid linked 1,4 disubstituted 1,2,3-triazoles, prepared by a simple work-up-free, solvent-free approach

Novel amino acid (i.e. N-protected L-alanine, benzoyl-protected L-phenylalanine) or dipeptide containing 1,2,3-triazole molecules were synthesized by an efficient, green strategy using 1,8- diazabicyclo [5.4.0] undec-7-ene (DBU) acetate ionic liquid under a solvent- and external base-free condition. Out of 21, four molecules showed promising activity with MIC 3.12 (n=2) and 6.25(n=2) µg/ml against *Mtb*, and were non-toxic to mouse macrophages. One compound with MIC 3.12 µg/ml also showed activity against both Gram-positive and Gram-negative bacterial strains. *In-silico* analysis of these promising compounds exhibited good activity with the DprE1 target protein of *Mtb*. Drug-likeness studies also showed these molecules as potential anti-TB drug candidates (***ACS Omega, 2020, 5, 29830-37).***

1.1.2 Biological Screening

1.1.2.1 Assay summary of compounds screened against *M. tuberculosis*

Compounds Received	Activity (µM)				
	> 50	50	25	12.5	6.25
195	164	30	0	01	00

Compounds with activity are being further optimized to improve efficacy.

1.1.2.2 Assay summary of compounds against ESKAPE pathogens

	Total compounds received	Total compounds screened	Pending	Hits in ESKAPE
CBRS	247	247	0	43
MOES	0	0	0	0
Maybridge	47	47	0	3

Compounds with activity are being further optimized to improve efficacy.

1.1.2.3 Antitubercular activity of 2, 3-diaryl benzofuran derivatives

Seventeen 2, 3-diaryl benzofuran hybrids were synthesized and studied for antitubercular activity. Out of these seventeen, four compounds showed significant activity with MIC ranging from 12.5 to 50 µg/ml. Out of these four, one active derivative (9E, MIC 12.5 µg/ml) was further supported by the molecular docking energy (−8.4 kcal/mol) with respect to the first line antitubercular drug, isoniazid (−6.2 kcal/mol) on the target Polyketide synthase-13. No derivative showed cytotoxicity towards normal lung cell line L-132 ***(Bioorganic Chem, 2020, 99, Article 103784).***

Table: Details of docking binding energy (kcal/mol) of derivatives 8C, 9A, 9E and 9G on putative *Mtb* targets catalase peroxidase, dihydrofolate reductase and enoyl-ACP reductase

Name	Catalase-peroxidase (PDB: 1SJ2)	Dihydrofolate reductase (PDB: 4M2X)	Enoyl ACP reductase (PDB: 4TRO)
Isoniazid	−6.0	−5.6	−5.9
8C	−7.8	−8.5	−8.0
9A	−8.5	−8.5	−8.6
9E	−9.7	−8.5	−8.8
9G	−8.9	−9.0	−8.9

1.1.2.4 Brevifoliol and its analogs: A new class of antitubercular agents

Brevifoliol is an abeo-taxane isolated from the *Taxus wallichiana* needles; eighteen semisynthetic ester derivatives of brevifoliol were prepared by Steglich esterification and evaluated for their antitubercular potential. The 3- [chloro (7)] and 3, 5-[dinitro (8)] benzoic acid ester derivatives were found most active (MIC 25.0 µg/ml) against *Mycobacterium tuberculosis* H37Ra (*Mtb*-Ra). Both derivatives (7 and 8) showed no cytotoxicity towards healthy liver cell line CHANG. *In-silico* docking studies with mycobacterial enzyme InhA (enoyl-ACP reductase), derivative 7 gave the LibDock score of 152.68 and binding energy of -208.62 and formed three hydrogen bonds with SER94, MET98, and SER94. Derivative 8 gave the LibDock score of 113.55 and binding energy of -175.46 and formed a single hydrogen bond with GLN100 and Pi-

interaction with PHE97. These molecular docking and binding patterns indicated that compounds 7 and 8 bind quite well within the binding pocket of InhA and show a higher binding affinity than the isoniazid (LibDock score of 61.63, binding energy of -81.25 and formed one hydrogen bond with ASP148). ***(Current Topics in Medicinal Chemistry, 2020, 20, 1-11).***

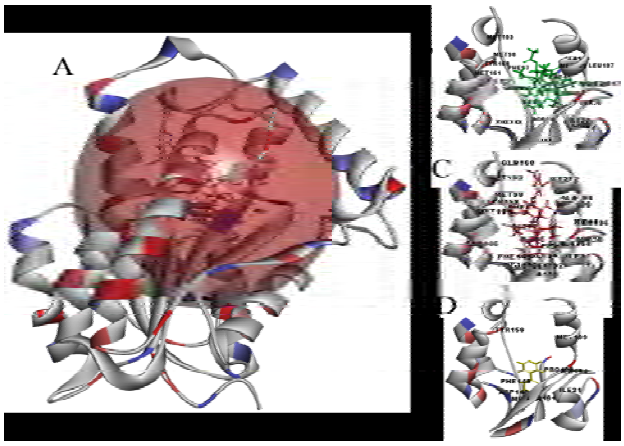


Figure. The above figure shows the structural model of enoyl-ACP reductase (PDB ID: 4TRO) with the ligand-binding site (orange sphere). (B-D) Binding site pocket residues with best fit confirmation of compound 7 (green colour), compound 8 (red colour) and isoniazid (yellow colour)

1.2 Advancing Knowledge Frontiers

1.2.1 Mycobacterium tuberculosis branched-chain amino acids biosynthesis as a source of new targets

The emergence of drug resistant tuberculosis (TB) has severely restricted the chemotherapeutic options. The therapeutic options available for treatment of resistant TB are associated with toxicity, increased cost and a need for prolonged treatment. This necessitates identification of novel pathways or targets, which are different from the targets inhibited by existing drugs. Among the various pathways, the branched-chain amino acids (BCAAs) biosynthetic pathway, which is responsible for biosynthesis of isoleucine, leucine and valine, is present in *Mycobacterium tuberculosis* H37Rv (*Mtb*-Rv), while it is absent in humans. This makes it an attractive pathway to target for inhibition. Among various enzymes involved in BCAAs biosynthesis, the ketol acid reductoisomerase (IlvC, Rv3001c) is part of the main branch, while 3-isopropylmalate dehydrogenase (LeuB, Rv2995c) is part of leucine biosynthetic arm. Both these are essential for *in-vitro* survival of *Mtb*-Rv; however, so far they have not been biochemically and functionally characterized. For IlvC functional characterization we have developed an *E. coli* knockout and studied its growth under nutrient limiting as well as under nutrient rich conditions. Also, for growth rescue the knockout complemented with *Mtb*-Ra copy of IlvC was developed. Further studies using nutrient combinations and growth response to these supplementations have been completed. The IlvC enzyme assay using a coupled two-step protocol has been developed. Also, *Mtb*-Ra silenced strain with down-regulated LeuB has been developed.

1.2.2 Targeting *Mycobacterium tuberculosis* enoyl-acyl carrier protein reductase using computational tools for identification of potential inhibitor and their biological activity

Enoyl-acyl carrier protein reductase (InhA) of type II fatty acid synthase system is involved in the synthesis of mycolic acids which is a major component of the bacterial cell wall. These are the key enzymes playing a very significant role in the FASII pathway of the bacterium. In this study, we have developed a workflow for identification of InhA inhibitors by utilizing *in-silico* virtual screening approaches based on various machine learning algorithms followed by pharmacophore based virtual screening.

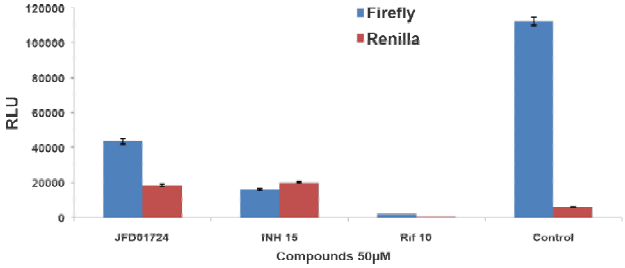


Figure. Test compound JFD01724 is similar to isoniazid (INH), which inhibits InhA and in turn FAS-II pathway. It inhibits the expression of Firefly luciferase gene (blue) but induces the expression of Renilla luciferase gene (red) with respect to untreated control, while rifampicin which does not inhibit InhA reduces the expression of both Firefly and Renilla luciferase genes as a result of general inhibition of mycobacterial growth.

The hits screened from the models were further subjected to molecular docking. Further, based on the XP docking score best twenty compounds were subjected to molecular dynamics study. Finally, nine compounds were shortlisted on the basis of best stable ligand RMSD, c-alpha RMSD, and RMSF plot for biological evaluation studies. Experimental validation of the shortlisted compounds identified one compound JFD01724 having potent inhibitory activity and was able to inhibit the growth of *Mtb*. Further medicinal chemistry efforts may help to improve the inhibitory potency of the identified compound ***(Mol. Informatics, 2020, 39, 2000211)***.

1.2.3 Identification and functional characterization of a *Mycobacterium tuberculosis* protein that helps in biofilm dispersal

Several species of mycobacteria are known to form biofilms in the environment and on the surface of

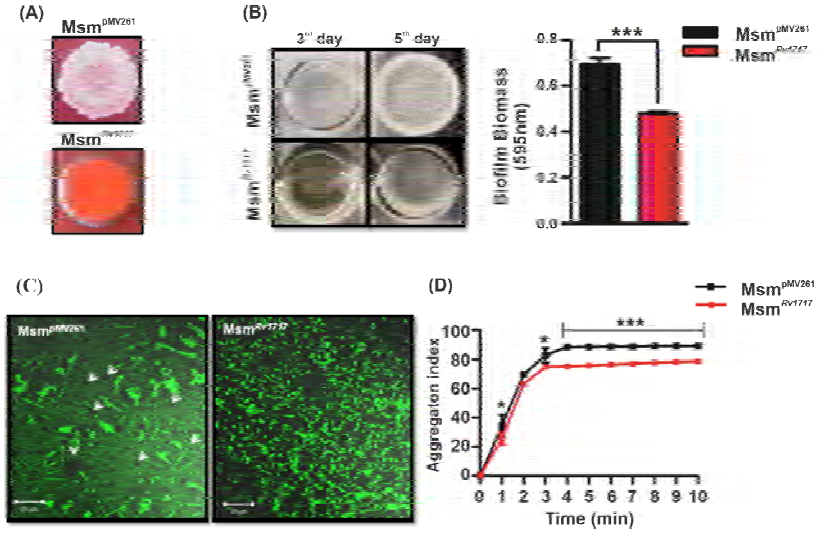


Figure. Rv1717 expression in *M. smegmatis* impairs biofilm growth and autoaggregation. **(A)** Colony colour and morphology of Msm^{Rv1717}and Msm^{pMV261} on Middlebrook 7H10-Congo red agar plates (**B)** Pellicle formation and biofilm biomass (day 5) by Msm^{Rv1717}and Msm^{pMV261} (**C)** Confocal laser scanning microscopy image of biofilms stained with BacLight Green™ fluorescent stain obtained using 63× oil immersion objective. Arrow heads in left panel point to possible nutrient/water channels **(D)** Autoaggregation property of either strain measured as aggregation index (% fall in OD_{600}).

prosthetic devices. *Mycobacterium tuberculosis* (*Mtb*), the causative agent of tuberculosis, has the ability to persist, albeit as a small population, in the infected host for years despite the antitubercular therapy and a competent immune system. Observations in animal models of tuberculosis suggest that *Mtb* may persist as biofilms in the host tissue. In general, biofilm growth is a cyclic process of attachment of microbe to a surface, multiplication and secretion of biofilm matrix and eventually a voluntary dispersal from the deteriorating biofilm to spread to new locations (dissemination). We have identified that Rv1717, a conserved hypothetical protein of *Mtb* is a β-D-galactosidase, specific for the pyranose form rather than furanose form. The form in which galactose exists in the cell wall arabinogalactan. When expressed in *M. smegmatis* (*Msm)* which lacks an ortholog, the protein was found to localize to the cell wall with a preference to the poles. *Msm^{Rv1717}* showed significant changes in colony morphology and cell surface properties. Most striking observation was reduced ability to form biofilms, pellicles and autoagglutination. Exogenous Rv1717 not only prevented biofilm formation in *Msm*, but also degraded preformed biofilms, suggesting that its substrate likely exists in the exopolysaccharides of the biofilm matrix. Presence of galactose in the EPS has not been reported before and hence we used the galactose/N-acetylgalactosamine-specific *Wisteria floribunda* lectin to test the same. The lectin extensively bound to *Msm* and *Mtb*-Ra EPS, but not the bacterium per se. Purified Rv1717 also hydrolysed purified exopolysaccharides from *Msm*. Eventually, to decipher its role, we down-regulated the expression of the homologous gene in *Mtb*-Ra and demonstrate that the strain is unable to disperse from *in-vitro* biofilms, unlike the wild-type. Biofilms exposed to carbon starvation showed a sudden upregulation of Rv1717 transcripts supporting the potential role of Rv1717 in *Mtb* dispersing from a deteriorating biofilm ***(Front. Microbiol., doi: 10.3389/fmicb.2020.611122).***

1.2.4 A dual-action pneumolysin derived peptide with antimicrobial and immunomodulatory activity

Host defense peptides have many desirable characteristics of a new class of antibiotics and immunomodulatory function to supplement traditional antibiotic therapy. These peptides may exist independently or lie hidden in the protein precursors. Here in this study, we adapted template-based screening of peptide sequences and used Pneumolysin (PLY), a virulence factor from the pathogenic bacteria *Streptococcus pneumoniae,* as the target protein. It displays multifaceted immunomodulatory functions like alterations in cell state, complement activation via the classical pathway, and induction of various cytokine and chemokine gene expression in macrophages, neutrophils, and neuronal cells at its sub-lytic levels. Previous microarray studies have revealed more than 100 immunoregulatory molecules' activation upon exposure to wild-type *S. pneumoniae* in THP-1.

All this background information propelled us to explore the effects of peptide sequences derived from PLY for their antibacterial and immunomodulatory functions, hoping to lead us to therapeutic lead candidates. Our antimicrobial studies showed that 3 peptide sequences derived from Pneumolysin have profound activity against *S. aureus* in physiological

conditions. Further immunomodulatory data showed that PLY-derived peptides lowered the quantity of pro-inflammatory cytokine TNF-α, and IL-6 significantly and enhanced the MCP1 production. One of the peptides, LKQ-12, significantly reduced the production of IL-1β, Caspase-1, and ASC proteins associated with molecules for inflammasome formation. LKQ-12 has been shown to elevate cytokines' expression like IL-8, MCP-3, caspases (4 and 6) by influencing the pathways like MAPK and PI3K. We have discovered a peptide template from pneumolysin, which shows profound antimicrobial and immunomodulatory activity through anti-pyroptosis. Overall we could get a peptide that has a dual-action, antimicrobial as well as immunomodulatory.

1.2.5 A novel temporin L-analogue with *in-vivo* antibacterial and anti-endotoxin activities, and non-membrane-lytic mode of action

Though frog antimicrobial peptide, temporin L (TempL) is an attractive molecule for the design of lead antimicrobial agents due to its short size and versatile biological activities, TempL-variants with desirable biological activities have rarely been reported. TempL-analogue, Q3K,TempL is water-soluble and possesses significant anti-endotoxin property along with comparable cytotoxicity to TempL. A phenylalanine residue, located at the hydrophobic face of Q3K,TempL and the 'd' position of its phenylalanine zipper sequence was replaced with a cationic lysine residue. This analogue, Q3K,F8K,TempL, showed reduced hydrophobic moment and was non-cytotoxic with lower antimicrobial activity. Interestingly, swapping between tryptophan at 4th and serine at 6th positions turned Q3K,F8K,TempL into totally amphipathic with clusters of hydrophobic and hydrophilic residues and the highest hydrophobic moment among these peptides. Surprisingly, this analogue, SW,Q3K,F8K,TempL was as non-cytotoxic as Q3K,F8K,TempL, but showed augmented antimicrobial and anti-endotoxin properties, comparable to that of TempL and Q3K,TempL. SW,Q3K,F8K,TempL exhibited appreciable survival of mice against *P. aeruginosa* infection and LPS challenge. Unlike TempL and Q3K,TempL; SW,Q3K,F8K,TempL adopted an un-ordered secondary structure in bacterial membrane-mimetic lipid vesicles and did not permeabilize them or depolarize bacterial membrane. On the whole, the results demonstrate the design of a non-toxic TempL-analogue that possesses clusters of hydrophobic and hydrophilic residues with impaired secondary structure and shows non-membrane-lytic

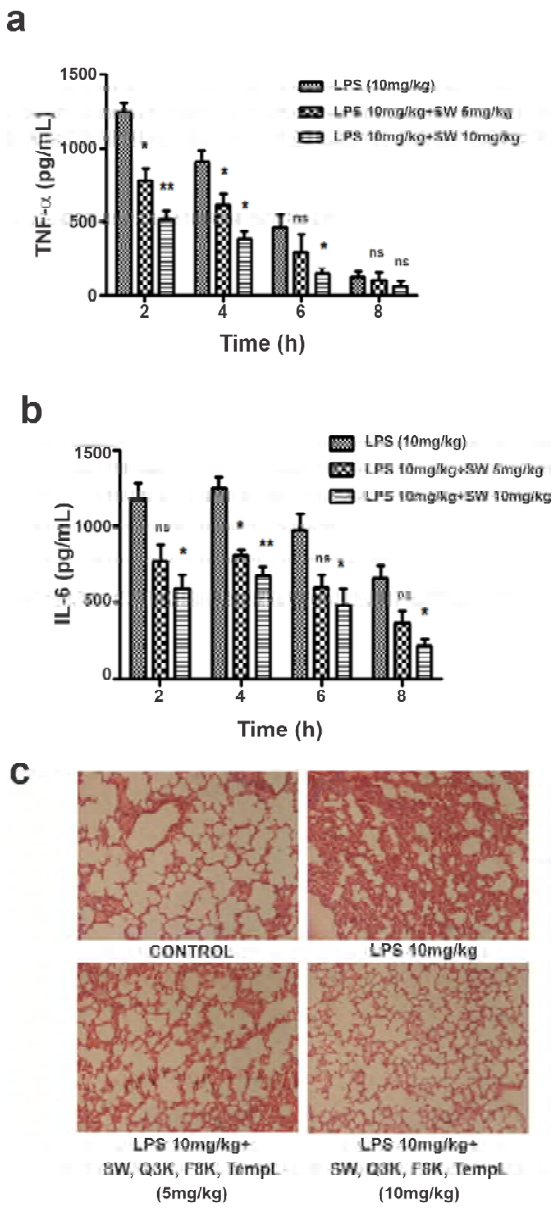
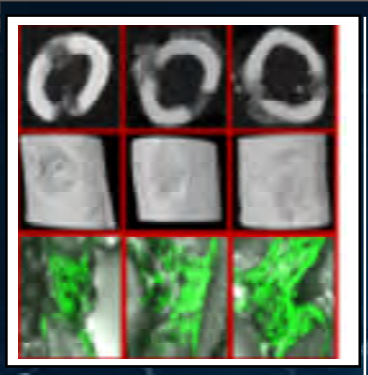


Figure. The above figure shows anti-endotoxin activity of SW,Q3K,F8K,TempL. (a) and (b) Levels of TNF-α and IL-6 in BALB/c mice (25 g) were estimated with ELISA kits. BALB/c mice were injected 10 mg/kg of LPS (i.p.) followed by peptide treatment 5 mg/kg and 10 mg/kg. Blood was collected after 0, 2, 4, 6 and 8 h post-infection. (c) Histology of representative lung sections. Sections were stained with hematoxylin and eosin. Control group. Lipopolysaccharide (LPS) group, LPS+ SW,Q3K,F8K,TempL 5mg/kg and LPS+ SW,Q3K,F8K,TempL 10 mg/kg, less damage or almost no difference was observed as compared to the LPS group. Error bars show the possible amount of error in each dataset. P value was calculated by using one-way analysis of variance using Tukey's test (*P≤ 0.05;**P≤ 0.01)

mechanism and *in-vivo* anti-endotoxin and antimicrobial activities. This paradigm of design of antimicrobial peptide with clusters of hydrophobic and hydrophilic residues and high hydrophobic moment but low secondary structure could be attempted further ***(ACS Infectious Diseases, 2020, 6, 2369-85).***

1.2.6 *Mycobacterium tuberculosis* class II apurinic/apyrimidinic-endonuclease/ 3'-5' exonuclease (XthA) engages with NAD+ -dependent DNA ligase A (LigA) to counter futile cleavage and ligation cycles in Base Excision Repair

Class-II AP-endonuclease (XthA) and NAD^+-dependent DNA ligase (LigA) are involved in initial and terminal stages of bacterial DNA base excision repair (BER), respectively. XthA acts on abasic sites of damaged DNA to create nicks with 32'-OH and 5'-deoxyribose phosphate (5'-dRP) moieties. Co-immunoprecipitation using mycobacterial cell-lysate, identified MtbLigA-MtbXthA complex formation. Pull-down experiments using purified wild-type, and domain-deleted MtbLigA mutants show that LigA-XthA interactions are mediated by the BRCT-domain of LigA. Small-Angle-X-ray scattering, $^{15}N/^{1}H$-HSQC chemical shift perturbation experiments and mutational analysis identified the BRCT-domain region that interacts with a novel $_{104}$DGQPSWSGKP$_{113}$ motif on XthA for complex-formation. Isothermal-titration calorimetry experiments show that a synthetic peptide with this sequence interacts with MtbLigA and disrupts XthA–LigA interactions. *In vitro* assays involving DNA substrate and product analogs show that LigA can efficiently reseal 32 OH and 52 dRP DNA termini created by XthA at abasic sites. Assays and SAXS experiments performed in the presence and absence of DNA, show that XthA inhibits LigA by specifically engaging with the latter's BRCT-domain to prevent it from encircling substrate DNA. Overall, the study suggests a coordinating function for XthA whereby it engages initially with LigA to prevent the undesirable consequences of futile cleavage and ligation cycles that might derail bacterial BER.



BONE HEALTH AND METABOLIC BONE DISEASES

Coordinators: Dr. Naibedya Chattopadhyay, Dr. Atul Goel and Dr. Ritu Trivedi

2

Vision and Goal:

- Development of novel agents for fracture healing and management of osteoporosis through modern drug design, scientific validation of traditional remedies and generation of new knowledge.

Core Competencies and Activities:

- Design, synthesis and bioevaluation of novel molecules/isolates from natural sources for new lead generation and/or development of agents for the management of osteoporosis, and bone related disorders
- Scientific validation of traditional remedies
- Therapeutic repurposing
- Molecular mechanism of action of promising agents;
- Advancing in knowledge frontiers

Research Group

Front row (L to R): Dr. K.V. Sashidhara, Dr. Sabyasachi Sanyal, Dr. T. Narender, Dr. Prem Prakash Yadav, Dr. Rajdeep Guha, Dr. Atul Goel (Area Coordinator), Dr. Naibedya Chattopadhyay (Area Coordinator), Dr. Ritu Trivedi (Area Coordinator), Dr. Arun Kumar Trivedi, Dr. Divya Singh, Dr. Prabhat Ranjan Mishra & Dr. Sanjeev Kanojiya.

Back Row (L to R): Dr. Jiaur Rahaman Gayen, Dr. Wahajuddin & Dr. Rabi Sankar Bhatta.

2.1 New drug discovery & development, and therapeutic repurposing

2.1.1 IND filing of S007-1500 (Fracture healing agent)

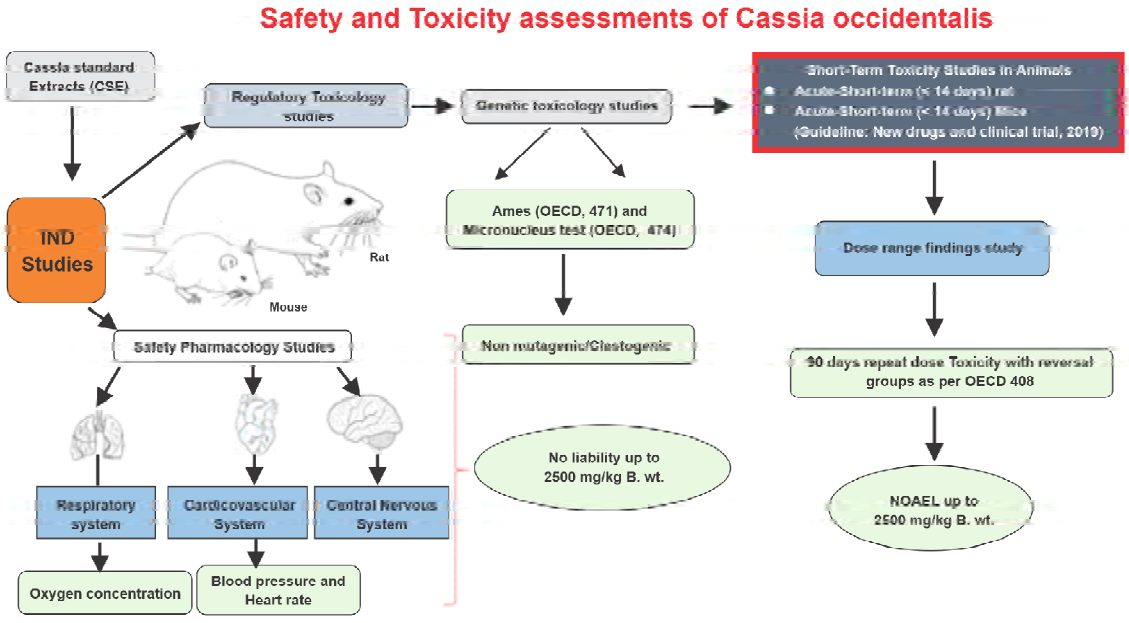
IND application dossier has been submitted for Approval of Phase I Clinical Trial (IND/CT04/FF/2020/22897; dated Dec 14, 2020). DCGI permission for Phase I clinical Trial received on 8 January 2021. RNA samples from S007-1500 treated samples were sent to Agrigenome Pvt Ltd for transcriptome analysis. Transcriptome analysis is complete and few targets have been chosen to identify molecular target using silencing studies approach.

2.1.2 Simultaneous quantification of five biomarkers in ethanolic extract of *Cassia occidentalis* Linn. stem using liquid chromatography tandem mass spectrometry: Application to its pharmacokinetic studies

Cassia occidentalis L. stem extract is used as a purgative, febrifuge, and diuretic, and in the treatment of flu, fever, fracture and bone diseases. Pharmacological studies prove the osteogenic and antiresorptive effects of *Cassia occidentalis* L. ethanolic extract (COEE), which may be due to apigenin, apigenin-6-*C*-glucopyranoside, luteolin, 32 ,42 ,7-trihydroxyflavone and emodin. The objectives of this study was to develop a selective and sensitive LC-MS/MS method and validate for the simultaneous determination of the above five biomarkers in rat plasma after oral administration of COEE at a dose of 500 mg kg^{-1}. The analytes were separated on a Phenomenex Luna C18 column (4.6 × 150 mm, 3.0 µm) with an isocratic mobile phase consisting of methanol-10 mM ammonium acetate buffer (95: 05, v/v). Run time was for 5.5 min with LLOQ of 1 ng mL^{-1} for all the analytes. The mass spectrometer was operating in negative ionization mode for quantification of the analytes. The calibration curves were linear (r^2 > 0.99) for all the analytes. The intra- and inter-day precisions were less than 8.17% and the relative error was between “8.57% and 7.28%. Analytes were rapidly absorbed in the oral pharmacokinetic study. The biomarkers were stable in simulated gastric and intestinal fluids but underwent metabolism in rat liver microsomes. This is the first report on *in vivo* oral pharmacokinetics and *in vitro* stability studies of osteogenic compounds present in COEE. These results will be helpful for further understanding of pharmacodynamics behaviour of COEE and the bioanalytical method will be useful for further preclinical/clinical trials. (***RSC Adv DOI: 10.1039/C9RA07482A***)

2.1.3 Regulatory safety pharmacology and toxicity assessments of a standardized stem extract of *Cassia occidentalis* Linn. in rodents

Cassia occidentalis Linn (CO) is an annual/perennial plant having traditional uses in the treatments of ringworm, gastrointestinal ailments and piles, bone fracture, and wound healing. Previously, we confirmed the medicinal use of the stem extract of CO (henceforth CSE) in fracture healing at 250mg/kg dose in rats and described an osteogenic mode of action of four phytochemicals present in CSE. Here we studied CSE’s preclinical safety and toxicity. CSE was prepared as per regulations of Current Good Manufacturing Practice for



human pharmaceuticals/phytopharmaceuticals and all studies were performed in rodents in a GLP-accredited facility. In acute dose toxicity in rats and mice and ten-day dose range-finding study in rats, CSE showed no mortality and no gross abnormality at 2500 mg/kg dose. Safety Pharmacology showed no adverse effect on central nervous system, cardiovascular system, and respiratory system at 2500 mg/kg dose. CSE was not mutagenic in the Ames test and did not cause clastogenicity assessed by *in vivo* bone marrow genotoxicity assay. By a sub chronic (90 days) repeated dose study in rats, the no-observed-adverse-effect-level was found to be 2500 mg/kg assessed by clinico-biochemistry and all organs histopathology. We conclude that CSE is safe up to 10X the dose required for its osteogenic effect.

2.1.4 A butanolic fraction from the standardized stem extract of *Cassia occidentalis* L delivered by a self-emulsifying drug delivery system protects rats from glucocorticoid-induced osteopenia and muscle atrophy

We recently reported that a butanol soluble fraction from the stem of *Cassia occidentalis* (CSE-Bu) consisting of osteogenic compounds mitigated methyl prednisone (MP)-induced osteopenia in rats, albeit failed to afford complete protection thus leaving a substantial scope for further improvement. To this aim, we prepared an oral formulation that was a lipid-based self-nano emulsifying drug delivery system (CSE-BuF). The globule size of CSE-BuF was in the range of 100-180 nm of diluted emulsion and the zeta potential was -28 mV. CSE-BuF enhanced the circulating levels of five osteogenic compounds compared to CSE-Bu. CSE-BuF (50 mg/kg) promoted bone regeneration at the osteotomy site and completely prevented MP-induced loss of bone mass and strength by concomitant osteogenic and anti-resorptive mechanisms. The MP-induced downregulations of miR29a (the positive regulator of the osteoblast transcription factor, Runx2) and miR17 and miR20a (the negative regulators of the osteoclastogenic cytokine RANKL) in bone was prevented by CSE-BuF. In addition, CSE-BuF protected rats from the MP-induced sarcopenia and/or muscle atrophy by downregulating the skeletal muscle atrogenes, adverse changes in body weight and composition. CSE-BuF did not impact the anti-inflammatory effect of MP. Our preclinical study established CSE-BuF as a prophylactic agent against MP-induced osteopenia and muscle atrophy. (***Sci Rep, PMID: 31932603***).

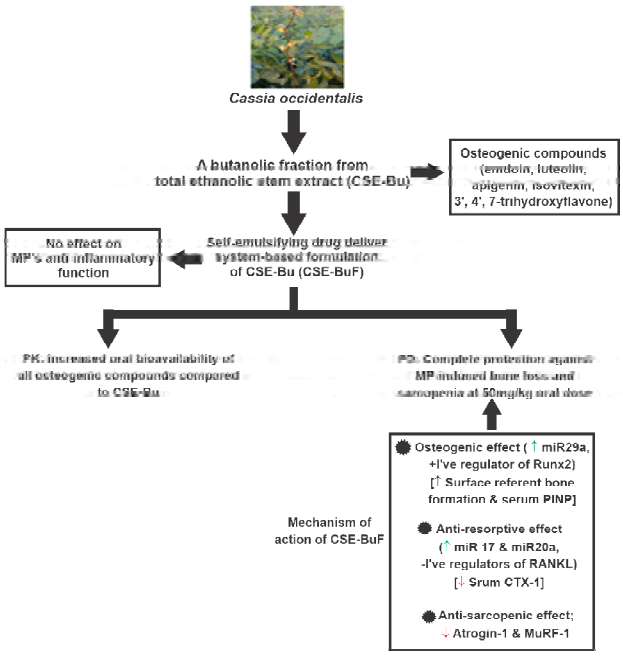
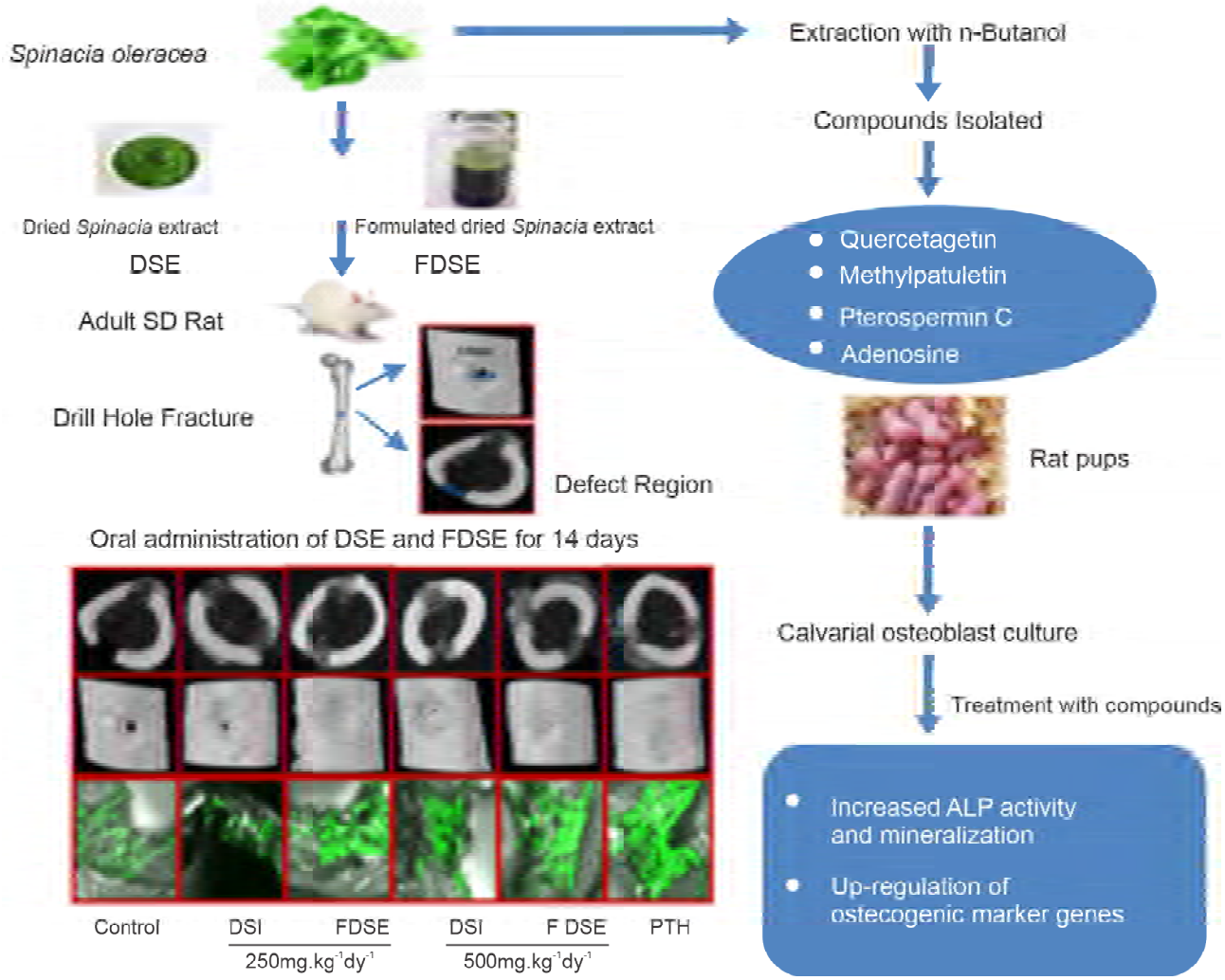


Figure: A schematic diagram illustrating the effects of CSE-Bu or CSE-BUF on rat bones and skeletal muscle given concurrently with MP treatment. PK, pharmacokinetics and PD: pharmacodynamics.

2.1.5 Self-emulsifying formulation of *Spinacia oleracea* reduces the dose and escalates bioavailability of bioactive compounds to accelerate fracture repair in rats

Spinach (*Spinacia oleracea*) is a rich source of flavonoids and therefore widely used therapeutically as an antioxidant agent in traditional medicine. The present study was undertaken to study the bone regenerating property of dried *Spinacia oleracea* extract (DSE) and self-emulsifying formulation of the extract (FDSE) on drill-hole model of fracture repair in rats. 0.8 mm hole was drilled in the diaphyseal region of femur in adult SD rats. DSE and formulated extract (FDSE) was administered orally and fractured femur was collected after treatment regimen. Micro-CT, transcriptional analysis and measurement of calcein intensity of callus formed at the injured site was performed to study the efficacy of the extract and formulation on bone regeneration. Further, compounds from extract were assessed for *in-vitro* osteoblast activity.

Micro-architecture of the regenerated bone at injured site exhibited 26% ($p < 0.001$) and 35% ($p < 0.01$) increased BV/TV (bone volume /tissue volume) and Tb.N. (trabecular number) for DSE (500 mg.kg^{-}1). Further, FDSE exhibited similar augmentation in BV/TV ($p < 0.01$) and Tb. N ($p < 0.01$) parameters at dose of 250 mg.kg $^{-}$1. Analogous results were obtained from transcriptional analysis and calcein intensity at the fractured site. 3-O-Methylpatuletin, one of the compound isolated from the extract stimulated the differentiation and mineralization of primary osteoblast and depicted concentration dependent antagonizing effect of H2O2 in osteoblast

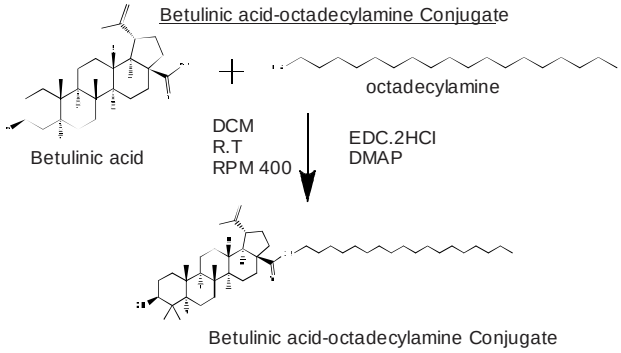


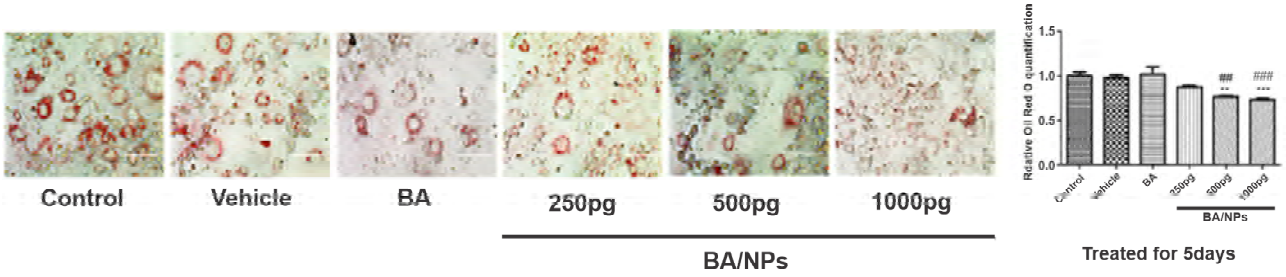
apparently, minimizing ROS generation thus affectivity in fracture repair. The present study showed that bone regenerating property of spinach was augmented by formulating extract to deliverable form and can be further studied to develop as therapeutic agent for fracture repair. ***(Clinical Phytoscience, doi.org/10.1186/s40816-020-00190-z)***

2.2 Advancing Knowledge Frontiers

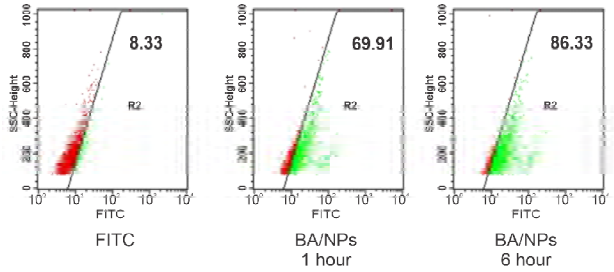
2.2.1 Lupane anchored Pharmacosomes for improved osteogenic activity.

Ligand directed self-assembled vesicles having composite core has been engineered to enhance osteogenic efficacy. The Low molecular weight osteotropic lipid was synthesized using stearic acid and palmitic acid through succinylation followed by carbodiimide reaction. The lipid was characterized through IR, Mass and NMR that established the successful conjugation of lipid. The proof of concept has been established. This prototype formulation resulted in interplay of different pathway stimulation. This formulation has resulted an inherent differentiation and mineralization of osteoblasts. It increased expression of osteogenic genes Bmp-2, OCN and Runx2 activating the Wnt-beta-catenin signaling pathway.





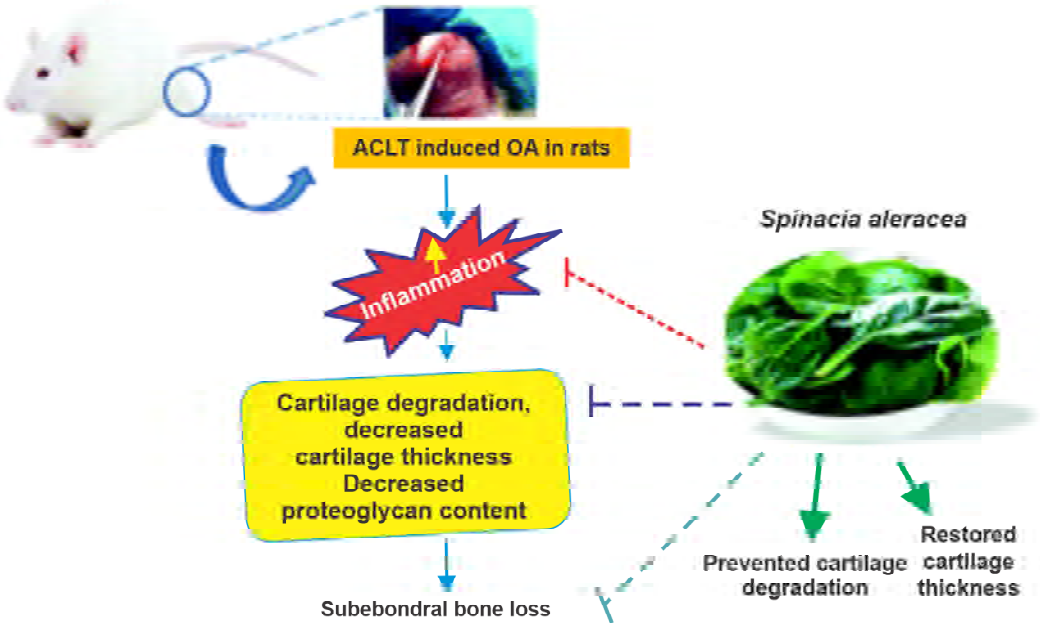
Treatment with the prototype formulation resulted in the decrease in number of adipocyte and simultaneously inhibited the adipogenic potential by down regulating the SREBP-1c, CEBP alpha and FABP4 .



Quantification of cellular uptake of BA/NPs inside the osteoblast cells

2.2.2 Inhibition of cartilage degeneration and subchondral bone deterioration by *Spinacia oleracea* in human mimic of ACLT-induced osteoarthritis

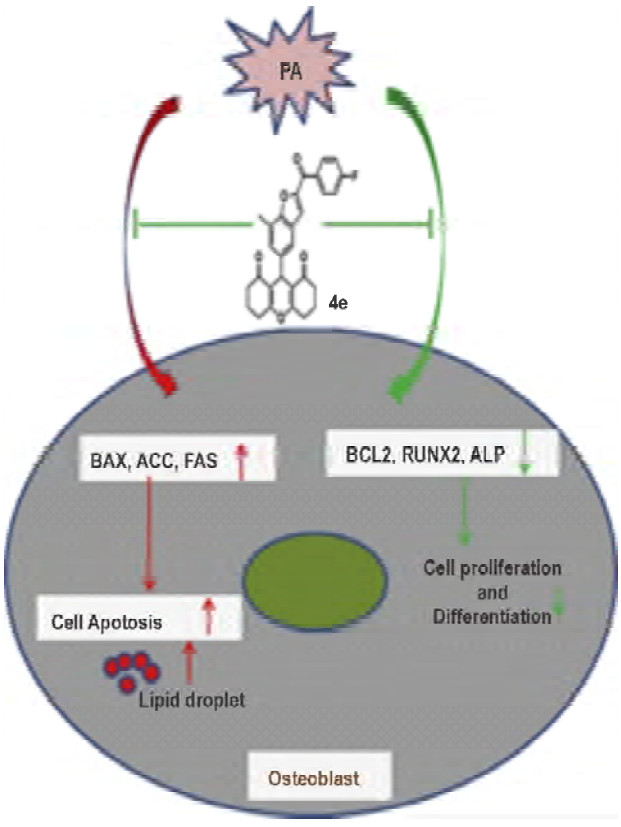
Osteoarthritis (OA) is an aging disorder characterized by degenerated cartilage and sub-chondral bone alteration in affected knee joints. Globally, millions of people suffer from this disease. However, there is a lack of safe and promising therapeutics, making the exploration and development of leads from natural sources urgent. Accordingly, food as medicine may be the most suitable approach for the treatment of this degenerative disease. Herein, we elucidated the protective role of *Spinacia oleracea* extract (SOE) in an anterior cruciate ligament transection (ACLT) model of osteoarthritis as a mimic of the human condition. ACL transection was done in the tibio-femoral joints of rats. SOE was orally administered at the dosage of 125 and 250 mg $kg^{-}1$ $day^{-}1$ for four weeks. It was shown that the animals with SOE treatment had better joint morphology than the ACLT animals, as evident by the shiny appearance of their cartilage. Hematoxylin and safranin-o staining showed that the number of chondrocytes was significantly reduced in the OA model, which was prevented with SOE treatment. The reduction in the cartilage thickness was well observed by toluidine blue staining. The reduced stain by safranin-o and toluidine blue, indicated proteoglycan loss in the ACLT-induced osteoarthritis model. The proteoglycan content and cartilage thickness



were restored in the SOE group upon treatment at an SOE dosage of 125 and 250 mg kg^{-1} day^{-1}. The micro-CT parameters of subchondral bone (SCB) and cartilage degradation markers in the serum corroborated our findings of the protective effects of SOE. In summary, our study suggests that SOE has therapeutic potential, which if taken regularly as a food supplement, can have beneficial effects. ***(Food Funct. PMID: 32901645)***

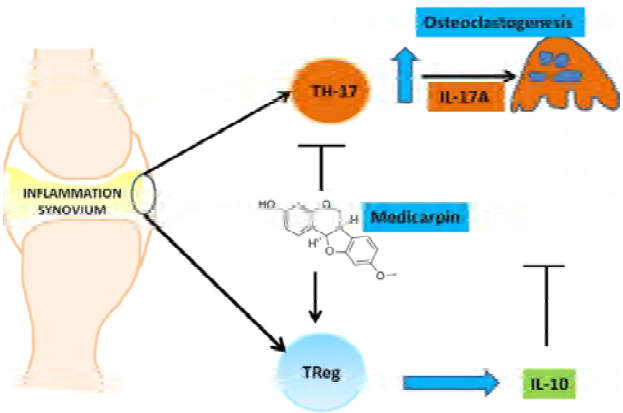
2.2.3 Benzofuran pyran compound rescues rat and human osteoblast from lipotoxic effect of palmitate by inhibiting lipid biosynthesis and promoting stabilization of RUNX2

Obesity and ageing increases bone marrow fat which in turn is associated with lower bone mass. Marrow adipocytes by secreting cytokines, adipokines and free fatty acids change the bone marrow milieu and thus the number of osteoblasts. Palmitate is the common saturated fatty acid, an unavoidable ingredient we consume with food, which kindles cell apoptosis. Compound 4e is osteogenic in nature. We examined the effect of compound 4e in palmitate induced lipotoxicity in rat osteoblasts. Design of benzofuran Pyran hybrid compound (4e) was found to be effective in inhibiting palmitate induced cell apoptosis. In this study an *in vitro* model of palmitate was contrived. Anti-apoptotic effect of compound 4e was assessed by Annexin/PI and LDH (Lactate dehydrogenase) assay. Compound 4e also increased osteoblast differentiation and mineralization. It also increased expression of osteogenic markers (RUNX2 and BMP2), assessed by Real time PCR and immunofluorescence, which was impeded by palmitate. Acetyl Co-Carboxylase (ACC) and Fatty acid synthase (FAS), two prominent mediators of lipid biosynthesis were increased by palmitate exposure. Compound 4e modulated lipid biosynthesis by inhibiting ACC and FAS as reflected visually and after quantification of less lipid droplet formation suggesting that 4e is osteogenic and simultaneously anti-lipotoxic ***(Toxicol In Vitro; PMID: 32330564).***



2.2.4 Medicarpin prevents arthritis in post-menopausal conditions by arresting the expansion of TH17 cells and pro-inflammatory cytokines

Autoimmune diseases are characterized by alteration in balance of various cytokines. Rheumatoid arthritis is a well-known inflammatory disease leading to destruction of cartilage at knee and hands. Collagen-induced arthritis (CIA) is a common autoimmune model for rheumatoid arthritis study. We have investigated the therapeutic role of medicarpin, a natural pterocarpan with known anti-osteoclastogenic activities, in postmenopausal polyarthritis model of DBA/1J mice. For this, mice were ovariectomized and CIA was induced in OVx animals with primary immunization. After 21 days, booster dose was injected in Ovariectomy (OVx) mice to develop postmenopausal poly-arthritis mice model. Medicarpin treatment in mice at dose of 10.0 mg/kg/body wt was started after 21 days of primary immunization for one month of time period every day orally. We found that medicarpin prevented alteration of TH-17/Treg ratio in CIA model leading to reduced osteoclastogenesis. Micro Computed Tomography (Micro-CT) analysis demonstrated that medicarpin prevents cartilage erosion in joints and restores loss of trabeculae parameters in distal tibia. Treatment with medicarpin also prevented alteration of various cytokines level by down-regulating



various pro-inflammatory cytokines like TNF-α, IL-6 and IL-17A, while up-regulating anti-inflammatory cytokine IL-10 in CIA model of mice. Biological marker of arthritis is cartilage oligomeric matrix protein (COMP). COMP level was up-regulated in CIA induced mice while treatment with medicarpin significantly restored the serum level of COMP compared with untreated groups. Cartilage staining by Safranin-O also indicates that cartilage destruction in joints of CIA mice was prevented by medicarpin treatment. From this study, we can conclude that medicarpin is effective in preventing arthritis in post-menopausal conditions ***(International Immunopharmacology, PMID: 32097846).***

2.2.5 *Fasciola* helminth defense molecule 1 protects against experimental arthritis by inhibiting osteoclast formation and function without modulating the systemic immune response

An inverse correlation between helminth infection and the autoimmune disease appears to be contributed by the anti inflammatory factors produced by these organisms. Suppressing osteoclast function without affecting the systemic immunological response is an emerging therapeutic strategy for rheumatoid arthritis (RA). We observed that a synthetic peptide corresponding to 34 amino acids of C terminal sequence of *Fasciola* helminth defense molecule 1 (C FhHDM 1) inhibited RANKL induced osteoclast formation and lysosomal acidification with an attendant upregulation of sequestome 1/p62, a negative regulator of NF kB expression. C FhHDM 1 also suppressed RANKL production from osteoblasts. Macrophages are the major inflammatory cells in the joints of RA and C FhHDM 1 suppressed ICAM 1 (an inflammatory surrogate) expression in these cells. In a murine model of collagen II induced arthritis (CIA), C FhHDM 1 improved clinical score, protected against cartilage destruction, and maintained bone mass and bone architecture of joints compared with the CIA group. C FhHDM 1 suppressed the CIA induced expression of TNF, IL 17, and IFN γ in joints but not their serum levels. The peptide also had no effect on the CIA induced suppression of T regulatory response. We conclude that C FhHDM 1 has a joint specific protective effect in experimental arthritis without mitigating systemic inflammation, and thus could become an adjuvant anti arthritis therapy to prevent RA induced osteopenia. (***FASEB Journal, PMID: 31914677***)

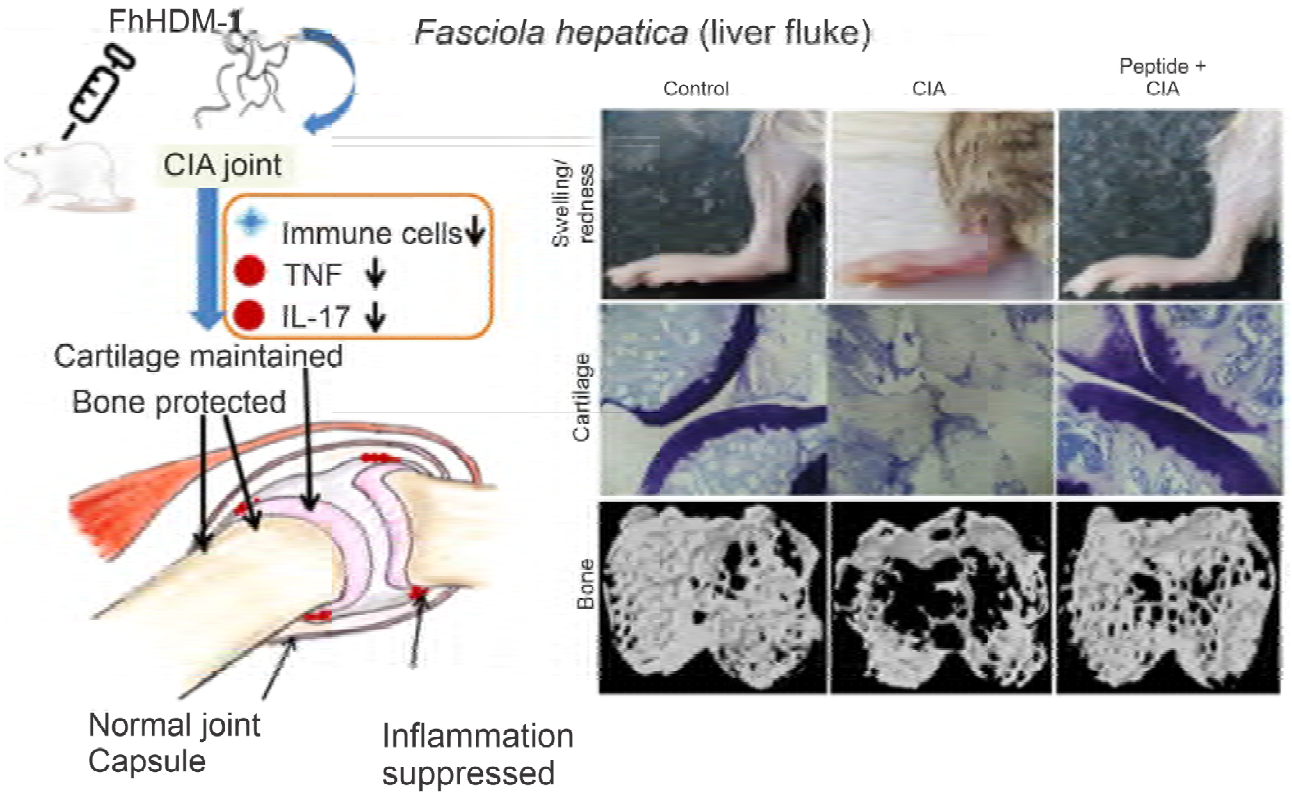


Figure: Left panel: a schematic diagram showing protection of joint structures by FhHDM-1 by local inhibition of inflammatory responses and right panel: showing mitigation of paw swelling, preservation of cartilage tissue (toluidine blue staining) and trabecular structure at proximal femur.

2.2.6 Increased bone marrow-specific adipogenesis by clofazimine causes impaired fracture healing, osteopenia and osteonecrosis without extra-skeletal effects in rats

Mycobacterium leprae infection causes bone lesions and osteoporosis, however, the effect of anti-leprosy drugs on the bone is unknown. We, therefore, set out to address it by investigating osteogenic differentiation from bone marrow (BM)-derived mesenchyme stem cells (MSCs). Out of seven anti-leprosy drugs, only clofazimine (CFZ) reduced MSCs viability (IC50~1μM) and their osteogenic differentiation but increased adipogenic differentiation on a par with rosiglitazone, and this effect was blocked by a peroxisome proliferator-activated receptor gamma (PPARγ) antagonist, GW9662. CFZ also decreased osteoblast viability and resulted in impaired bone regeneration in a rat femur osteotomy model at 1/3rd human drug dose owing to increased callus adipogenesis as GW9662 prevented this effect. CFZ treatment decreased BM-MSCs population and homing of MSCs to osteotomy site despite drug levels in BM being much less than it's *in vitro* IC50 value. In adult rats, CFZ caused osteopenia in long bones marked by suppressed osteoblast function due to enhanced adipogenesis and increased osteoclast functions. A robust increase in marrow adipose tissue (MAT) by CFZ did not alter hematologic parameters but likely reduced BM vascular bed leading to osteonecrosis (ON) characterized by empty osteocyte lacunae. However, CFZ had no effect on visceral fat content and was not associated with any metabolic and hematologic changes. Levels of unsaturated fatty acids in MAT were higher than saturated fatty acids and CFZ further increased the former. From these data, we conclude that CFZ has skeletal toxicity and could be used for creating a rodent ON model devoid of extra-skeletal effects. **(*Toxicol Sci, PMID: 31393584*)**

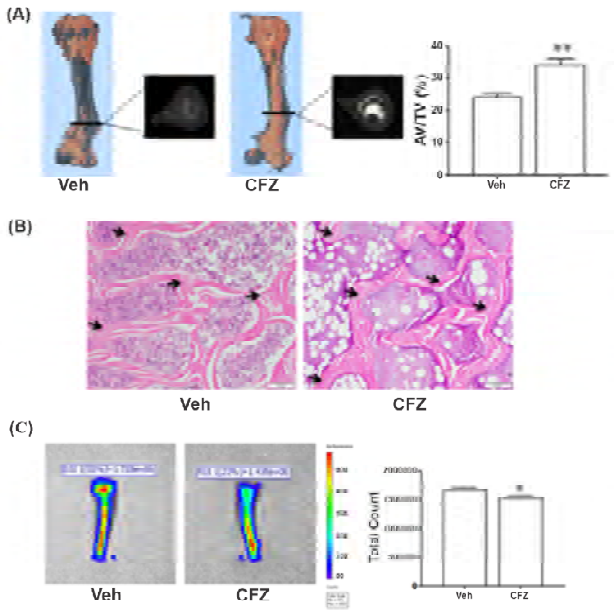


Figure caption: Chronic CFZ treatment in adult rats resulted in osteonecrotic changes in femur. **(A)** Decalcified femurs from vehicle or CFZ treated rats were incubated in OsO_4 solution to study the distribution and volume of adipose tissue in BM. 3-D mCT images showing adipose tissue (orange colour) in femurs and 2-D of indicated cross-sections from femurs showing adipocyte abundance (shinning white region in CFZ group). Adipose volume/tissue volume (AV/BV) of femur of indicated groups was quantified by mCT (right). **(B)** Photomicrographs of decalcified femurs stained with H&E showing increased adipocytes and marrow necrosis in CFZ group. Arrows indicate pyknotic nuclei and empty lacunae in osteocytes. Scale bar, 100 μm. **(C)** Epi-florescence in tibia representing the labelled vasculature. Red-orange range represents higher labelling thus indicating better vasculature (vehicle) whereas that towards green-blue range indicates lower labelling corresponding to poor vasculature (CFZ). Representative images with ROI in panel left, and quantification in panel right.

2.2.7 Selective dietary polyphenols induce differentiation of human osteoblasts by adiponectin receptor 1-mediated reprogramming of mitochondrial energy metabolism

Anabolic therapies for osteoporosis including dietary polyphenols promote osteoblast function by influencing its energy metabolism. Among the dietary polyphenols, the beneficial skeletal effects of genistein (an isoflavone), kaempferol (a flavone), resveratrol (RES, a stilbenoid) and epigallocatechin gallate (EGCG, a catechin) have been reported in preclinical studies. We studied the action mechanism of these nutraceuticals on osteoblast bioenergetics. All stimulated differentiation of human fetal osteoblasts (hFOB). However, only EGCG and RES stimulated mitochondrial parameters including basal and maximum respiration, spare respiratory capacity and ATP production (a measure of the activity of electron transport chain/ETC). Increases in these parameters were due to increased mitochondrial biogenesis and consequent upregulation of several mitochondrial proteins including those involved in ETC. Rotenone blocked the osteogenic effect of EGCG and RES suggesting the mediatory action of mitochondria. Both compounds rapidly activated AMPK, and dorsomorphin (an AMPK inhibitor) abolished ATP production stimulated by these compounds. Moreover, EGCG and RES upregulated the mitochondrial biogenesis factor, PGC-1α which is downstream of AMPK activation, and silencing PGC-1α blocked their stimulatory effects on ATP production and hFOB differentiation. Adiponectin receptor 1 (AdipoR1) is an upstream regulator of PGC-1α, and both compounds increased the expression of AdipoR1 but not AdipoR2. Silencing AdipoR1 blocked the upregulation of EGCG/RES-induced PGC-1α and hFOB differentiation. In rat calvarium, both compounds increased AdipoR1, PGC-1α, and RunX2 (the osteoblast transcription factor) with a concomitant increase in

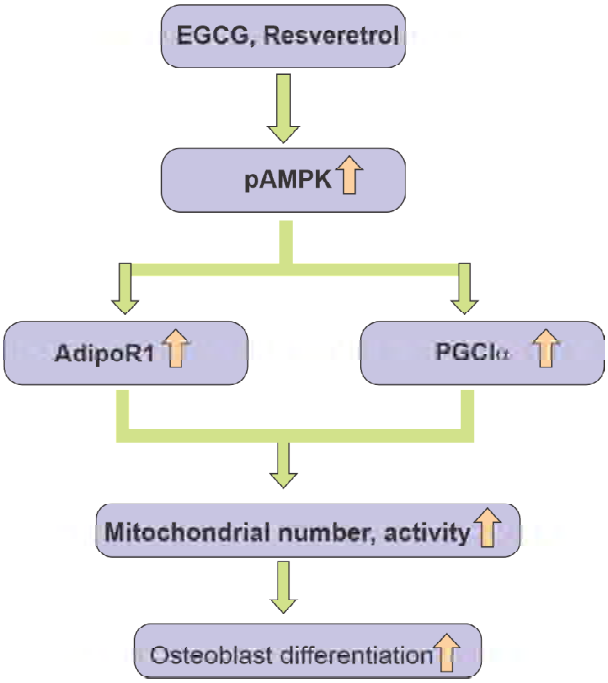
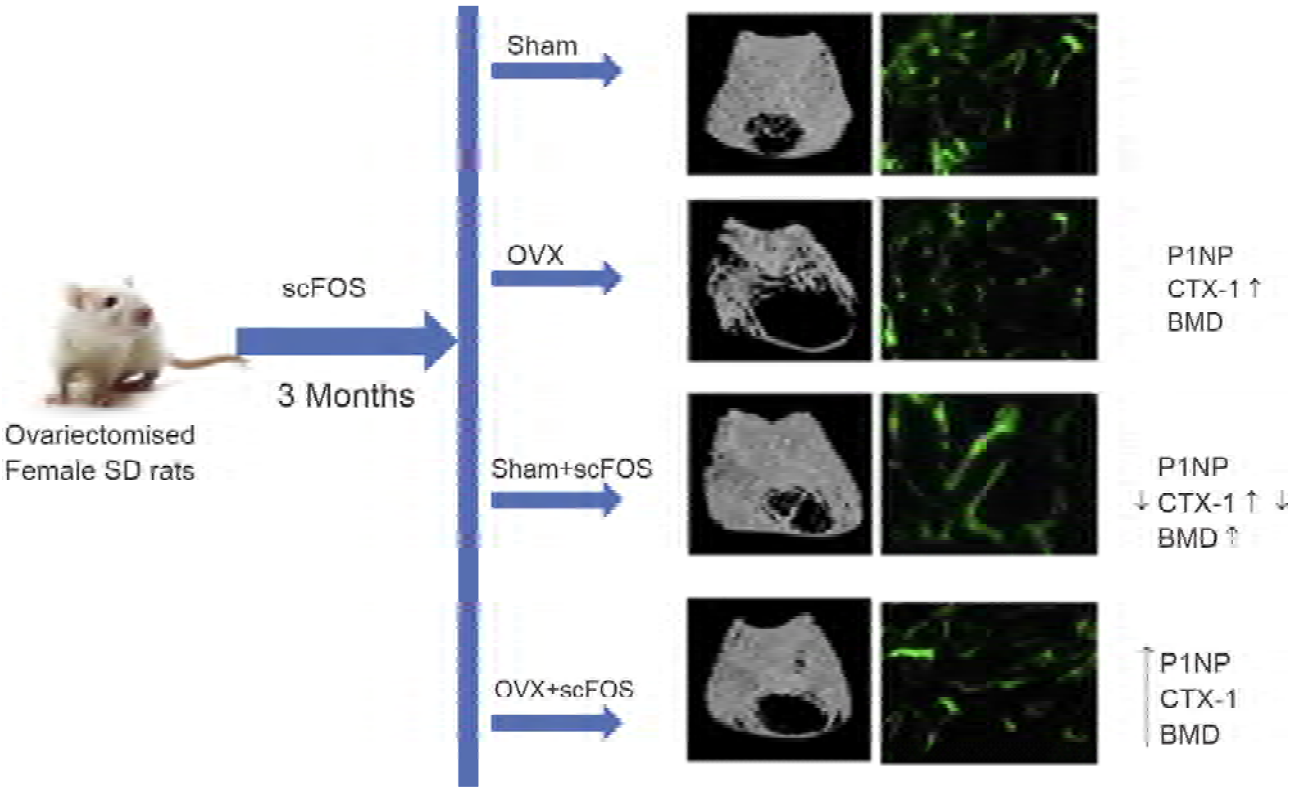


Figure: Schematic illustration showing EGCG- and RES-induced signalling pathway that involves increased mitochondrial activity leading to osteoblast differentiation.

mitochondrial copy number and ATP levels. We conclude that EGCG and RES display osteogenic effects by reprogramming osteoblastic bioenergetics by acting as the AdipoR1 agonists. (***Biomed Pharmacother, PMID: 32422565***).

2.2.8 A prebiotic, short-chain fructo-oligosaccharides promotes peak bone mass and maintains bone mass in ovariectomized rats by an osteogenic mechanism

In preclinical studies, fructooligosaccharide (FOS) showed beneficial skeletal effects but its effect on peak bone mass (PBM) and bone loss caused by estrogen (E2) deficiency has not been studied, and we set out to study these effects in rats. Short-chain (sc)-FOS had no effect on body weight, body composition, and energy metabolism of ovary intact (sham) and ovariectomized (OVX) rats. scFOS did not affect serum and urinary calcium and phosphorus levels, and on calcium absorption, although an increasing trend was noted in the sham group. Sham and OVX rats given scFOS had better skeletal parameters than their respective controls. scFOS treatment resulted in a higher bone anabolic response but had no effect on the catabolic parameters. scFOS increased serum levels of a short-chain fatty acid, butyrate which is known to have osteogenic effect. Our study for the first time demonstrates that in rats scFOS at the human equivalent dose enhances PBM and protects against E2 deficiency-induced bone loss by selective enhancement of new bone formation, and implicates butyrate in this process. (***Biomed Pharmacther, PMID: 32776872***).

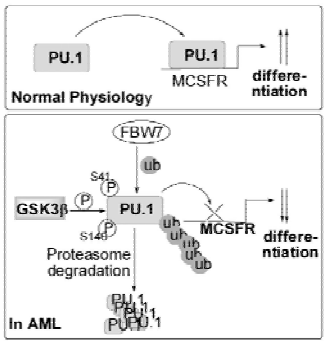


2.2.9 Calcium repletion to rats with calcipenic rickets fails to recover bone quality: A calcipenic "memory"

Calcipenic rickets is prevalent in underprivileged children in developing countries. Calcipenic rickets resulting from dietary calcium (Ca) deficiency decreases bone mass and deteriorates bone microstructure in humans. The effect of dietary Ca replenishment (CaR) on rachitic bones in animal models depends on the amount, critical period and duration of replenishment, however, the extent of recovery in various bone parameters including bone quality remains unclear. We investigated the effect of CaR in rat skeleton after inducing calcipenic rickets. Female SD rats (postnatal 28 days/P28) were rendered calcipenic by feeding calcium deficient (CaD) diet (0.1% Ca) till P70 while control SD rats were fed Ca sufficient diet (0.8% Ca). At P70, calcipenic rats were switched to 0.8% Ca diet till P150 for one group and P210 for another group (endpoint). The CaD groups received 0.1% Ca diet throughout the study (P210). In the CaD groups, serum Ca and phosphate, and bone mineral density (BMD) were significantly decreased whereas serum alkaline phosphatase (ALP), iPTH and CTX-1 were increased compared to age-matched controls. Moreover, at the endpoint, the CaD group had reduced bone mass, surface referent bone formation parameters, tissue mineralization and strength accompanied by the increased osteoid thickness and microarchitectural decay (measured by trabecular geometric parameters) with poor crystal packing. The CaR group showed complete recovery in serum Ca, iPTH, ALP and CTX-1, and BMD, however, the bone quality parameters including bone strength, microarchitectural decay, tissue mineralization, and crystallinity were incompletely restored. Decreased surface referent bone formation and increased unmineralized bones (osteoid) indicative of osteomalacia were also observed in the CaR group at P210 compared with control despite prolonged replenishment. We conclude that a prolonged Ca repletion following the induction of calcipenic rickets in rats although shows the recovery of biochemical measures of bone metabolism and bone mass, however, the bone quality remains compromised. This suggests that a "memory" of calcipenia occurring at the early growth stage persists in the skeleton of adult rats despite a prolonged Ca replenishment **(*Bone, PMID: 32730922*).**

2.2.10 Skeletal restoration by phosphodiesterase 5 inhibitors in osteopenic mice: Evidence of osteoanabolic and osteoangiogenic effects of the drugs

Phosphodiesterases (PDEs) hydrolyze cyclic nucleotides and thereby regulate diverse cellular functions. The reports on the skeletal effects of PDE inhibitors are conflicting. Here, we screened 17 clinically used non-xanthine PDE inhibitors (selective and non-selective) using mouse calvarial osteoblasts (MCO) where the readout was osteoblast differentiation. From this screen, we identified sildenafil and vardenafil (both PDE5 inhibitors) having the least osteogenic EC_{50}. Both drugs significantly increased vascular endothelial growth factor (VEGF) and VEGF receptor 2 (VEGFR2) expressions in MCO and the nitric oxide synthase inhibitor L-NAME completely blocked VEGF expression induced by these drugs. Sunitinib, a tyrosine receptor kinase inhibitor that also blocks VEGFR2 blocked sildenafil-/vardenafil-induced osteoblast differentiation. At half of their human equivalent doses, i.e. 6.0 mg/kg sildenafil and 2.5 mg/kg vardenafil, the maximum bone marrow level of sildenafil was 32% and vardenafil was 21% of their blood levels. At these doses, both drugs enhanced bone regeneration at the femur osteotomy site and completely restored bone mass, microarchitecture, and strength in OVX mice. Furthermore, both drugs increased surface referent bone formation and serum bone formation marker (P1NP) without affecting the resorption marker (CTX-1). Both drugs increased the expression of VEGF and VEGFR2 in bones and osteoblasts and increased skeletal vascularity. Sunitinib completely blocked the bone restorative and vascular effects of sildenafil and vardenafil in OVX mice. Taken together, our study suggested that sildenafil and vardenafil at half of their adult human doses completely reversed osteopenia in OVX mice by an osteogenic mechanism that was associated with enhanced skeletal vascularity ***(Bone, PMID: 32126313)***.



3

CANCER BIOLOGY

Area Coordinators: Dr. Dipak Datta and Dr. Dipankar Koley

Vision and Goal:

Discover, Develop and Deliver Affordable Cancer Care for patients

Core Competencies and Activities:

- Development of high value generic anti cancer targeted therapies at affordable cost
- Discovery of New Chemical Entity (NCE) against clinically validated anti cancer targets
- Development of Phytopharmaceuticals and traditional medicine
- In depth understanding of disease biology to discover new potential targets
- New knowledge creation with respect to Cancer Metastasis, Therapy Resistance and Relapse

Research Group

(L to R): Dr. Ravindra Kumar, Dr. Pintu Kumar Mandal, Dr. Dibyendu Banerjee Dr. Gautam Panda, Dr. Dipankar Koley (Area Coordinator), Dr. D P Mishra, Dr. Atul Kumar, Prof. Tapas K. Kundu (Director, CSIR-CDRI), Dr. Dipak Datta (Area Coordinator), Dr. Ajay Kumar Srivastava, Dr. Arun Kumar Trivedi, Dr. Kishor Mohanan, Dr. T. Narender, Dr. Jayanta Sarkar, Dr. Nayan Ghosh & Dr. Namrata Rastogi

3.1 Promising anti-cancer leads

S-016-1348, a synthetic novel small molecule lead for colon-cancer

- Designed and synthesized as patentable Smac mimetic
- targets Inhibitor of apopotosis proteins (IAP)
- unique dual protein binding efficiency in the low nanomolar range
- *In vivo* activity against against drug resistant cancer cells.
- More efficacious than the current Phase-II Smac mimetic clinical trial

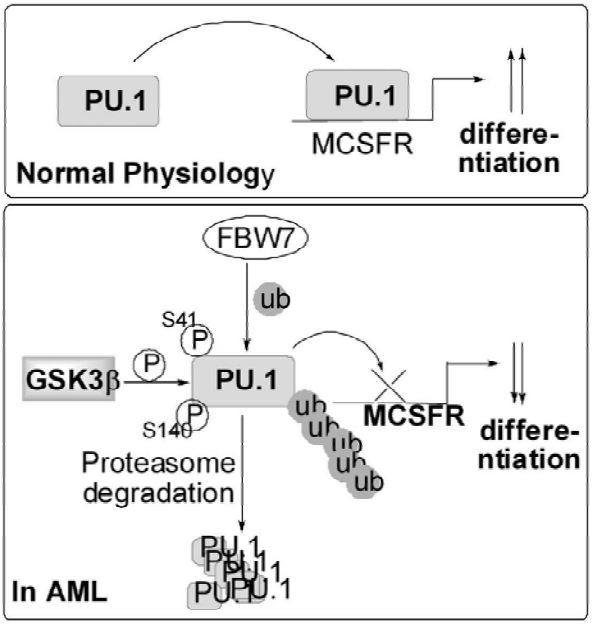
3.2 Advancing Knowledge Frontiers

3.2.1 Salinomycin inhibits epigenetic modulator EZH2 to enhance death receptors in colon cancer stem cells.

Drug resistance is one of the trademark features of Cancer Stem Cells (CSCs). Although it is known that the paucity of functional death receptors (DR4/5) on the cell surface of tumor cells plays a major role in developing drug resistance, their involvement in the context of in CSCs is poorly understood. By harnessing CSC specific cytotoxic function of salinomycin, it was discovered that EZH2, an epigenetic modulator takse part important role in regulating the expression of DRs in colon CSCs. Unbiased proteome profiler array approach followed by ChIP analysis of salinomycin treated cells indicated that the expression of DRs, especially DR4 is epigenetically repressed in colon CSCs. Concurrently, EZH2 knockdown demonstrated increased expression of DR4/DR5, significant reduction of CSC phenotypes such as spheroid formation *in-vitro* and tumorigenic potential *in-vivo* in colon cancer. TCGA data analysis of human colon cancer clinical samples shows strong inverse correlation between EZH2 and DR4. Taken together, this study provides an insight about epigenetic regulation of DR4 in colon CSCs and advocates that drug-resistant colon cancer can be therapeutically targeted by combining TRAIL and small molecule EZH2 inhibitors. (***Epigenetics. 2020; 1-18. doi: 10.1080/15592294.2020.1789270***).

3.2.2 FBW7 inhibits myeloid differentiation in acute myeloid leukemia via GSK3-dependent ubiquitination of PU.1

GSK3β, an ubiquitously expressed serine/threonine kinase is reported to be overexpressed and hyperactivated in cancers including Acute Myeloid Leukemia where it promotes self-renewal, growth and survival of AML cells. Therefore, GSK3β inhibition results in AML cell growth inhibition and myeloid differentiation. Master transcription factor PU.1 of monocyte-macrophage differentiation pathway has been identified as potential GSK3β target. It is also demonstrated that GSK3β phosphorylates PU.1 at Ser41 and Ser140 leading to its recognition and subsequent ubiquitin-mediated degradation by E3 ubiquitin ligase FBW7. This GSK3-dependent degradation of PU.1 by FBW7 inhibited monocyte-macrophage differentiation. In addition, it was demonstrated that a phospho-deficient PU.1 mutant (PU.1-S41, S140A) neither binds to FBW7 nor is degraded by it. Consequently, PU.1-S41, S140A retained its transactivation, DNA binding ability and promoted monocyte-macrophage differentiation of U937 cells even without PMA treatment. Further, it was found that FBW7 overexpression inhibited both PMA as well as MCSF-induced macrophage differentiation of myeloid cell lines and PBMCs from healthy volunteers respectively. Contrarily, FBW7 depletion promoted differentiation of these cells even without any inducer suggesting for a robust role of GSK3β-FBW7 axis in negatively regulating myeloid differentiation. The similar result was also observed in PBMCs isolated from leukemia patients where FBW7 over expression markedly inhibited endogenous PU.1 protein levels. In addition, PBMCs also showed enhanced differentiation when treated with M-CSF and GSK3 inhibitor (SB216763) together compared to M-CSF treatment alone. Taken together, these data demonstrate a plausible mechanism behind PU.1 restoration and induction of myeloid differentiation upon GSK3β inhibition and further substantiates potential of GSK3β as a therapeutic target in AML. (***Mol Cancer Res. 2020 (PMID: 33188146***)



3.2.3 Microtubule disrupting agent-mediated inhibition of cancer cell growth is associated with blockade of autophagic flux and simultaneous induction of apoptosis.

Given that the autophagy inhibition is a feasible way to enhance sensitivity of cancer cells towards chemotherapeutic agents, identifying potent autophagy inhibitor has obvious clinical relevance. In this endeavour the ability of TN-16, a microtubule disrupting agent, on modulation of autophagic flux and its significance in promoting *in vitro* and *in vivo* cancer cell death was investigated. The effect of TN-16 on cancer cell proliferation, cell division, autophagic process and apoptotic signalling was assessed by various biochemical (Western blot and SRB assay), morphological (TEM, SEM, confocal microscopy) and flowcytometric assays. *In vivo* anti-tumour efficacy of TN-16 was investigated in syngeneic mouse model of breast cancer. TN-16 inhibited cancer cell proliferation by impairing late-stage autophagy and induction of apoptosis. Inhibition of autophagic flux was demonstrated by accumulation of autophagy-specific substrate p62 and lack of additional LC3-II turnover in the presence of lysosomotropic agent. The effect was validated by confocal micrographs showing diminished autophagosome-lysosome fusion. Further studies revealed that TN-16-mediated inhibition of autophagic flux promotes apoptotic cell death. Consistent with *in vitro* data, results of our *in vivo* study revealed that TN-16-mediated tumour growth suppression is associated with blockade of autophagic flux and enhanced apoptosis. Our data signify that TN-16 is a potent autophagy flux inhibitor and might be suitable for (pre-) clinical use as standard inhibitor of autophagy with anti-cancer activity. ***(Cell Prolif. 2020 53(4): e12749.***

3.2.4 Androgen deprivation upregulates SPINK1 expression and potentiates cellular plasticity in prostate cancer

Emergence of an aggressive androgen receptor (AR)-independent neuroendocrine prostate cancer (NEPC) after androgen-deprivation therapy (ADT) is well-known. Nevertheless, the majority of advanced-stage prostate cancer patients, including those with SPINK1-positive subtype, are treated with AR-antagonists. Here, it is showed that AR and its corepressor, REST, function as transcriptional-repressors of SPINK1, and AR-antagonists alleviate this repression leading to SPINK1 upregulation. Increased SOX2 expression during NE-transdifferentiation transactivates SPINK1, a critical-player for maintenance of NE-phenotype. SPINK1 elicits epithelial-mesenchymal-transition, stemness and cellular-plasticity. Conversely, pharmacological Casein Kinase-1 inhibition stabilizes REST, which in cooperation with AR causes SPINK1 transcriptional-repression and impedes SPINK1-mediated oncogenesis. Elevated levels of SPINK1 and NEPC markers are observed in the tumors of AR-antagonists treated mice, and in a subset of NEPC patients, implicating a plausible role of SPINK1 in treatment-related NEPC. Collectively, our findings provide an explanation for the paradoxical clinical-outcomes after ADT, possibly due to SPINK1 upregulation, and offers a strategy for adjuvant therapies. ***(Nat Commun. 2020;11(1):384).***

3.2.5 N-acetyl-cysteine in combination with celecoxib inhibits Deoxynivalenol induced skin tumor initiation via induction of autophagic pathways in swiss mice

Deoxynivalenol is a trichothecene mycotoxin which naturally contaminates small grain, cereals intended for human and animal consumption. Investigations for dermal toxicity of DON has been needed and highlighted by WHO. Previous studies on dermal toxicity suggest that DON has DNA damaging potential leading to skin tumor initiation in mice skin. However, considering its toxicological manifestations arising after dermal exposure, strategies for its prevention/protection are barely available in literatute. Collectively, our study demonstrated that N-acetylcysteine (NAC), precursor of glutathione, significantly alters the genotoxic potential of DON. Further NAC in combination with Celecoxib (CXB) inhibits tumor growth by altering antioxidant status and increasing autophagy in DON initiated *Swiss* mice. Despite the broad spectrum use of CXB, its use is limited by the concerns about its adverse effects on the cardiovascular system. Serum parameters and histology analysis revealed that CXB (2 mg) when applied topically for 24 weeks did not impart any cardiovascular toxicity which could be because skin permeation potential of CXB was quite low when analyzed through HPLC analysis.

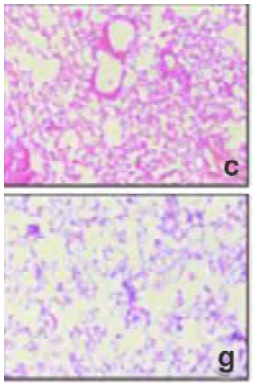
Although the anticancer effects of CXB and NAC have been studied, however, the combination of NAC and CXB has yet not been explored for any cancer treatment. Therefore, our observations provide additional insights into the therapeutic effects of combinatorial treatment of CXB and NAC against skin tumor prevention. This approach might form a novel alternative strategy for skin cancer treatment as well as skin associated toxicities caused by mycotoxins such as DON. This combinatorial approach can overcome the limitations associated with the use of CXB for long term as topical application of the same seems to be safe in comparison to the oral mode of administration. (**Free Radical Biology and Medicine, 2020, 156, 70-82)**

3.2.6 Cytotoxicity, apoptosis and ameliorative potential of *Lawsonia inermis* extract in human lung, colon and liver cancer cell line

Cancer has emerged as a major public health issue in developed as well as in developing countries. Plant-derived molecules are widely being used in the treatment of cancer due to their minimum side effects. *Lawsonia inermis* (Henna) is one of the medicinal plants containing many therapeutic properties. In the present study, bioactive components of *L. inermis* extract were analyzed by LCMS/MS method and validated. Lawsone (3.5%) is primarily responsible for cytotoxic and anti-cancerous activities. These properties were studied on human lung carcinoma (A549), colorectal cancer (DLD1) and Hepatocellular carcinoma (HepG2) cancer cell lines. The activities were assessed by MTT assay, evaluation of apoptosis by measuring the production of Reactive Oxygen Species (ROS) and mitochondrial membrane potential of the cancer cell lines. Moreover, apoptosis in the respective cancer cell lines was also determined by chromatin condensation and DNA fragmentation using Hoechst 33528 and propidium iodide (PI) staining. The preliminary *in vitro* result of MTT showed that the henna extract induces cytotoxic properties against A549, DLD1, HepG2 with IC_{50}values 490, 480 and 610 µg/ml respectively (more than 40% growth inhibition). In addition, the extract induced a concentration-dependent rise in ROS production which was 84, 102, and 110% in HepG2, DLD1 AND A549 respectively at 300 µg/ml, whereas at 400 µg/ml concentration it was 86, 102, and 106% in respective cell lines while decreasing mitochondrial membrane potential was more than 20% in the investigated cell lines. The extract also provoked changes associated with apoptosis and the data indicate that the ROS production leads to a diminution in mitochondrial membrane potential and this correlated with the extract cytotoxicity **(Cancer Invest. 2020; PMID: 32845783)**

3.3 Facility development

CDRI Cancer biology area repository has more than 30 cancer cell lines of mouse and human origin covering most of the solid tumors and blood cancers. Like NCI-60, initial hits can be tested in CDRI-30 cancer cell line panel. Recently, the Nude mice facility has also been established as an integral part of cancer drug discovery program. Utilizing this facility, different xenograft and allograft tumor models of breast and colon cancers have been developed. Therefore, with live animal imaging facility and xenograft model, the cancer biology group is looking forward to achieve its goal and vision.



4

CARDIOVASCULAR BIOLOGY

Area Coordinator: Dr. Manoj Barthwal and Dr. K.V. Sashidhara

Vision and Goal:

- Development of novel therapeutic agents for Cardiovascular disorders, through modern drug design, scientific validation of traditional remedies.
- Basic research to delineate the molecular mechanisms of cardiovascular, cardiometabolic disorders as well as associated comorbidities so as to identify suitable targets for drug discovery, as well as to analyze the possible mechanism(s) of action of the candidate drugs.
- Creation of appropriate platform for interdisciplinary collaborative research.

Core Competencies and Activities:

- Development of experimental models of hypertension, dyslipidemia, thrombosis, myocardial ischemia and atherothrombosis to identify anti-hypertensive, hypolipidemic, anti-thrombotic, anti-ischemic drugs, respectively and identification of the mechanism of action of test substances. As well as development of experimental models to study the cardiometabolic disorders and associated comorbidities e.g. insulin resistance, chronic kidney disease, fatty liver, inflammatory bowel disease, etc. and to identify novel therapies to combat them.
- Design, synthesis and bio-evaluation of novel molecules/isolates from natural sources for new lead generation for atherosclerosis, dyslipidemia, diabetes, obesity, hypertension myocardial infarction, chronic kidney disease and inflammatory bowel disease. Scientific validation of traditional remedies for cardiovascular, cardiometabolic disorders and associated comorbidities.
- Molecular mechanism of action of promising agents.
- New knowledge generation in the area cardiovascular biology

Research Group

Front row (L to R): Dr. Kashif Hanif, Dr. Ajay Kumar Srivastava, Dr. Anil Gaikwad, Dr. K.V. Sashidhara (Area Coordinator), Dr. Manoj K. Barthwal (Area Coordinator) & Dr. Kumaravelu Jagavelu.

Back Row (L to R): Dr. Shashi Kumar Gupta, Dr. Shrikant R. Mulay, Dr. A.K. Tamrakar, Dr. Sadan Das, Dr. Amit Lahiri & Dr. Sachin Kumar

4.1 Summary of drug discovery and development activities

During the reporting period several compounds were synthesized and evaluated for cardiovascular activities in cell culture and in various animal models of cardiovascular diseases. A total of 157, 174, 20, 68, and 22 compounds were submitted for screening of an anti-adipogenic, anti-inflammatory, anti-hyperlipidemic, anti-angiogenic, and anti-NAFLD activity, respectively. Out of this, 6 compounds were found to have anti-adipogenic activity while none was found to have anti-inflammatory, anti-hyperlipidemic, anti-angiogenic, and anti-NAFLD activity in primary screening. The secondary screening of these compounds is ongoing. Next, we will do detail study of active compounds for their possible role to combat obesity and associated disorders. Following secondary screen, if we find any lead, then we will perform analysis of lead compound in *in-vivo* model of high-fat diet-induced dyslipidemia and obesity.

4.2 Advancing Knowledge Frontiers

4.2.1 Non-coding RNAs are novel regulators of valvular calcification

There is currently a growing global burden of valvular heart diseases due to aging populations and changing lifestyles. Valvular heart diseases mainly include the malfunctioning of aortic and mitral valves and are characterized by extensive tissue remodeling, which includes calcification, endothelial dysfunction, and endothelial mesenchymal transition. These valvular remodeling processes are known to be regulated by protein-coding genes as well as non-coding genes. We recently published a review summarizing the role of non-coding RNA in valvular calcification. Here, we have summarized studies highlighting the non-coding RNA mediated regulation of valvular tissue remodeling and their potential therapeutic benefits. Additionally, studies investigating the diagnostic capability of circulating non-coding RNA molecules in valvular diseases are also summarized. Overall, of the various candidates, several studies have highlighted miR-214 and miR-204 as central regulators of valvular calcification ***(Journal of Molecular and Cellular Cardiology, 2020, 142, 14-23).***

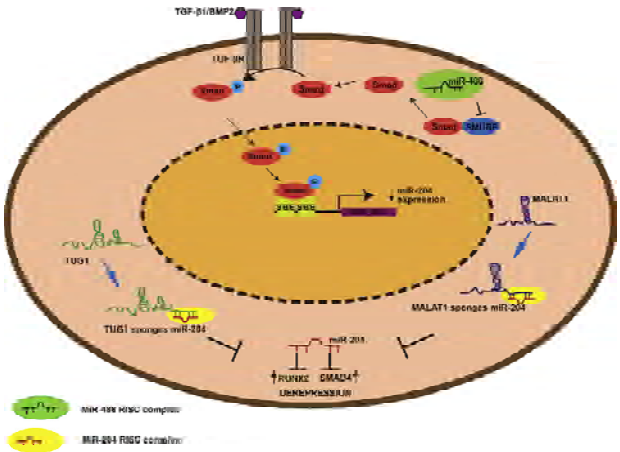


Figure 1. MiR-204 has an anti-osteogenic function in VICs.

4.2.2 Role of gut bacteria in Inflammatory Bowel Disease

Inflammatory Bowel Disease (IBD) results from an inappropriate inflammatory response to intestinal microbes in a genetically susceptible host. GWAS studies have implicated the importance of host-microbe interaction in IBD pathogenesis. We and others have further shown that in the susceptible host, an altered gut flora leads to unbalanced cytokine production and tight junction dysfunction resulting in chronic inflammation and pain in the intestine. Macrophages, dendritic cell, T and B cells infiltrated in the lamina propria (LP) produce cytokine during this inflammation and decide the pathology of the disease and more studies are required to know the cytokine regulation during IBD. Furthermore, studies using germ free mice have definitely proved that microbiota have direct role in deciding and maintaining the host immune function. When germ free (GF) mice are compared with the specific pathogen free (SPF) animals it has been found that the GF animals have defective gut associated lymphoid tissues, smaller peyers patch and mesenteric lymph nodes. In the IBD patients also, the diversity of mucosa associated gut bacteria, specifically the firmicutes and bacteroidetes are reduced. On the other hand, the actinobacteria, and proteobacteria species are increased in both CD and UC patients when compared to the healthy controls clearly indicating microbiota plays a crucial role in dictating IBD progression. There is currently no remedy for IBD and most importantly, IBD is the main reason for the development of colorectal cancer in India. Cytokine blockers like infliximab, adalimumab are used to treat IBD, however, in India, due to latent TB infection, they raise

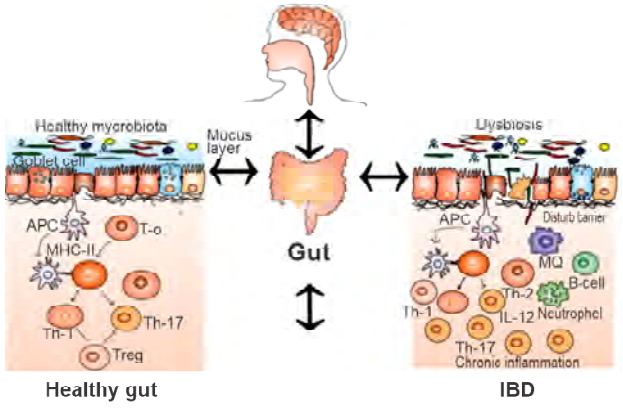


Figure 2. Role of gut bacteria in Inflammatory Bowel Disease

significant secondary infection risk in the patients. Both antibacterial and antiviral immune signalling are determined by the bacterial population in the gut and we would like to address how gut microbes regulate immune activation during IBD.

4.2.3 The gut-liver-kidney axis: Novel regulator of fatty liver associated chronic kidney disease

Increased interest in understanding the liver-kidney axis in health and disease during the last decade unveiled multiple recent evidences that suggested a strong association of fatty liver diseases with chronic kidney disease (CKD). Low-grade systemic inflammation is thought to be the major contributing factor to the pathogenesis of CKD associated with fatty liver. However, other contributing factors largely remained unclear, for example, gut microbiota and intestinal barrier integrity. Homeostasis of the gut microbiome is very crucial for the health of an individual. Imbalance in the gut microbiota leads to various diseases like fatty liver disease and CKD. On the contrary, disease conditions can also distinctly change gut microbiota. In this review, we propose the pathogenic role of the gut-liver-kidney axis in the development and progression of CKD associated with chronic fatty liver diseases, either non-alcoholic fatty liver disease or non-alcoholic steatohepatitis in experimental models and humans. Further, we discuss the therapeutic potential and highlight the future research directions for therapeutic targeting of the gut-liver-kidney axis. ***(Pharmacol Res. 2020, 152:104617.)***

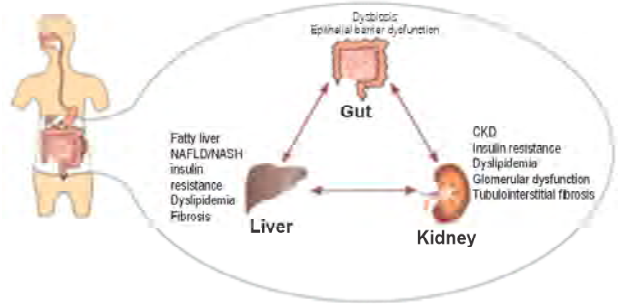


Figure 3. The gut-liver-kidney axis

4.2.4 Molecular regulation of neutrophilic inflammation in metabolic disorders

Meta-inflammation has been observed to play a central role in metabolic disorders like diabetes and obesity. Role of T cells and macrophages have been investigated in type 2 diabetes, insulin resistance, destruction of pancreatic β-cells. But understanding of neutrophils, the most abundant leukocytes and early responders remain least explored. In patients, neutrophil count increases during insulin resistant and diabetic conditions, but neutrophil functions dampen significantly. Studies have also found an early infiltration of neutrophils to adipose tissue during the development of diet-induced obesity. Our group is focusing to reveal precise role of neutrophil in diabetes and other metabolic syndrome development. Using animal models of T2DM, insulin resistance and lung injury, our data so far suggest important role of neutrophil infiltration in tissue damage and metabolic insults. Redox enzymes- NADPH Oxidase and iNOS deficient mice exhibited insulin resistance and neutrophils in these mice exhibit defective anti-microbial functions. Further, Rho signalling seems to regulate neutrophil recruitment to site of insults via selectin shedding and Akt activation and therapeutic applicability need further investigations. Additionally, classical view of neutrophils as homogenous population has also been challenged recently. Results from our lab identified a distinct population of neutrophils in different metabolic organs. We are further investigating therapeutic targets through molecular mechanism approaches to target neutrophil plasticity. For that, we are utilizing immuno-modulatory approach from novel small molecules, natural products or herb extract and also uncovering immuno-modulatory effects of molecules currently in use. In particular, we are investigating NETs modulation using pre-approved drugs and found out some of very potent drug with anti-NETosis activities. The other major area of investigation is HSC biology, that we probing in metabolic disorder and NADPH Oxidase and iNOS deficient mice that are providing key knowledge for their role/impact on stem cells and progenitors.

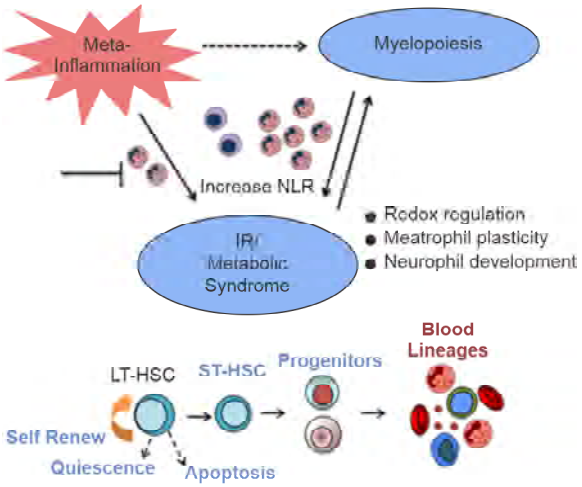


Figure 4. Molecular regulation of neutrophilic inflammation in metabolic disorders

4.2.5 Autophagy inhibition by Chloroquine prevents increase in blood pressure and preserves endothelial functions

In this work, the effect of lysosomal inhibition of autophagy by chloroquine (CHQ) on hypertension-

associated changes in the endothelial functions was studied. Angiotensin II (Ang II)-treated human endothelial cell line EA. hy926 and renovascular hypertensive rats were subjected to CHQ treatment (*in vitro*: 0.5, 1, and 2.5 μM; *in vivo:* 50 mg/kg/day for three weeks). Changes in the protein expressions of LC3b II (autophagosome formation marker) and p62 (autophagy flux marker) were assessed using immunoblotting. Cell migration assay, tubule formation assay (*in vitro*), and organ bath studies (*in vivo*) were performed to evaluate the endothelial functions. Hemodynamic parameters were measured as well. A higher expression of LC3b II and a reduced expression of p62 observed in the Ang II-treated endothelial cells, as well as in the aorta of the hypertensive rats, indicating enhanced autophagy. Treatment with CHQ resulted in reduced autophagy flux (*in vitro* as well *as in vivo*) and suppressed Ang II-induced endothelial cell migration and angiogenesis (*in vitro*). The treatment with CHQ prevented increase in blood pressure in hypertensive rats and preserved acetylcholine induced relaxation in phenylephrine-contracted aorta from the hypertensive rats. In addition, chloroquine attenuated Ang II-induced contractions in the aorta of normotensive as well as hypertensive rats. These observations indicated that CHQ lowers the blood pressure and preserves the vascular endothelial function during hypertension. ***(Tropical Journal of Pharmaceutical Research 2020; 19 (4): 789-796).***

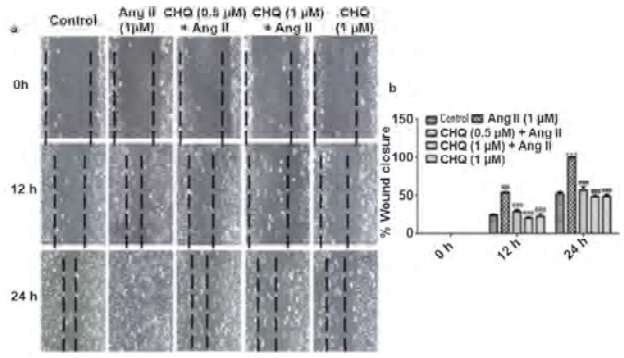


Figure 5. Lysosomal inhibition of autophagy by chloroquine inhibits the Angiotensin II-induced endothelial cell migration.

4.2.6 Discovery of PKM2 as a link between aerobic glycolysis, metabolic inflammation and foam cell formation in the macrophages

This unique study was designed to study the role of PKM2 and aerobic glycolysis in macrophage foam cell formation and inflammation. PKM2 regulates lipid uptake and efflux. DASA-58, a PKM2 activator, downregulated LXR-α, ABCA1, and ABCG1, and augmented FASN and CD36 protein expression. Peritoneal macrophages showed similar results. Ox-LDL induced PKM2- SREBP-1 interaction and FASN expression in a PKM2-dependent manner. Therefore, this study suggests a role for PKM2 in Ox-LDL-induced aerobic glycolysis, inflammation, and macrophage foam cell formation ***(J Lipid Res. 2020 Mar; 61(3): 351-364)***.

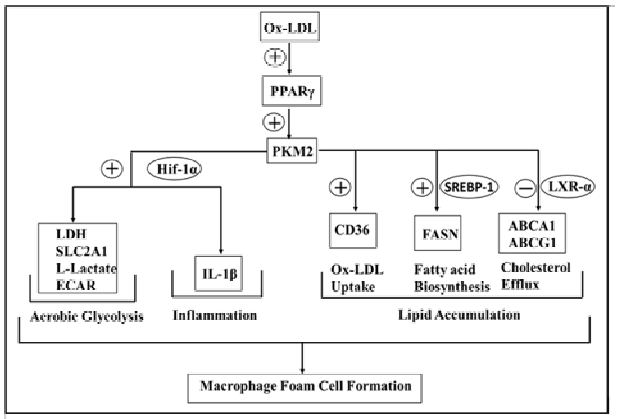


Figure 6. Role of PKM2 in Ox-LDL induced foam cell formation

4.2.7 Lin28B regulates Angiotensin II-mediated Let-7c/miR-99a microRNA formation consequently affecting macrophage polarization and allergic inflammation

Angiotensin-II (Ang-II) receptor plays a role in allergic airway inflammation; however, the underlying mechanism and role of macrophages need better understanding. In the present study, angiotensin-II infusion (1 μg/kg/min) in ovalbumin-induced airway inflammation mice model significantly decreased immune cell infiltration, goblet cell hyperplasia, and eosinophil numbers in lungs. Ang-II infusion increased M1 and decreased M2 macrophage population in bronchoalveolar lavage fluid and respective macrophage markers in lung macrophages. Similarly, *in vitro* Ang-II treatment in murine bone marrow-derived macrophages (BMDMs) induced M1 and reduced M2 macrophage phenotype with enhanced bactericidal activity. Mechanistically, Ang-II inhibits Let-7c and miR-99a expression in BMDMs and in vivo as well. Lentiviral overexpression of Let-7c and miR-99a miRNAs in BMDMs abrogated Ang-II-induced M1 phenotype activation and promoted M2 phenotype, which is governed by targeting TNFα by miR-99a. In lung macrophages, ovalbumin-induced TNFα inhibition was rescued after Ang-II treatment. In BMDMs, knockdown of TNFα abrogated Ang-II-induced M2 to M1 macrophage phenotype switch and associated bactericidal activity. Ang-II affects mature miRNA formation by enhancing Lin28B levels in macrophages *in vivo* and *in vitro*. Furthermore, Lin28B knockdown prevented Ang-II-mediated inhibition of mature Let-7c/miR-99a miRNA formation, M2 to M1 macrophage phenotype switch, and increased

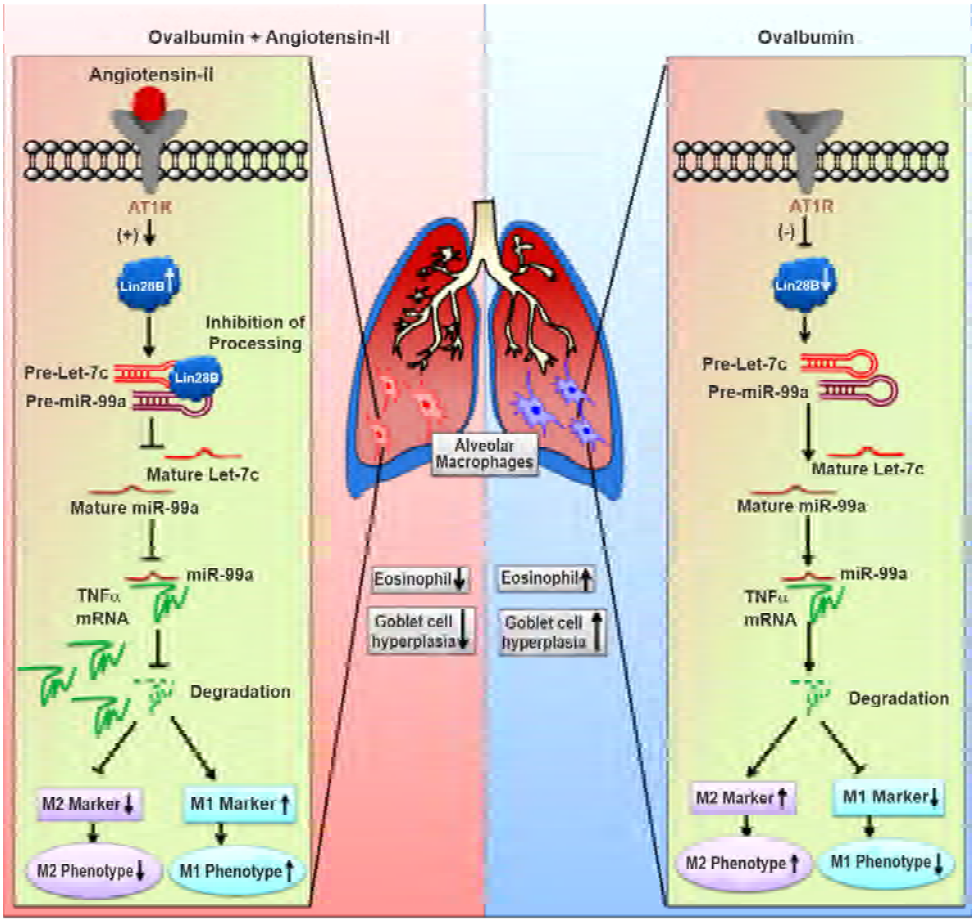


Figure 7.Role of miR-99a and Let-7c in airway inflammation

bactericidal activity. Therefore, present study suggests a role of Lin28B in Ang-II-induced Let-7c/miR-99a miRNA formation that consequently affects TNFα production, M1 phenotype activation, and allergic airway inflammation. Graphical Abstract Ovalbumin inhibits LIN28B expression thereby fails to inhibit premature to mature Let-7c/miR-99a miRNA formation. Mature miR-99a miRNA that inhibits TNFα consequently promotes M2 polarization and allergic airway inflammation. While Ang-II induces Lin28B, which inhibits Let-7c/miR-99a miRNA processing and mature miRNA formation, this results in increased TNFα levels that lead to M1 polarization and allergic airway inflammation inhibition. ***(Inflammation 2020; 43(5): 1846-1861).***

4.2.8 Standardized *Xylocarpus moluccensis* fruit fraction mitigates collagen-induced arthritis in mice by regulating immune response

In this study effect of *Xylocarpus moluccensis* fruit fraction (F018) on the pathogenesis of collagen-induced arthritis in mice was evaluated. F018 at 3 and 10 mg/kg significantly reduced paw thickness, clinical score, mononuclear cell infiltration and collagen layer depletion in the knee section of collagen-induced arthritis (CIA) mice when compared with collagen-induced arthritis mice alone. Furthermore, F018 treatment in collagen-induced arthritis mice significantly recovered bone volume and trabecular number and decreased the trabecular space by modulating RANKL and OPG mRNA expression in the synovial tissue. F018 treatment in collagen-induced arthritis mice significantly attenuated spleen index, lymphocyte proliferation and paw myeloperoxidase (MPO) activity, pro-inflammatory cytokine TNFα, IL1β, and IL6 mRNA expression and enhanced IL10 mRNA expression in paw tissue. Furthermore, F018 treatment in collagen-induced arthritis mice significantly reduced splenic dendritic cell maturation and Th17 cells. In culture, F018 significantly decreased collagen-induced arthritis-FLS proliferation and promoted apoptosis. Therefore, F018 may serve as a potential curative agent for arthritis. ***(J Pharm Pharmacol 2020; 72(4): 619-632).***

4.2.9 Cigarette smoke extract triggers neoplastic change in lungs and impairs locomotor activity through wnt3a-β-catenin signalling in aged COPD rodent model

Chronic cigarette smoking primes immense decline in lung functions and retardation of motor functions with increase in age. This raise the question of whether

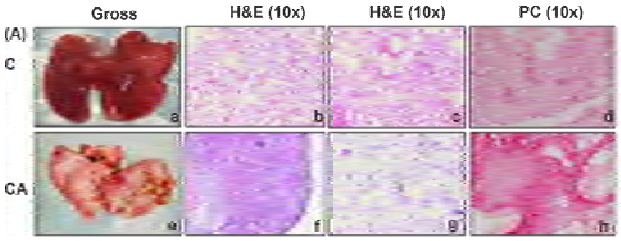


Figure 8. Effect of sub chronic cigarette smoke exposure on lung morphology and histology

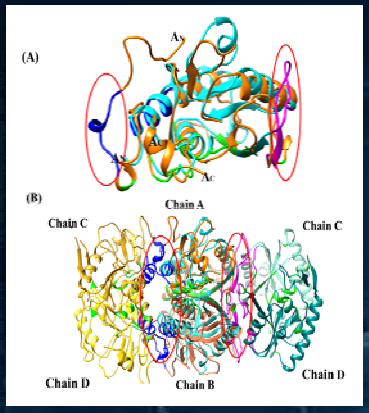
age status overwhelms the susceptibility to smoking induced lung inflammatory diseases and neuro-motor dysfunctions. To study the hypothesis 11–12 month old aged wistar rats (n¼6) were administered cigarette smoke extract (CSE) through intraperitoneal route (0.5 ml/rat) twice a week for 2 months. Sub-chronic CSE exposure worsened the lung functions including decreased tidal volume ($p<0.05$), peak inspiratory flow ($p<0.05$) and enhanced pause ($p<0.05$). Grossly, solid neoplastic lesions were visible on the supra-lateral surface of the lungs of the CSE treated animals. Histopathological examination revealed immune cell infiltration, dominated with macrophages and alveolar type II cells stained positive for PCNA. Increased expression of BAX, PCNA, Wnt-3a, p-b-catenin ($p<0.05$) was seen in the lungs of CSE treated aged animals. Elevated expression of inflammatory markers including NF-kB, TNF-α, TNF-R1, p-AKT was found in CSE treated lung tissues. Moreover, our result showed increased MCP-1, VEGF and IL-6 levels in BALF and plasma ($p<0.01$) which might lead to neo-vascularization and excessive cell proliferation in lungs of CSE induced rats. Sub-chronic cigarette smoke exposure retarded the motor activity with suppression of D1 and D2 receptor expression in brain tissues. Brain tissue revealed the abundance of hyperchromatic and pyknotic nuclei suggesting neuronal degeneration. In conclusion, chronic cigarette smoking in old age creates susceptibility to fast onset of lung inflammatory diseases and neuro-motor retardation than their non-smoker counterparts.***(Exp Lung Res. 2020; 46(8): 283-296)***

4.2.10 Role of brown adipose tissue in modulating adipose tissue inflammation and insulin resistance in high-fat diet fed mice

Hyperinsulinemia precedes obesity and then it results in chronic activation of innate immune system and followed by diabetes. Brown adipose tissue is also major player in obesity development. Its role in obesity is not clearly studied in tissue resident immuno-metabolic alteration. Towards this, we performed both BAT transplantation as well as extirpation experiments in the mouse model of high-fat diet (HFD)-induced obesity. Following experimentations, we performed immune cell profiling in the stromal vascular fraction (SVF) isolated from epididymal white adipose tissue (eWAT). Upon transplantation BAT reversed HFD-induced increase in body weight gain and insulin resistance without altering diet intake. BAT transplantation attenuated the obesity-associated adipose tissue inflammation in terms of decreased pro-inflammatory M1-macrophages, cytotoxic CD8a T-cells and restored anti-inflammatory regulatory T-cells (Tregs) in the eWAT. BAT transplantation also improved endogenous BAT activity by elevating protein expression of browning markers (UCP-1, PRDM16 and PGC1α). BAT transplantation promoted the eWAT expression of various genes involved in fatty acid oxidation (such as Elvol3 and Tfam). In contrast, extirpation of the interscapular BAT exacerbated HFD-induced obesity, insulin resistance and adipose tissue inflammation (by increasing M1 macrophages, CD8a T-cell and decreasing Tregs in eWAT). Taken together, our results suggested an important role of BAT in combating obesity-associated metabolic complications. These results open a novel therapeutic option to target obesity and related metabolic disorders like type 2 diabetes ***(Eur J Pharmacology. 2019; 854:354-364).***

4.2.11 NOD1 activation induces oxidative stress via NOX1/4 in adipocytes

Activation of innate immune components promotes cell autonomous inflammation in adipocytes. Oxidative stress links pattern recognition receptor-mediated detection of inflammatory ligands and the immune response. Reactive oxygen species (ROS) may mediate the effect of nucleotide-binding oligomerization domain protein-1 (NOD1) activation on inflammation in adipocytes. We defined the potential role of NADPH oxidase (NOX)-derived ROS in NOD1-mediated inflammatory response in adipocytes. NOD1 activation potently induced ROS generation in 3T3-L1 adipocytes. Of the NOX family members, expression of NOX1 and NOX4 was increased upon NOD1 activation, in a PKCδ-dependent manner. siRNA-mediated down-regulation of NOX1 or NOX4 inhibited NOD1-mediated ROS production and increased the expression of antioxidant defense enzyme catalase and superoxide dismutase (SOD). siRNA-mediated lowering of NOX1 or NOX4 also suppressed NOD1-mediated activation of JNK1/2 and NF-kB, and consequent activation of inflammatory response in 3T3-L1 adipocytes. In summary, our findings demonstrate that NOD1 activation provokes oxidative stress in adipocytes via NOX1/4 and that oxidative stress, at least in part, contributes to induction of inflammatory response. Defining the source of ROS after immune response engagement may lead to new therapeutic strategies for adipose tissue inflammation ***(Free Radical Biology and Medicine. 2021; 162: 118-128).***



MALARIA AND OTHER PARASITIC DISEASES

Area coordinators: Dr. Saman Habib and Dr. Sanjay Batra

5

Vision and Goal:

- Development of new drugs/drug combinations as therapeutic interventions for malaria, leishmaniasis and filariasis;
- Identification of unique targets and pathways for future interventions;
- Investigations on parasite biology and host-parasite interactions.

Core Competencies and Activities:

- Design and synthesis of novel molecules as potential parasiticidal agents;
- Bioevaluation of synthetic molecules and natural products for antimalarial, antileishmanial and antifilarial activities against in vitro and in vivo models;
- Preclinical development of combination therapy regimens with novel compounds/ known drugs;
- Mechanism of drug action / drug resistance;
- Characterization of drug targets using molecular approaches;
- Development of immunoprophylactic modalities;
- Development of improved screening models/drug delivery systems.

5.1 Malaria

5.2 Leishmaniasis

5.3 Lymphatic Filariasis

5.4 Medicinal Chemistry

5.5 Anti-parasitic screening for drug discovery

Front row (L to R): Dr. Niti Kumar, Dr. Mohammed Imran Siddiqi, Dr. Neena Goyal, Dr. Sanjay Batra (Area Coordinator) & Dr. Gautam Panda

Middle row (L to R): Dr. Damodara Reddy N., Dr. Kalyan Mitra, Dr. Pintu Kumar Mandal, Dr. Namrata Rastogi, Dr. Saman Habib (Area Coordinator), Dr. Ramesh Chintakunta, Dr. Prem Prakash Yadav, Dr. Kishor Mohanan & Dr. Malleswara Rao Kuram

Back Row (L to R): Dr. Satish Mishra, Dr. Susanta Kar & Dr. Mrigank Srivastava

5.1 Malaria

5.1.1 *Pf*KsgA1 functions as a transcription initiation factor in parasite mitochondria

The 6 kb repeat mitochondrial genome (mtDNA) of the malaria parasite transcribes its genes polycistonically but its promoter element(s) are not identified. An unusually large *P. falciparum* candidate mitochondrial phage-like RNA polymerase (*Pf*mtRNAP) with an extended N-ter region is encoded by the parasite nuclear genome. It has been established that *Pf*mtRNAP was targeted exclusively to the mitochondrion and interacted with mtDNA. Phylogenetic analysis showed that it is part of a separate apicomplexan clade. Search for *Pf*mtRNAP-associated transcription initiation factors by sequence homology and *in silico* protein-protein interaction network analysis identified *Pf*KsgA1 as a possible interacting partner of *Pf*mtRNAP. *Pf*KsgA1 is a dual cytosol- and mitochondrion-targeted protein that functions as a SSU rRNA dimethyltransferase in ribosome biogenesis (Gupta et al., *Mol. Biochem. Parasitol*. 2018). *Pf*KsgA1 bound mtDNA and interaction of *Pf*mtRNAP with *Pf*KsgA1 was confirmed by *in vivo* crosslinking and pull-down experiments. *Pf*KsgA1 served as a transcription initiation factor as demonstrated by complementation of yeast Mtf1 function in Rpo41-driven *in vitro* transcription. Pull-down experiments using *Pf*KsgA1 and *Pf*mtRNAP domains indicated that the N-ter region of *Pf*mtRNAP interacts primarily with the *Pf*KsgA1 C-terminal domain with some contacts being made with the linker and N-terminal domain of *Pf*KsgA1. Solution structures of yeast Rpo41 complexes with Mtf1 or *Pf*KsgA1 were determined by Small Angle X-ray Scattering (Fig. 1). Protein interaction interfaces thus identified matched with those reported earlier for Rpo41-Mtf1 interaction and also overlaid with the *Pf*mtRNAP-interfacing region identified experimentally for *Pf*KsgA1. Results demonstrated that in addition to a role in mitochondrial ribosome biogenesis, *Pf*KsgA1 has an independent function as a transcription initiation factor for *Pf*mtRNAP ***[Int. J. Parasitol. 2020; PMID: 32896572].***

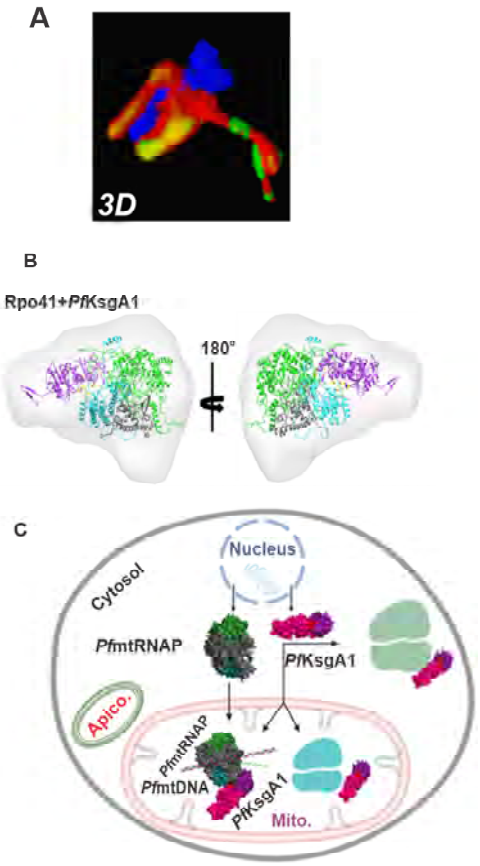


Fig. 1. A, 3-dimensional reconstruction of *Pf*mtRNAP co-localization with Mitotracker Red. B, SAXS-based reconstruction of *Pf*KsgA1 interaction with yeast RNA pol Rpo41. C, dual role of *Pf*KsgA1 in ribosome biogenesis and transcription initiation in the parasite mitochondrion.

5.1.2 Understanding the structural–functional diversity of malaria parasite's *Pf*HSP70-1 and *Pf*HSP40 chaperone pair

An interesting research question is how the human malaria parasite is able to keep its aggregation-prone proteome in a functional state. Co-evolutionary analysis has revealed that the parasite has evolved highly diverged proteostasis machinery which allows it to survive under hostile microenvironment. However, the components of proteostasis machinery have not been comprehensively investigated in malaria parasite. As HSP70–40 system forms the central hub in cellular proteostasis, the protein folding capacity of *Pf*HSP70-1 and *Pf*HSP40 chaperone-

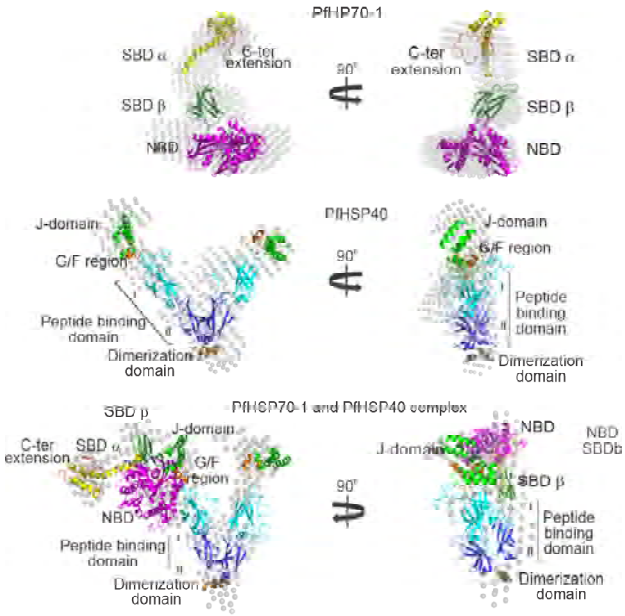


Fig. 2. SAXS analysis of PfHSP70-1, PfHSP40 and their complex. Superimposition of homology models of PfHSP70-1 and PfHSP40 onto the ab initio dummy-atom envelope constructed through DAMMIF from experimental small angle x-ray scattering. SASBDB-IDs are SASDHU5 (PfHSP70-1) and SASDHR5 (PfHSP40). The samples for solution scattering of PfHSP70-1 and its complex with PfHSP40 was prepared in presence of ADP and NR-peptide. (Anas et al, Biochemical Journal 2020)

pair was investigated and compared with their human orthologs. Biochemical experiments revealed that *Pf*HSP70-1 and *Pf*HSP40 chaperone pair has better protein folding, aggregation inhibition, oligomer remodeling and disaggregase activities than their human orthologs. Better chaperoning ability of *Pf*HSP70-1 and *Pf*HSP40 is driven by functional diversity of *Pf*HSP40 (type-I cytosolic HSP40) which gives an edge over its human ortholog in driving HSP70-mediated protein folding. Structural investigation through small angle x-ray scattering gave insights into the conformational architecture of *Pf*HSP70-1 (monomer), *Pf*HSP40 (dimer) and their complex (Fig. 2). Overall, the research investigations reveal that human malaria parasite has distinct structural-functional properties which may open avenues for the exploration of small-molecule based antimalarial interventions ***(Biochemical Journal 2020; PMID: 32893851).***

5.1.3 Development of novel therapies against malaria

To develop the novel therapies against malaria, we extensively characterized the secreted protein with altered thrombospondin repeat (SPATR) using conditional mutagenesis system. We show that SPATR plays an essential role during blood stage. Mutant *Spatr* salivary gland sporozoites exhibit normal motility, hepatocyte invasion, liver stage development and rupture the parasitophorous vacuole membrane to egress from hepatocytes in the form of merosomes. Furthermore, mutant hepatic merozoites failed to establish a blood-stage infection *in vivo* (Fig. 3 and Table 1). We provide direct evidence that SPATR is not required for hepatocyte invasion but plays an essential role during the blood stages of *P. berghei* ***(Mol. Microbiol, 2020;113:478–491).***

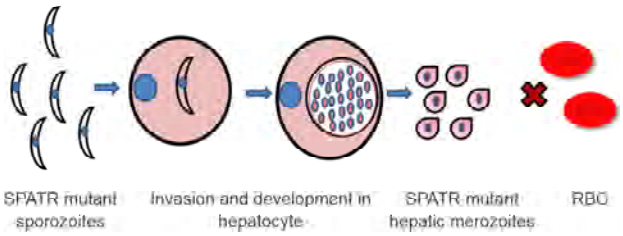


Fig. 3. SPATR mutant sporozoites failed to establish blood stage infection.

Table 1. Infectivity of *Spatr* cKO sporozoites in C57BL/6 mice. Mice were inoculated i.v. with *Spatr* cKO or TRAP/FlpL sporozoites.

Parasites	Number of sporozoites injected	Mice positive/ mice injected	Pre-patent period (days)	Genotype of recovered parasites
TRAP/FlpL	5,000	12/12	3	*Spatr* (+)
Spatr cKO	5,000	16/16	4	*Spatr* (+)

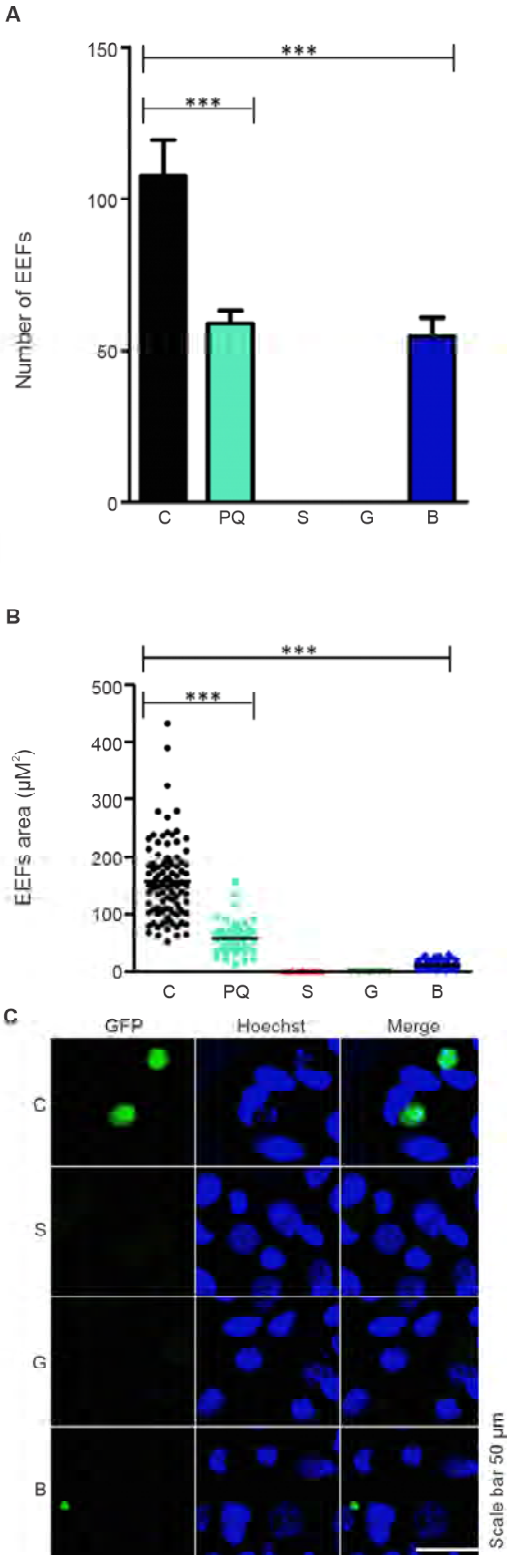


Fig. 4. DQN loaded liposomes result in either complete abolishment or heavily stunted growth of EEFs in vitro. (A) Number of EEFs per 25 fields is shown for untreated control and DQN loaded liposomes. Representative data of two independent experiments. Error bars represent SD. $p < 0.0001$. (B) Quantitation of EEF area in untreated control and DQN loaded liposomes at 40 h p.i. EEF areas were quantified using Nikon NIS elements BR imaging software. $p < 0.0001$. (C) Representative EEF images used for quantification. Scale bar, 50 μm. Representative data of two independent experiments. Error bars represent SD. C – Untreated Control, PQ – Primaquine, S – SAG-modified liposomes G – GM-modified liposomes, B – Conventional liposomes.

Targeting the development of liver-stage *Plasmodium* parasites represents a promising strategy for the development of malaria prophylaxis. Primaquine continues to remain the gold standard molecule with an incumbent toxicity profile, as far as radical treatment of malaria is concerned. Better molecules are available at experimental level but their targeted delivery is a challenge. Decoquinate (DQN) as a repurposed, safer drug molecule with a potential to function as a replacement for primaquine active against liver-stage malaria. We demonstrate that differently designed DQN loaded liposomes targeted to liver efficiently and kill the malaria parasite (Fig. 4) ***(Int. J. Pharmaceutics, 2020; PMID: 32739383).***

5.1.4 Identification the role of Calcyclin binding protein (CacyBP) in rodent malaria parasite

CacyBP plays important roles in several cellular processes such as ubiquitination, proliferation, apoptosis, differentiation, cytoskeleton organization, tumerogenesis, or regulation of transcription by interacting with target proteins. It is distributed in the cytoplasm, however, due to elevation of intracellular calcium ion, it can translocate to the nucleus. CacyBP is still unexplored in malaria parasite. Plasmodial CacyBP has ~35% similarity with human and other eukaryotes. The detailed study of CacyBP from malaria parasite has not been performed till date. We hypothesized that the CacyBP might play important role in survival of malaria parasite and in the development of multidrug resistance.

We cloned, over expressed and purified the CacyBP from rodent malaria parasite *Plasmodium yoelii nigeriensis* MDR. Polyclonal antibody was raised in rabbit. Immunofluorescence (IF) analysis was performed in different intra-erythrocytic asexual stages of the parasite to check the localization of *Py*MDR-CacyBP. The subcellular localization of *Py*MDR-CacyBP during the asexual developmental cycle was studied by Confocal microscopy using *Py*MDR-CacyBP antibody and Alexafluor488 tagged secondary anti-rabbit antibody, (green) (Fig. 5). The results of the study revealed that

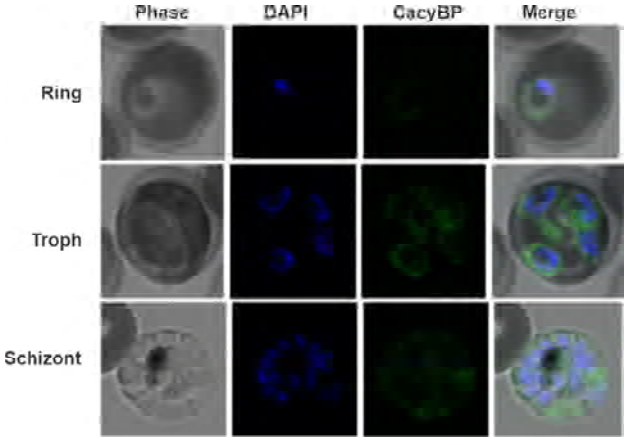


Fig. 5: Subcellular localization of *Py*MDR-CacyBP (green, Alexa fluor488) analyzed during the different intra-erythrocytic stages of *P. yoelii* MDR by immunofluorescence studies using anti-CacyBP antibody. DAPI stain (blue colour) showing parasite nucleus within RBC. Merge is composite of the DAPI (blue) and CacyBP (green) images.

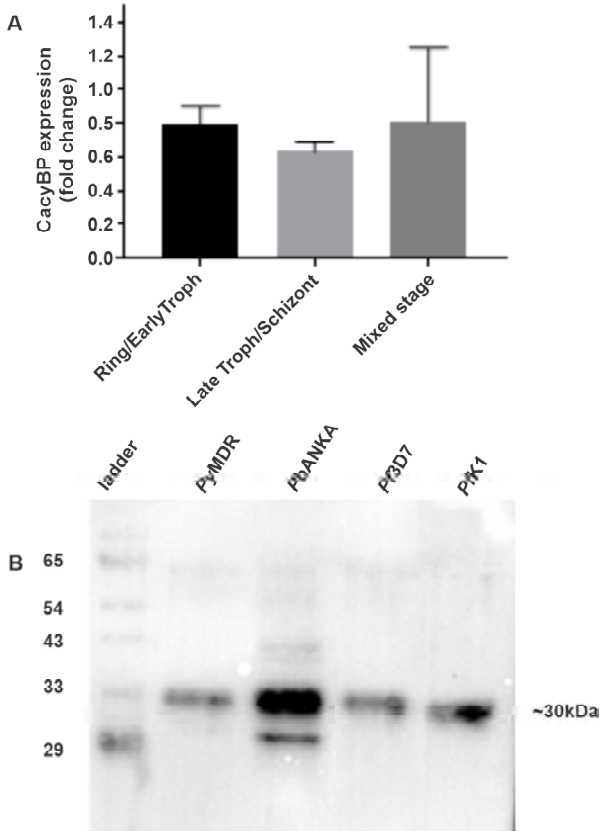


Fig. 6 (A) Relative expression of mRNAs for *PyMDR*-CacyBP gene investigated using Real-time PCR in ring /early trophozoite, late trophozoite/ schizont and mixed stages of parasite. Each experiment was performed in triplicate. All quantifications were normalized to the housekeeping gene 28S rRNA. (B) CacyBP protein expression in different species of *Plasmodium* parasite. Lane1: ladder; Lane2: lysate of *Py*MDR; Lane3: lysate of *Pb*ANKA; Lane4: lysate of *Pf*3D7; Lane5: lysate of *Pf*K1

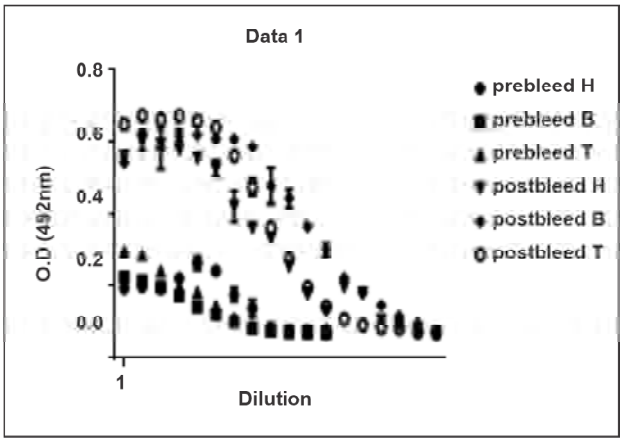


Fig. 7: Antibody titration analysis in balb/c mice immunized with *PyMDR*-CacyBP recombinant protein. ~3 fold increased antibody titre was found in immunized mice compared with pre-immunized mice.

*Py*MDR-CacyBP is cytosolic in localization and ubiquitously expressed during all intra-erythrocytic stages. We have checked the relative mRNA expression of the *Py*MDR-cacybp gene in the ring/early trophozoite, late trophozoite/schizont stages and mixed stage of parasite. The results of the study revealed that *Py*MDR-cacybp gene expression relatively same in all stage of parasite (Fig. 6A). *Py*MDR-CacyBP protein expression in different species of plasmodium was checked through western blot analysis. The results of western blot showed that *Py*MDR-CacyBP protein expresses in all these species of *Plasmodium* (Fig. 6B). To test the *Py*MDR-CacyBP protein immunogenicity, Balb/c mice were immunized with *Py*MDR-CacyBP recombinant protein and antibody titre was measured by ELISA. The results of ELISA showed the ~3 fold increased antibody titre in immunized mice compared with pre-immunized mice (Fig. 7).

5.1.5 Casein Kinase 2 (CK2) expression in experimental cerebral malaria.

Cerebral malaria is the most severe pathology caused by the malaria parasite, *Plasmodium falciparum*. The pathogenic mechanisms leading to cerebral malaria are still poorly defined as studies have been hampered by limited accessibility to human tissues. Protein kinase CK2 (casein kinase 2) is a eukaryotic serine/threonine protein kinase with multiple substrates and has a dual role in cellular processes, namely its involvement in growth and proliferation as well as in suppression of apoptosis especially in cancer cells. CK2 activity promotes the activation of NF-kB, PI3K–Akt–mTOR and JAK–STAT pathways. In case of experimental cerebral malaria, inhibition of these entire pathways reduces the risk of this disease. Since casein kinase 2 activity promotes the activation of these pathways, thus, identification of its inhibitors and development of adjunctive therapies acting in concert with existing antimalarials, can reduce the disease severity.

We established that the mRNA expression of CK2α (Fig. 8) was significantly increased in brain of symptomatic mice compared to healthy control, while there was no significant changes was detected in CK2α', CK2β1 and CK2β2. The protein expression of CK2á was significantly increased in brain of symptomatic mice compared to healthy control, while no significant changes were detected in CK2α' and CK2β subunits. *Pf*CK2α, a novel protein kinase in *Plasmodium falciparum* is also involved in the parasite replication in host RBCs. Inhibitors of *P. falciparum* CK2 may provide several unique approaches as novel curative agents, transmission blockers, and potential multi-targeted agents in the treatment of malaria. Here we found that the casein kinase 2α inhibitors CX-4945 and DMAT are inhibiting *Plasmodium* growth at 8.78 and 47.65 μM concentrations. In addition, on the basis of molecular docking of maybridge library casein kinase inhibitors against

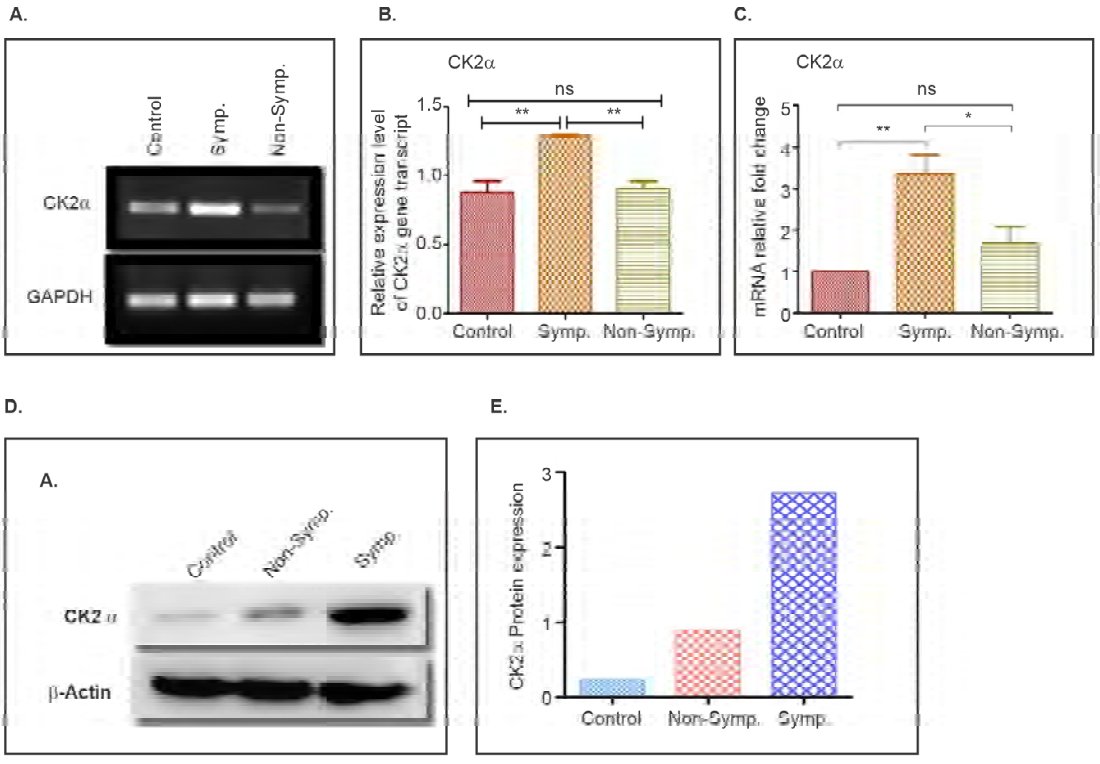


Fig. 8. (A) mRNA level **CK2α** by semi-quantitative PCR, (B) Densitometry analysis of semi-quantitative PCR, (C) Quantitative real-time PCR analysis,(D) Protein expression by western blotting, (E) Densitometry analysis of protein expression.

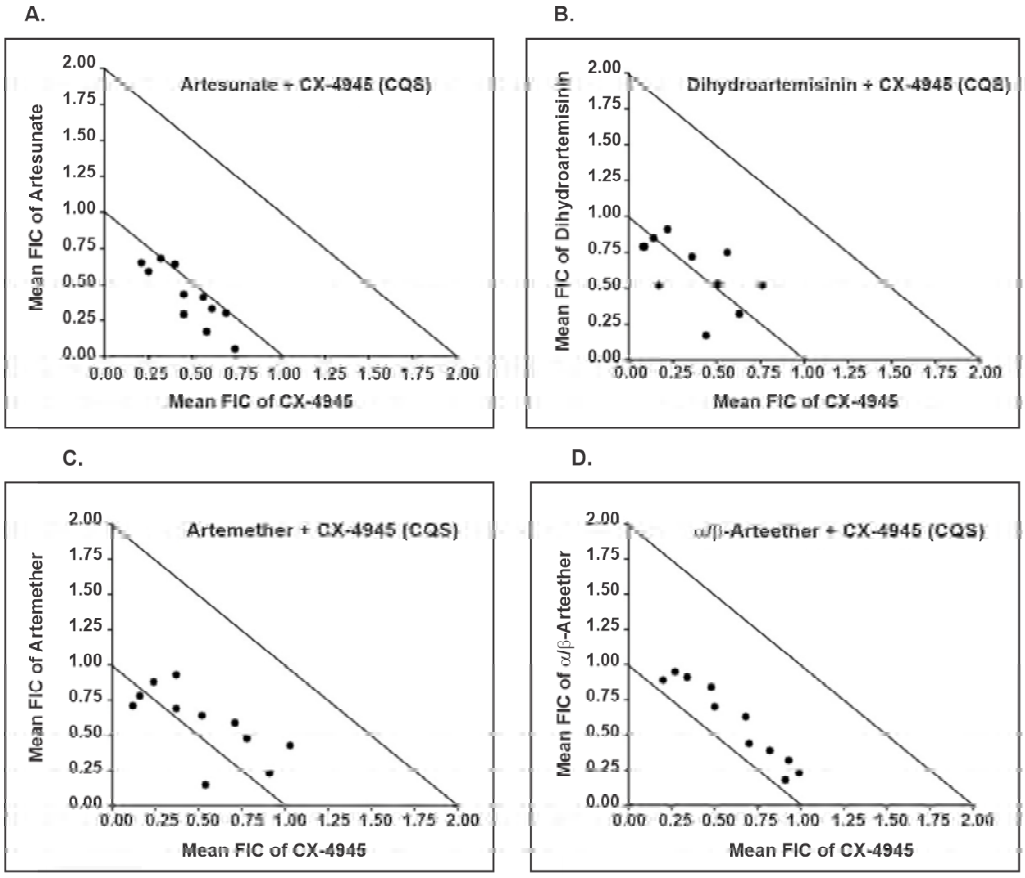


Fig. 9 (A): *In-vitro* interactions between **artesunate** and **CX-4945** against CQ sensitive *Pf*3D7 strain. (B): *In-vitro* interactions between **Dihydroartemisinin** and **CX-4945** against CQ sensitive *Pf*3D7 strain. (C): *In-vitro* interactions between **artemether** and **CX-4945** against CQ sensitive *Pf*3D7 strain. (D): *In-vitro* interactions between **arteether** and **CX-4945** against CQ sensitive *Pf*3D7 strain.

plasmodium CK2α, one compound namely CD07054 inhibited 50% growth of *P. falciparum* at 5.50 µM concentration. Interaction studies of artemisinin derivatives with CX-4945 were found to be synergistic with artesunate, artemether and DHA (Fig. 9).

5.2 Leishmaniasis

5.2.1 Effect of overexpression of of LdMAPK1 on Leishmania phosphoproteome

Mitogen-activated protein kinases (MAPKs) are well-known mediators of signal transduction of eukaryotes, regulating important processes, like proliferation, differentiation, stress response, and apoptosis. In Leishmania, MAPK1 plays various roles in regulating the critical cellular activities like parasite survival, infectivity and drug resistance. Earlier, we have shown that LdMAPK1 modulates antimony susceptibility by downregulating P-glycoprotein (P-gp) efflux pump and plays a vital role in the post-translational modification and possibly the regulation of heat shock proteins. With an aim to identify target phosphoproteins of LdMAPK1, a comparative phosphoproteomics analysis of wild type (Dd8+/+), LdMAPK1 over-expressing (Dd8++/++) and LdMAPK1 single deletion (Dd8+/-) mutant parasites was carried out utilizing LC-MS/MS approach. The MS data was analyzed using the label free quantitation algorithm for quantitation of the precursor ion in Proteome-Discoverer software [Thermo-Scientific, V2.3]. The data obtained from the LC-MS/MS analyses was searched simultaneously on the Mascot server and Sequest database using Swiss port database and uniprot_UP000008153, UP000318821, UP000255414 for *Leishmania donovani* strain database respectively. Carbamidomethylation [C] was used as a fixed modification.

5.2.2 Functional characterization of TCP1g of *L. donovani*

LdTCP1γ is essential for growth and infectivity: T-complex protein-1 (TCP1) is a chaperonin protein known to fold various proteins like actin and tubulin. In *Leishmania donovani* only one subunit of TCP1 that is gamma subunit (LdTCP1γ) has been functionally characterized. It not only performs ATP dependent protein folding but is also essential for survival and virulence. Gene replacement studies indicate that LdTCP1γ is essential for parasite survival as efforts to generate null mutant failed and single-allele replacement mutants exhibited retarded growth and decreased infectivity in mouse macrophages compared to wild-type parasites. Modulation of LdTCP1γ expression in promastigotes also

modulated cell cycle progression. Suramin, initially developed as a treatment for human African sleeping sickness, exhibited significant inhibition of LdTCP1γ refolding activity and multiplication of amastigotes with low toxicity to mammalian cells. The interaction of suramin with LdTCP1γ was observed both by isothermal titration calorimetry and computational molecular docking studies. The study suggests that LdTCP1γ is an essential gene, hence a potential drug target. It also provides a framework for the development of a new class of drugs ***(Antimicrob Agents Chemother 2020; PMID: 32457112).***

LdTCP1γ also has a role in miltefosine resistance: Overexpression of LdTCP1γ in *L. donovani* promastigotes results in decreased sensitivity of parasites towards miltefosine, while single-allele replacement mutants exhibited increased sensitivity as compared to wild-type promastigotes. This response was specific to miltefosine with no cross-resistance to other drugs. The LdTCP1γ-mediated drug resistance was directly related to miltefosine-induced apoptotic death of the parasite, as was evidenced by 2 to 3-fold decrease in cell death parameters in overexpressing cells and >2-fold increase in single-allele replacement mutants.

LdTCP1γ exhibits prophylactic efficacy: Treatment of VL is associated with the generation of Th1 type of cellular response and antigens that are involved in Th1 stimulation are considered as a suitable vaccine candidate. Interestingly, the recombinant protein, LdTCP1γ was found to be potent immunogenic in nature as it exhibited strong LTT response along with significant NO and ROS production in cure hamsters (treated with miltefosine) as compared to untreated infected controls. Further immunization of hamsters with LdTCP1γ results in significant reduced parasite burden in spleen and liver from day 45 onwards. While, hamsters vaccinated with rLdTCP1γ plus BCG suggesting an improved efficacy. In addition, hamsters immunized with rLdTCP1γ+BCG survived for 10 months as compared to the infected and BCG control hamsters with much shorter survival period. Further an enhanced serum levels of IgG2 and much lower levels of IgG and IgG1 in rLdTCP1γ+BCG vaccinated hamsters further favored disease resolution.

5.2.3 Characterization of leishmanial dipeptidylcarboxypeptidase as a potential vaccine molecule against visceral leishmaniasis

Peptidase from parasite origin are becoming important as vaccine candidate, among them cell surface metallopeptidase and lysosomal cysteine peptidase have shown immunoprophylactic activity. From our lab, dipeptidylcarboxypeptidase (LdDCP) a zinc metallopeptidase has been reported as a potent drug target. LdDCP was evaluated for its immunogenicity in cured hamster by XTT, NO and RO production. The study suggested that LdDCP has potential of developing as vaccine candidate against VL infection. Further immunization of hamsters with LdDCP results in significant reduced parasite burden in spleen and liver from day 45 onwards. While, hamsters vaccinated with LdDCP plus BCG suggesting an improved efficacy. Further vaccination also resulted in increase in body weight, decrease in liver and spleen weight as compare to infected controls followed by significant increase in iNOS and Th1 cytokine production i.e. IFNr, IL-12, TNFα, while inhibition of Th2 cytokine i.e. IL-10 and IL-4. Cell mediated immune response further activates humoral immune response and vaccination with rLdDCP+BCG has shown significant increase in IgG2. In contrast, Th2 immune response marker IgG and IgG1 are significantly down-regulated.

5.2.4 Identification of potential anti-leishmanial agents using Leishmanial trypanothione reductase LdTR as drug target

Trypanothione reductase of *L. donovani* is one such essential target whose inhibition could lead to a decline in parasite growth. Using virtual screening of Maybridge chemical library against LdTR, 10 compounds were identified which were evaluated for their inhibitory effect on trypanothione reductase followed by their antileishmanial efficacy. The study highlighted one compound as the potential anti-leishmanial agent, with IC50 value of 15.2 μM that can be further optimised with medicinal chemistry efforts to improve its activity ***(J. Biol. Struc. and Dynamics 2020; PMID: 31984862).***

5.2.5 Guanylate Binding Proteins (GBP) restrict *Leishmania donovani* growth in nonphagocytic cells

Interferon (IFN)-inducible guanylate binding proteins (GBPs) play important roles in host defense against many intracellular pathogens that reside within pathogen-containing vacuoles (PVs). We reported a critical role for both mouse and human GBPs in the cell-autonomous immune response against the vector-borne parasite *Leishmania donovani*. Although *L. donovani* can infect both phagocytic and nonphagocytic cells, it predominantly replicates inside professional phagocytes. The underlying basis for this cell type tropism is unclear. We for the first time demonstrated that GBPs restrict growth of *L. donovani* in both mouse and human nonphagocytic cells. GBP-mediated restriction of *L. donovani* replication occurs via a noncanonical pathway that operates independent of detectable translocation of GBPs to *L. donovani*-containing vacuoles (LCVs). Instead of promoting the lytic destruction

of PVs, as reported for GBP-mediated killing of Toxoplasma in phagocytic cells, GBPs facilitate the delivery of *L. donovani* into autolysosomal-marker-positive compartments in mouse embryonic fibroblasts as well as the human epithelial cell line A549. Together our results show that GBPs control a novel cell-autonomous host defense program, which renders nonphagocytic cells nonpermissible for efficient Leishmania replication ***(mBio, 2020; PMID: 32723921).***

5.2.6 Efficient antileishmanial activity of amphotericin B and piperine entrapped in enteric coated guar gum nanoparticles

Amphotericin B (AmB) exhibits potential antileishmanial activity, with only a little rate of recurrence. However, low bioavailability and severe nephrotoxicity are among the major shortcomings of AmB-based therapy. Various AmB nanoformulations have been developed, which to an extent, have reduced its toxicity and increased the drug efficacy. To further reduce the nonspecific tissue distribution and the cost of the treatment and increased bioavailability by oral route, the current AmB-based formulations require additional improvements. Combination of natural bioenhancers with AmB is expected to further increase its bioavailability. Therefore, we developed a nanoformulation of AmB and piperine (Pip), a plant alkaloid, known to enhance the bioavailability of various drugs, by entrapping them in guar gum, a macrophage targeting polymer. Owing to the ease of oral delivery, these nanoparticles (NPs) were coated with eudragit to make them suitable for oral administration. The formulated eudragit-coated AmB and Pip-loaded NPs (Eu-HDGG-AmB-Pip-NPs) exhibited controlled release of the loaded therapeutic agents and protected the drug from acidic pH. These NPs exhibited effective suppression of growth of both promastigotes and amastigotes of Leishmania donovani parasite under *in vitro*. *In vivo* evaluation of these NPs for therapeutic efficacy in golden hamster-*L. donovani* model demonstrated enhanced drug bioavailability, non-nephrotoxic nature, and potential antileishmanial activity with up to 96% inhibition of the parasite by oral route ***(Drug Deliv. Transl. Res.,* 2020*; PMID: 32016707)***.

5.2.7 *Leishmania donovani* subverts host immune response by epigenetic reprogramming of macrophage M (Lipopolysaccharides + IFN-γ)/M(IL-10) polarization

Reciprocal changes in histone lysine methylation/ demethylation of M(LPS + IFN-γ)/M(IL-10) genes is one of the factors that direct macrophage polarization and contribute to host defense/susceptibility towards infection. Although, histone lysine methyltransferases and lysine demethylases orchestrate these events, their role remains elusive in visceral leishmaniasis, a disease associated with macrophage M(IL-10) polarization. In this study, we observed that *L. donovani* induced the expression of histone lysine methyltransferases Ash1l, Smyd2, and Ezh2 and histone lysine demethylases Kdm5b and Kdm6b in J774 macrophages and BALB/c mice. Chromatin immunoprecipitation analysis revealed that *L. donovani* facilitated H3K36 dimethylation at TNF-α promoter by Smyd2 and H3K27 trimethylation at inducible NO synthase promoter by Ezh2 to suppress their expression in macrophages. Furthermore, infection-

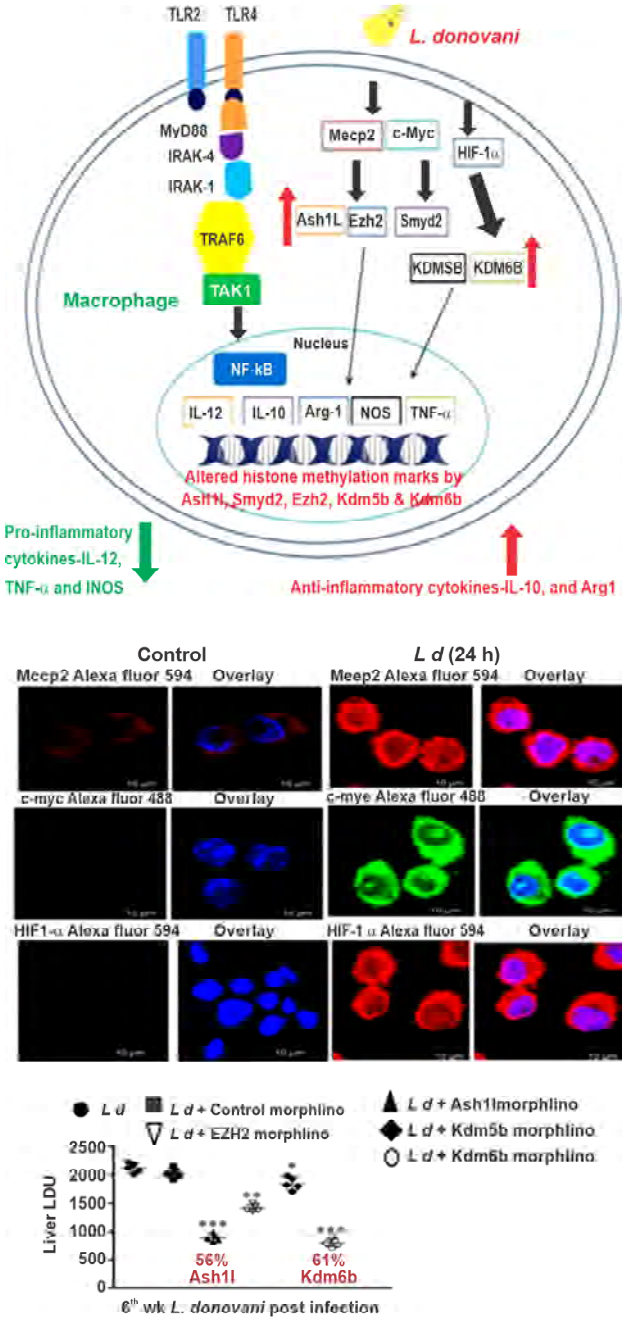


Fig. 10. *L. donovani* exploits Ash1l, Ezh2, Smyd2, Kdm5b and Kdm6b for modulation of TLR-responsive pro-anti inflammatory genes

induced Kdm5b and Kdm6b modulated H3K4 and H3K27 trimethylation at IL-12, TNF-α, and arginase-1 promoters, respectively, whereas H3K4 trimethylation by Ash1l at IL-10 promoter induced its expression. Analysis of transductional events revealed that HIF-1α upregulated Kdm5b and Kdm6b expression, whereas Ash1l and Ezh2 expression were induced by transcription factor MeCP2. Additionally, Smyd2 was induced by c-Myc in infected macrophages. Knockdown of Ash1l, Ezh2, Kdm5b, and Kdm6b by specific small interfering RNA and Vivo-Morpholino, as well as inhibition of Smyd2 by its specific inhibitor, AZ505, led to increased protective proinflammatory response and inhibited amastigote multiplication in infected J774 macrophages and BALB/c mice, respectively. Collectively, our findings demonstrate that *L. donovani* exploits specific histone lysine methyltransferases/demethylases to redirect epigenetic programming of M(LPS + IFN-α)/M(IL-10) genes for its successful establishment within the host. ***(J Immunol, 2020; PMD: 32277055).***

5.2.8 Characterization of RNA Editing Ligase 1 (REL1) of *Leishmania donovani* as drug target.

RNA editing is a unique posttranscriptional modification of mitochondrial mRNAs that regulates mitochondrial oxidative phosphorylation system. One of the important components of RNA editing is RNA editing ligase 1 (REL1). We aim to characterize the RNA editing pathway, particularly the enzyme, REL1 of *L. donovani* (LdREL1) in the context of parasite survival and infectivity.

To assess the biological functions of the LdREL1 protein in modulating mitochondrial RNA editing and oxidative phosphorylation, we attempted to create an LdREL1 null mutant cell line by targeted gene replacement strategy. Leishmania are asexual diploids and thus require two rounds of gene replacement. A 0.8 kb flanking sequence upstream (52 F) and 0.725 kB flanking sequence downstream (32 F) of LdREL1 were PCR-amplified from *L. donovani* g-DNA. 52 F and 32 F were cloned in pCR-2.1-TOPO TA vector and then sub-cloned in pX63NEO and pX63HYG vectors in between HindIII and SalI as well as SmaI and BglII sites to generate 52 F-pX63NEO-32 F and 52 F-pX63HYG-32 F constructs respectively. Both of these circular constructs were then digested with HindIII and BglII to generate linear constructs for transfection in Leishmania parasites. Therefore, we generated LdREL1-knockout constructs by gene replacement with either hygromycin- or neomycin-selectable markers. We transfected 52 F-pX63NEO-32 F construct in Leishmania parasite and generated LdREL1$^{-/+}$ (single knockout) parasite, maintained at 50 µg/mL G418. LdREL1$^{-/+}$ (single knockout) parasite was then transfected with 52 F-pX63HYG-32 F construct to generate double knockout parasite (LdREL1$^{-/-}$) and the transfectant was maintained in presence of both 50 µg/mL G418 and 50 µg/mL hygromycin. Through homologous recombination, both alleles of REL1 gene were replaced by NEO and HYG. LdREL1 gene deletion was conûrmed by PCR analysis of genomic DNA. Western blot analysis to confirm the loss of LdREL1 at protein level will also be performed after generating anti-LdREL1 antibody. Using these knockout parasites, loss of function of LdREL1 will be assessed and we will explore whether LdREL1 is responsible for mitochondrial mRNA editing in Leishmania as well as its role in mitochondrial oxidative phosphorylation and parasite survival inside host.

5.2.9 The *L. donovani* Hypoxanthine-Guanine PhosphoRibosyl Transferase tetramer is distinct from the human homolog

Purines are important molecules that play a vital role in energy metabolism, signaling, synthesis of vitamin/co-factors, in addition to being precursor molecules of RNA and DNA. Purines are synthesized either *de novo* or salvaged via a purine salvage pathway in most organisms. Kinetoplastids including *Leishmania* lack the *de novo* machinery and solely rely on the salvage pathway. Thus enzymes of the kinetoplastid purine salvage pathway are considered from a therapeutic purpose. A key enzyme of the *L. donovani* purine salvage pathway is the hypoxanthine-guanine phosphoribosyl transferase (HGPRT; EC2.4.2.8), that converts purine to its mono-phosphate product. HGPRTs exist either as dimers (*Trypanosoma brucei, L. tarentole*) or tetramers (*P.*

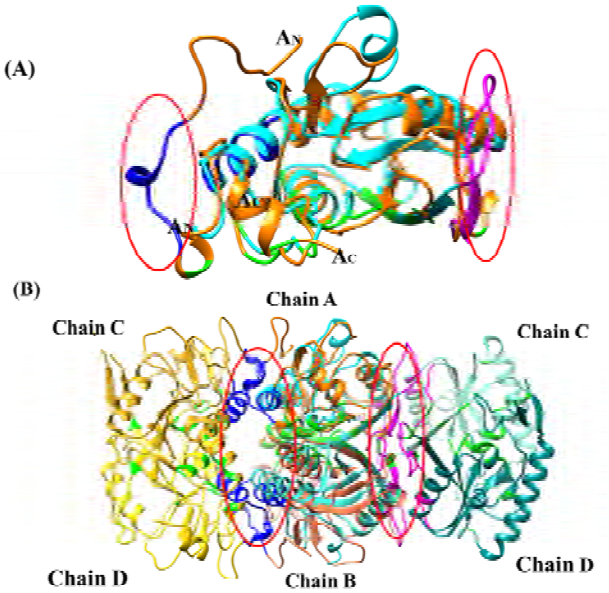


Fig. 11. Structural superposition of the *L. donovani* (orange) & human (cyan) HGPRT protomers (top) and the functional tetramers (bottom). Regions involved in oligomer association are coloured distinctly (dimer: green, tetramer: magenta & blue).

falciparum, human) or as both (*T. cruzi*). It was hypothesized that the dimer is the active form, but later reports show an active tetramer.The *L. donovani* HGPRT was cloned, expressed, purified and determined its structure, which showed that it assembles as a tetramer, consistent with solution studies and active. Comparison of the *L. donovani* and human HGPRT structures reveal that though the individual protomers (and dimers) are similar, the tetramers show a distinct difference, with the two dimers interacting via opposite faces (Fig. 11). Structure based sequence alignment studies indicate that an N-terminal insertion in the human HGPRT primarily contributes to tetramerization. Further studies are in process to utilize this distinct feature for therapeutic approaches ***(Biochem. Biophys. Res. Comm. 2020, PMID 32873391).***

5.2.10 Functional analysis of *Leishmania* actin

We have developed gene half-knockout mutant of actin with a depletion level of approximately 50% and have analysed the functional implications in Leishmania cells. Immediate phenotype observed was slow growth and significantly reduced flagellar length rendering the promastigotes non-motile. Detailed analysis revealed role of actin in cell division but not in DNA replication. The cell cycle progression was slow during G2/M transition, mainly pre-cytokinetic stages. The mutants also showed defects in flagellar assembly and flgallar pocket activity, mainly endocytosis/exocytosis slowdown, however, the cellular ATP levels were maintained high. More studies on mechanisms are underway.

5.2.11 Development of *Leishmania* vaccine

We have now selected three Th1 stimulatory proteins out of six that showed better immune response and efficacy. As per the plan, three chimeras were planned with permutation combinations of the three selected proteins and one of them containing Enolase and TPI was analysed and was found to suppress infection up to 75% when used with BCG as immune modulator. The other two chimeras containing Enolase-Aldolase and Aldolase-TPI have now been generated and are being optimized for their expression and purification processes. Once all three chimeras are in hand they will be analysed at the same plateform towards selecting the most potent one. The future plan includes different delivery formulations for oral as well as sub-cutaneous delivery of the vaccine prototype(s), stability analysis and dose optimization.

5.3 Lymphatic Filariasis

5.3.1 Role of Eosinophils in Tropical Pulmonary Eosinophilia (TPE)

Lymphatic Filariasis is a highly morbid disease that does not per se causes mortality. However, Tropical pulmonary eosinophilia (TPE) is a clinical manifestation of Filariasis that is caused by hypersensitive response to antigens from microfilariae of *Wuchereria bancrofti* and *Brugia malayi*. If left untreated or

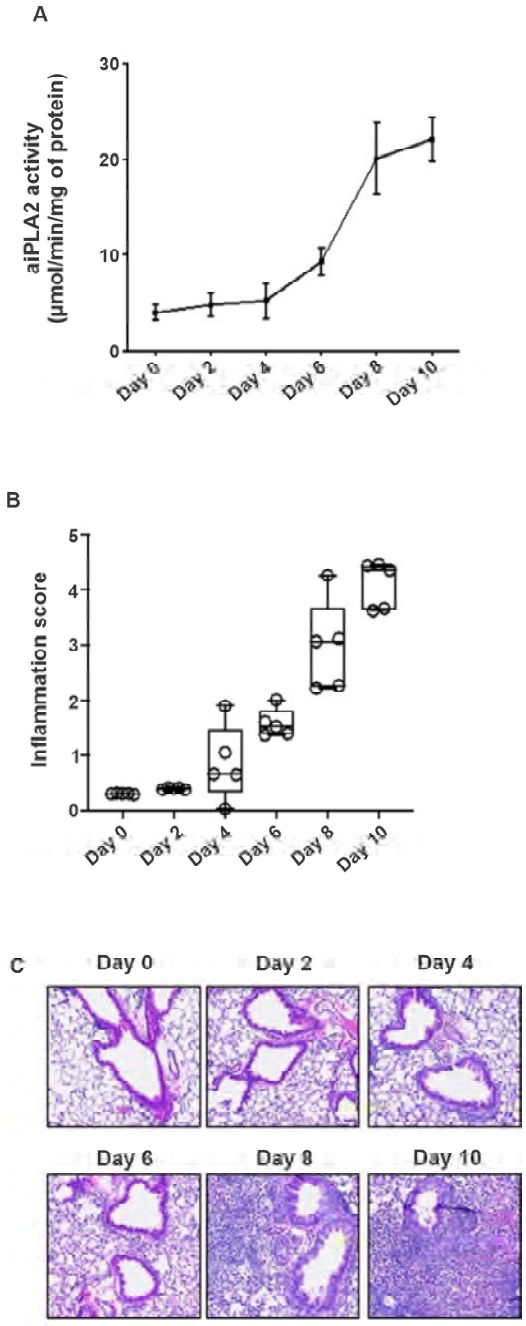


Fig 12. aiPLA2 activity correlates with lung pathology in TPE mice. aiPLA2 activity in TPE mouse lungs over the course of disease (A), lung inflammation score (B), and HE stained lung sections showing high leukocytic infiltration into the lungs of mice (C).

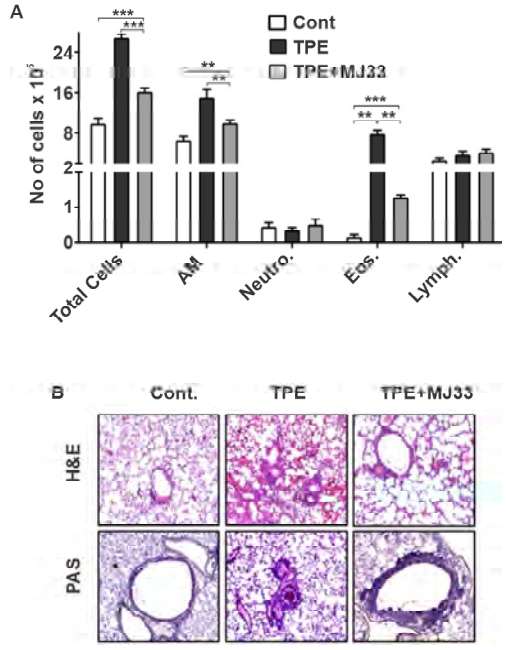


Fig 13. Inhibition of aiPLA2 activity abrogates eosinophils mediated lung inflammation in TPE mice. Leukocyte counts in the lungs of mice (A) and HE stained lung sections of mice post MJ33 administration showing resolution of inflammation (B).

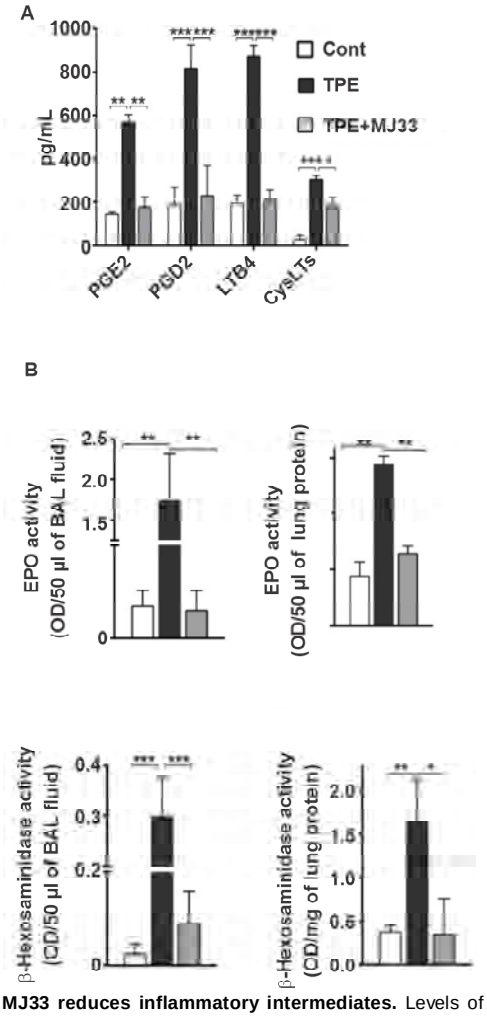


Fig 14. MJ33 reduces inflammatory intermediates. Levels of PGE2, PGD2, LTB4 and CysLTs in the lungs of mice post MJ33 treatment and reduced EPO and β-Hexosaminidase activity (B).

misdiagnosed, TPE can result in death. Eosinophils mediate pathological manifestations during TPE but the immunopathology of the disease is not completely understood. We identified acidic calcium independent phospholipase A2 (aiPLA2) as the master regulator of TPE pathogenesis. We showed that aiPLA2 activity increased during TPE (Fig 12A) which lead to high inflammation in the lungs (Fig 12B) resulting in lung damage (Fig 12C).

Administration of MJ33, a non-toxic inhibitor of aiPLA2 in mice, reduced eosinophil counts in the lungs (Fig 13A), and improved overall lung histopathology (Fig. 13B).

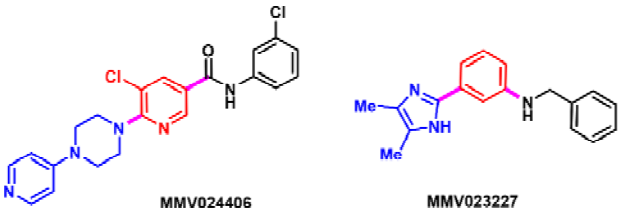
Further analysis showed that treatment with MJ33 also lead to reduced accumulation of inflammatory intermediates in the lungs viz. Prostaglandins (PGE2, PGD2), Leukotriene (LTB4) and Cysteinyl leukotrienes (Cys LTs) as well as prevented eosinophil degranulation as evident by diminished Eosinophil peroxidase (EPO) and β-Hexosaminidase activity in the BAL fluid and lung homogenate of MJ33 treated animals ***(J Immunol, 2021; PMID:33441441).***

5.4 Medicinal Chemistry

5.4.1 Malaria

In efforts to identify new chemical scaffolds with antiplasmodial activity during the period of reporting, several new compounds were synthesized and investigated. These include hybrids of 4-aminoquinoline with triazoline or triazole or peptidomimetics. Out of the first series of 32 quinoline-triazoline hybrids, 12 compounds were found to be active with IC50 values in the range of 0.01-0.2 mM for 3D7 and 0.02-0.94 mM for K1 strains. Likewise, out of a set of 24 compounds from the quinolone-triazole hybrid compounds, five displayed significant *in vitro* effect. However, nine quinolone peptidomimetic hybrids did not elicit any significant bioresponse. In addition, synthesis and evaluation of a series of twenty salicylamide compounds similar to histone acetyl transferase (HAT) activators was conducted, out of which S-020-382 displayed activity in submicromolar range. Further evaluation of the compounds in the *in vivo* assay is underway.

In a collaborative effort with Medicines for Malaria Venture, an open science project for optimizing the biological activity of aryl piperazine MMV024406 and aryl imidazole MMV023227 and surmounting the challenges of high CYP inhibition and low metabolic stability was inititiated. Under the program, more than twenty new compounds were synthesized which are under investigation for their antiplasmodial effect (see below).



5.4.2 Leishmaniasis

In the pursuit to discover new antileishmanial agents against Visceral Leishmaniasis, compounds belonging to triazolylbutenolide, quinolone acetamide, 3-isoxazolecarbamate, styrylazaarene class were investigated. Out of 24 compounds from the triazolybutenolide series, three compounds displayed promising activity against the amastigote stage and are being examined for their *in vivo* efficacy. From the 30 quinolone acetamide derivatives, only two hit compounds were identified. On the other hand, out of the 22 isoxazole derivatives, S-020-0099, 0120, 0125 displayed better activity against amastigotes of *L. donovani* as compared to the standard drug Miltefosine. The work on the isoxazole derivatives was compiled and the SAR (Fig. 15) was published (***RSC Med. Chem.* 2020**).

benzamide derivative, quinoline hybrid, trifluoro methyl triazoline derivative of chloroquinoline and Sulfonyl triazoline have shown promising *in vitro* antiplasmodial activity.

One benzamide derivative (S020-0382) presented its activity with IC_{50} values of 0.79 µM against CQ sensitive *Pf*3D7 and 1.28 µM against CQ resistant *Pf*K1 strains, respectively. Four quinoline hybrid compounds (S020-0365, 0366, 0367 and S020-068) exhibited IC_{50} values 0.13, 0.14, 0.09 and 0.13 µM, respectively against *Pf*3D7 and 0.31, 0.18, 0.13 and 0.25 µM, respectively against *Pf*K1. Twenty-five trifluoromethyl triazoline derivatives of chloroquinoline (S020-0244-0414, and 0416) had IC_{50} in the range of 0.009 to 0.153 µM against *Pf*3D7 and 0.02 to 0.66 µM against CQ *Pf*K1. Five sulfonyl triazolines (S020-0415, 0417 and 0419-0420 and 0421) exhibited IC_{50} in the range of 0.29 to 1.04 µM against *Pf*3D7 and 0.65 to 2.32 µM against *Pf*K1 strain. These molecules were also evaluated for cytotoxic profile against Vero cell line and found to be safe.

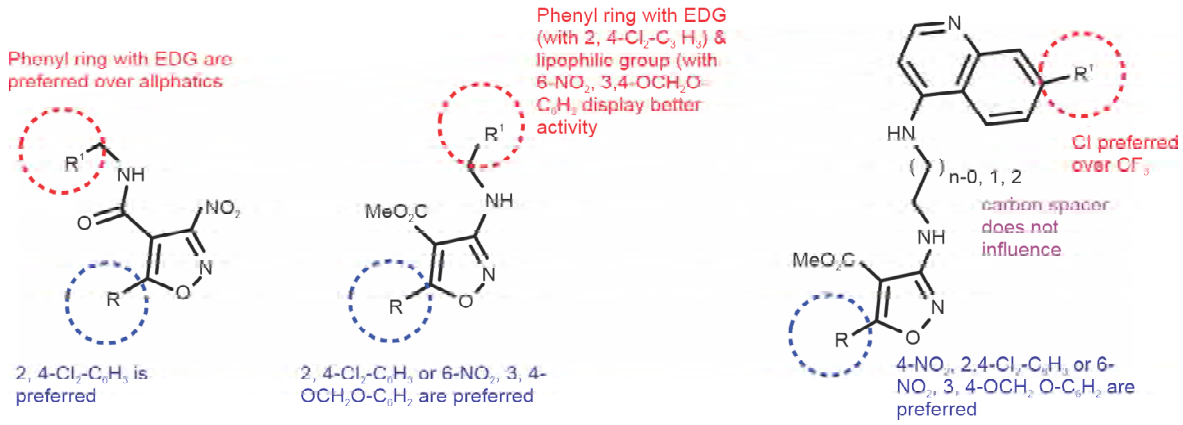


Fig. 15. SAR of the isoxazole derivatives

5.5 Anti-parasitic screening for drug discovery

5.5.1 Anti-malarial drug discovery

5.5.1.1 In-vitro antimalarial activity of CDRI Compounds

During the current year, 282 novel CSIR-CDRI compounds were screened against the human malaria parasite, *P. falciparum*. Out of these, 35 compounds belonging to the diverse chemical classes such as

Eight plant-extracts were also evaluated for their antimalarial activity. One of the extracts exhibited antimalarial activity of 12 µg/ml and had CC_{50} value as 57 µg/ml.

Under an MoU with Foundation for Neglected Disease Research (FNDR), Bangalore in vitro activity and toxicity of two compounds was evaluated. CDRI is also partner of 'Malaria Libre', an open source discovery initiative of the Medicines for Malaria Venture (MMV). As part of this international consortium, nine compounds were screened, of which five compounds showed promising antimalarial activity.

5.5.1.2 *In-vivo* antimalarial profile of CSIR-CDRI compounds against *P. yoelii nigeriensis* N67 (CQ resistant)

Five compounds namely S-019-0547, 0553, 0554, 0555 and 0564 (Quinoline triazoles) were administered for 4 days, at 100 mg/kg oral dose in *P. yoelii nigeriensis* N67 infected Swiss mice. All of these compounds showed 100% parasite suppression on day 4 post treatment but were not completely curative. Only three compounds- S-019-0547, 0555 and 0564 showed 20% survival till the end of observation period.

Four compounds namely S-019-0129, 0131, 0133 and 0137 (oxazole salts), were administered for 4 days, at 100mg/kg oral dose in *P. yoelii nigeriensis* N67 infected Swiss mice. These compounds showed only 27.6, 14.7, 44.7, and 53.7% parasite suppression on day 4 post-treatment and were not curative.

5.5.1.3 *In vivo* efficacy evaluation of compounds/ formulations received from other institutes, against *P. yoelii nigeriensis* N67 & MDR

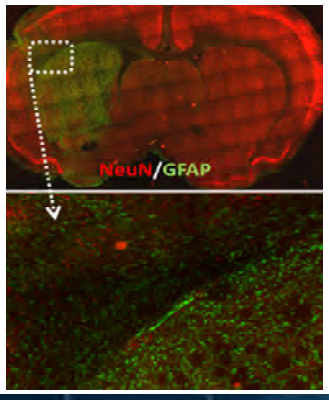
Two compounds from Foundation for Neglected Disease Research, Bengaluru were evaluated for anti-malarial efficacy in Swiss mice infected with *P. yoelli* N67, with different routes of administration also tested used for one of them; results were reported to FNDR. Formulations of DHA, quercetin and curcumin were also evaluated for *in vivo* antimalarial activity in Swiss mice infected with *P. yoelli nigeriensis* MDR.

5.5.2 Discovery and development of antileishmanials

296 compounds belonging to different chemical prototypes; phenanthridines, benzotriazoyl chalcones, pyridines, imidazole pyrimidine, quinoline piperazine, quinolone, dihydropyrimidinone nitroimidazole, isoxazole, indole dihydropyrimidinone, quinazolinone and pyrazolopyrimidinone dithiocarbamate, heterocyclic pyrrolo-quinolinone, pyrimidine-based heterocyclic, isoquinoline, pyranone derivatives, benzothiazole, phenylallylindole were screened against promastigotes and amastigotes of *L. donovani*. For each series six experiments were performed (primary and secondary) to estimate IC_{50}, CC_{50} and SI index. 22 Compounds exhibited IC_{50} <5 µM and SI >5. Compounds belonging to quinazolinone derivatives (S-019-0629, S-019-0645) series showed significant anti-amastigote activity (76.2% and 78.8% inhibition at 12.5 µM and 25 µM of amastigote multiplication respectively and SI greater than 5). The IC_{50} value of S-019-0629 and S-019-0645 were found to be 5.76 µM and 3.39 µM, respectively against intracellular amastigotes. S-019-0629 and S-019-0645 will be further evaluated for their anti-leishmanial activity in *L. donovani*-golden hamster model.

Target-based screening of 20 compounds from Maybridge library was performed against LdTR (*L. donovani* Trypanothione Reductase) at three concentrations 5 µM, 25 µM & 100 µM. Compound BTB13370 showed 50% inhibition at 50 µM.

Three compounds (S-019-0674, S-019-0676 and S-019-0682) were evaluated for their *in vivo* efficacy in *L. donovani*-Hamster model at a dose of 50 mg/Kg via intraperitonial administration. All compounds showed poor antileishmanial activity as only 25% reduction of parasite load on 28th day post treatment was observed.



6

NEUROSCIENCE AND AGEING BIOLOGY

Area Coordinators: Dr. Atul Kumar and Dr. Aamir Nazir

Vision and Goal:

- Development of novel therapeutic agents for CNS and age associated disorders.
- Fundamental research to delineate the molecular mechanism of ailments related to ageing and nervous system.
- Creation of appropriate platform for interdisciplinary collaborative research.

Core Competencies and Activities:

- Targeted design and synthesis of small molecules for nervous system related disorders.
- Neurobehavioral facility to conduct battery of behavioral assays like forced swim test, tail suspension test, light and dark test, elevated plus maze, open field locomotor activity, Morris water maze test, Grip Strength, Social interaction and rotarod test, which are being used to study depression, anxiety, stress, cognitive impairment and locomotor deficit.
- Extensive battery of physiological and behavioral assay systems to measure nociception (pain), such as Digital/electronic Von Frey system and Hargreaves system to record Allodynia and hyperalgesia and hot plate test system to record planter nociception.
- Functional assays that enable measurement of G-protein coupled receptor (GPCR) dependent formation of secondary messengers (cAMP using GloSensor, Ca++ flux using gCAMP6b biosensor) or ß-arrestin recruitment to GPCRs to discover selective agonist and antagonists of target GPCRs.
- Transgenic *C. elegans* strains expressing "human" alpha synuclein and "human" amyloid beta towards conducting screening of test compounds and to understand mechanistic aspects related to neurodegenerative diseases (Alzheimer's and Parkinson's disease).
- MPTP and 6-OHDA induced Rodent models for studies on Parkinson's disease.
- GLP accredited lab for essential CNS safety pharmacology studies of a test compound as per Schedule "Y", including animal activity monitoring by Optovarimax system, motor coordination by Rotarod, core body temperature, Analgesia activity by Hot Plate and gross behavior assessment.

Research Group

Front row (L to R): Dr. Nayan Ghosh, Dr. Durga Prasad Mishra, Dr. Gautam Panda, Dr. Ramesh Chintakunta, Dr. Sanjay Batra, Dr. Atul Goel, Dr. Ravindra Kumar, Prof. Tapas K. Kundu (Director, CSIR-CDRI), Dr. Atul Kumar (Area Coordinator), Dr. Aamir Nazir (Area Coordinator), Dr. Prem N. Yadav, Dr. Namrata Rastogi & Dr. Richa Pandey.

Back Row (L to R): Dr. Sarika Singh, Dr. Shubha Shukla, Dr. T. Narender, Dr. Vineeta Tripathi, Dr. Kishor Mohanan, Dr. Ajay Kumar Srivastava, Dr. Malleswara Rao Kuram, Dr. Damodara Reddy N, Dr. Pintu Kumar Mandal & Dr. Prem Prakash Yadav

6.1 Kappa opioid receptor agonist SB/ CDRI4/105 shows promise in treating neuropathic pain

Neuropathic pain is an extremely common condition and various estimates of the prevalence range from a low of about 3% to a high of over 12%, with most estimates settling at around 10% (WHO data). The number is likely to grow as the population ages, together with increase in the prevalence of type 2 diabetes. Those numbers together with difficulty to treat neuropathic pain due to lack of effectiveness and tolerability of currently available drugs makes it an important and growing health issue. Compounds that exhibit full agonist activity at the Kappa Opioid Receptor (KOR) are efficacious in preclinical models of pain, particularly visceral pain. Simultaneously, KOR agonists are devoid of inducing several side effects caused by Mu Opioid Receptor (MOR) agonists, including abuse liability, gastrointestinal transit inhibition and respiratory depression. Nonetheless, at analgesic doses, KOR agonists are reported to produce complicating side effects such as dysphoria and sedation. In parallel, it has been demonstrated that KOR selective G-protein biased agonist induce analgesia and aversion, but unlike unbiased KOR agonist they do not induce sedation and are free from anhedonia-like actions. This may also suggest that a mechanism other than G protein signalling mediates these effects. This underscores the need for the discovery of biased KOR agonists that retain sufficient efficacy to treat various types of pain and other symptoms or disease states associated with the KOR, while reducing the CNS side effects. In this context, we have discovered a series of compounds that display biased agonistic activity for the KOR. One of the compounds SB/ CDRI4/105 from the series has shown high affinity as KOR agonist (IC_{50}< 10 nM) and 100-fold biased towards G-Protein signalling in comparison to β-arrestin 2 signalling. During the *in-vivo* studies via oral administration at a dose of 10 mg/kg, this compound has been found to be highly efficacious in alleviating hyperalgesia and allodynia (hallmark symptoms of neuropathic pain) and interestingly did not induce sedation and neuromuscular incoordination as observed with unbiased full KOR agonist U50488. The compound has pronounced activity in the nerve ligation assay and has been found to be free of toxic effects in the preliminary assays. Further IND enabling studies are underway.

6.2 Synthesis and biological evaluation of multifunctional tacrine-triazole hybrids as potential candidates for the treatment of Alzheimer's disease

Alzheimer's disease is a brain disorder, characterized by the aggregation of senile plaques (SPs) and neurofibrillary tangles (NFTs). SPs and NFTs are primarily composed of Aβ and hyper phosphorylated tau protein, respectively. In the present study, twenty-two tacrin-triazole derivatives were synthesized and were evaluated for their effect on the aggregation of Aβ. Among these twenty-two compounds, six compounds (**45, 47, 49, 51, 54** and **56**) were found to reduce aggregation of Aβ by 1.5 (p<0.001), 1.3 (p<0.01), 1.9 (p<0.001), 1.6 (p<0.001), 2.1 (p<0.001) and 1.9 (p<0.001) folds, respectively with respect to vehicle control. We observed that three test compounds *viz* **45**, **47** and **49** showed a significant reduction in the levels of reactive oxygen species with respect to vehicle control by reducing the fluorescence intensity by 1.3 (p<0.05), 1.9 (p<0.01) and 4.1 (p<0.001) folds respectively as compared to control. Worms treated with test compounds (**45, 47, 49, 51, 54** and **56**) exhibited no tissue/ cell damage. Among six tested compounds, **47** possessed anti-oxidant potential as well as inhibited the AChE activity. Moreover, we examined the TcAChE–E2020 complex for analysis of the binding mode of newly synthesized compounds in the active site of TcAChE. Interestingly, strong non-covalent interactions (H-bond) between these inhibitor compounds and target site of AChE, π-π stacking interactions between aromatic rings of compounds and residues of the target site were observed.

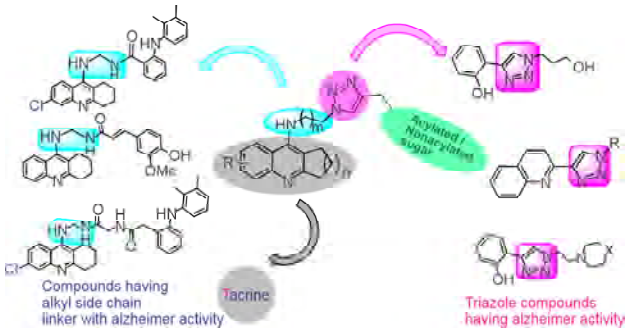
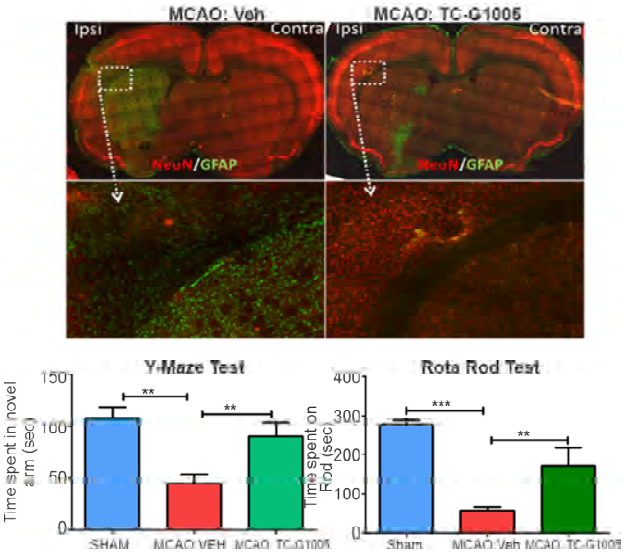


Figure: Strategy for designing of tacrine-triazole based hybrid molecules

6.3 Bile acid receptor confers neuroprotection in cerebral stroke

Transmembrane G protein-coupled receptor-5 (TGR5), also known as GPBAR1, has been identified as bile acid receptor, expressed in the gall bladder, kidney, brown adipose tissue, liver, intestine and brain. In the central nervous system (CNS), TGR5 activation exerts a beneficial effect on fat metabolism in mouse brains, alleviates microglial activation in hepatic encephalopathy and cognitive impairment. Since ischemic cerebral stroke is one of the most common causes of death and the main cause of long-term disability worldwide, we investigated the effect of CNS TGR5 activation in Middle Cerebral Artery Occlusion (MCAO) model of stroke in SD rats.

We administered TC-G1005 (a TGR5 selective agonist, 1 nM/2 µl/rat) via ICV route (to selectively engage brain specific TGR5) 1hr post occlusion. Interestingly, we observed that TGR5 activation significantly blocked activation of astrocytes and neuronal cell death. Also, treatment with TC-G1005 significantly alleviated cognitive (evaluated Y-Maze test) and motor impairment (Rota rod test) due to cerebral stroke. These results for the first time provide proof of concept data that TGR5 could be targeted for the development of novel therapeutics for cerebral stroke.



6.4 Dopamine D1 receptor agonism induce dynamin related protein-1 inhibition to improve mitochondrial biogenesis and dopaminergic neurogenesis in rat model of Parkinson's disease

Dopamine (DA) neurotransmitter act on DA receptors (D1-D5) to regulate motor functions, reward, addiction and cognitive behavior. The depletion of DA in midbrain due to degeneration of nigral dopaminergic (DAergic) neurons leads to Parkinson's disease (PD). DA agonist and levodopa (L-DOPA) are the only therapies used for symptomatic relief in PD. However, the role of DA receptors in PD pathogenesis and how they are associated with mitochondrial functions and DAergic neurogenesis is still not known. Here, we investigated the mechanistic aspect of DA D1 receptor mediated control of DAergic neurogenesis, motor behavior and mitochondrial functions in rat PD model. The pharmacological activation of D1 receptors markedly improved motor deficits, mitochondrial biogenesis, ATP levels, mitochondrial membrane potential and protected nigral DAergic neurons against 6-hydroxydopamine (6-OHDA) induced neurotoxicity in adult rats. However, the D1 agonist mediated effects were abolished following D1 receptor antagonist treatment in 6-OHDA lesioned rats. Interestingly, pharmacological inhibition of dynamin related protein-1 (Drp-1) by Mdivi-1 in D1 antagonist treated PD rats, significantly restored behavioral deficits, mitochondrial functions, mitochondrial biogenesis and increased the number of newborn DAergic neurons in substantia nigra pars compacta (SNpc). Drp-1 inhibition mediated neuroprotective effects in PD rats were associated with increased level of protein kinase-B/Akt and extracellular-signal-regulated kinase (ERK). Taken together, our data suggests that dopamine D1 receptor mediated reduction in mitochondrial fission and enhanced DAergic neurogenesis may involve Drp-1 inhibition which led to improved behavioral recovery in PD rats. ***(Behav Brain Res. 2020; 378:112304)***

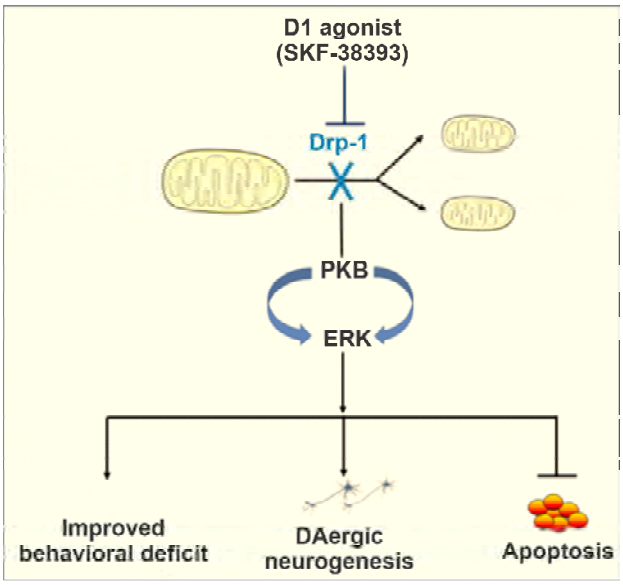


Figure: Inhibition of dynamin related protein-1 by dopamine D1 receptor agonist improve mitochondrial biogenesis and dopaminergic neurogenesis

6.5 Human insulin modulates α-synuclein aggregation via DAF-2/DAF-16 signaling pathway by antagonizing DAF-2 receptor in *C. elegans* model of Parkinson's disease

Insulin-signalling is an important pathway in multiple cellular functions and organismal ageing across the taxa. A strong association of insulin-signalling with Parkinson's disease (PD) has been proposed but the exact nature of molecular events and genetic associations are yet to be understood. We employed transgenic *C. elegans* strain harboring human α-synuclein YFP transgene, towards studying the aggregation pattern of α-synuclein, a PD-associated endpoint, under human insulin (HumINS) treatment and DAF-16/DAF-2

knockdown conditions, independently and in combination. The aggregation was increased when DAF-16 was knocked-down independently or alongwith a co-treatment of HumINS and decreased when DAF-2 was knocked-down independently or alongwith a co-treatment of HumINS; whereas HumINS treatment per se, reduced the aggregation. Our results depicted that HumINS decrease α-synuclein aggregation via DAF-2/DAF-16 pathway by acting as an antagonist for DAF-2 receptor. Knockdown of reported DAF-2 agonist (INS-6) and antagonists (INS-17 and INS-18) also resulted in a similar effect on α-synuclein aggregation. Further by utilizing bioinformatics tools, we compared the differences between the binding sites of probable agonists and antagonists on DAF-2 including HumINS. Our results suggest that HumINS treatment and DAF-16 expression play a protective role against α-synuclein aggregation and its associated effects. ***(Oncotarget 2020; 11(6):634-649)***.

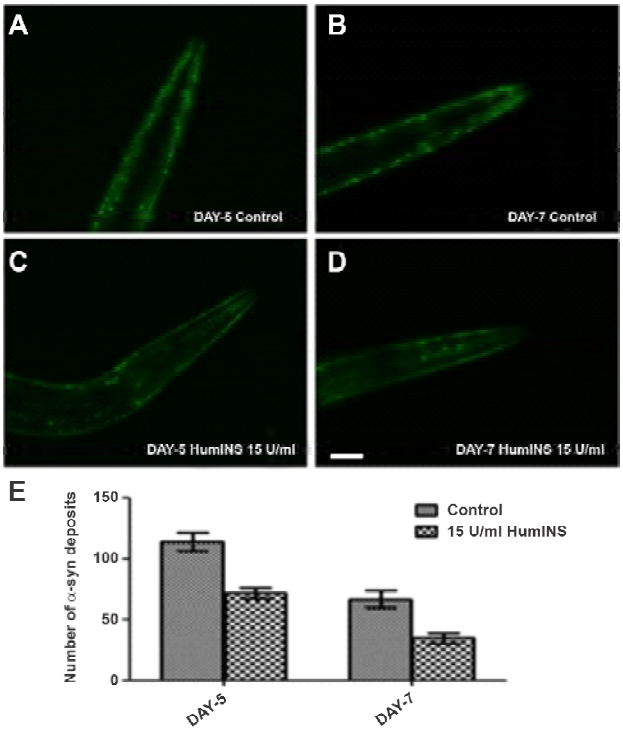
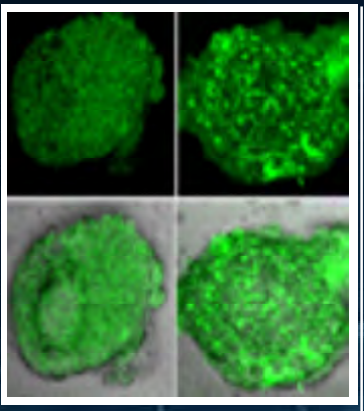


Figure: HumINS decrease aging-dependent aggregate accumulation. *(A–D) The aggregation of α-syn was assayed in NL5901 transgenic strain of C. elegans that expresses human α-syn YFP transgene in their body wall muscles at day 5 and day 7. Representative image (A) represents 5-day-old worms fed on OP50; (B) represents 7-day-old worms fed on OP50; (C) 5-day-old worms treated with 15 U/ml HumINS; (D) 7-day-old worms treated with 15 U/ml HumINS. (E) Graphical representation for numbers of α-syn deposits as quantified using DotCount image analysis software. *** p < 0.001, Scale bar, 100 μm.*



7

REPRODUCTIVE HEALTH

Area Coordinators: Dr. Rajender Singh and Dr. T Narender

Vision and Goal:

- Development of novel therapeutic agents for fertility regulation (male/female), diagnostics/therapeutics for male/female infertility and endocrine disorders through modern drug design, scientific validation of traditional remedies.
- Basic research to delineate the molecular mechanisms of these biologies, pathologies / abnormalities so as to identify suitable targets for drug discovery, as well as to analyze the possible mechanism(s) of action of the candidate drugs.
- Creation of appropriate platform for interdisciplinary collaborative research.

Core Competencies and Activities:

- Design, synthesis and bio-evaluation of novel molecules/isolates from natural sources for new lead generation for:
- Female or male contraceptives.
- Female and male infertility
- Cervical, prostate and endometrial disorders.
- Scientific validation of traditional remedies for reproductive health disorders.
- Molecular mechanism of action of promising agents.
- New knowledge generation in the areas of reproductive endocrinology, fertility regulation and endocrine disorders.

(L to R): Dr. T. Narender (Area Coordinator), Dr. Rajesh Kumar Jha, Dr. Gopal Gupta, Prof. Tapas K. Kundu (Director, CSIR-CDRI), Dr. Rajender Singh (Area Coordinator), Dr. K.V. Sashidhara.

7.1 Should we fear assisted reproduction in COVID-19 season?

COVID-19 is infecting and killing millions of people worldwide. Specialists in every medical field are concerned about the penetrance of the virus in specific organs. We investigated the influence of COVID-19 on male fertility and its sexual transmission. The much-awaited first study on semen samples was conducted in China, which showed that 15.8% (6 out of 38) COVID-19 patients have the virus in the semen samples, of which 10.5% (4 out of 38) were in the acute phase and 5.26% (2 out of 38) in the recovery phase of disease. This study made headlines on various media platforms across the world, suggesting sexual transmission of the virus not only between sexual partners but also to the fetus and may have also resulted in the reduction of IVF cycles taken in the last six months. However, another study refuted the claims regarding the presence of SARS-CoV-2 in the semen samples as they failed to detect virus in 34 COVID-19 patients after a median of 31 days. An important investigation on SARS-CoV (coronavirus pandemic 2002-2003) reported that SARS-CoV was not found in the testis, though the immune response in the host resulted in a significant damage to the testicular tissue. Further, none of the above studies analyzed the impact of SARS-CoV-2 on fertility or semen parameters though it is highly likely to affect fertility because of various factors discussed by us recently. However, the impact of infection on semen parameters remained to be assessed until recently.

Now with more Covid-19 negative reports in semen transpiring, the possibility of the presence of the virus in patients' semen appears brink. Another study showed the absence of the virus by RT-PCR after analysing eighteen semen samples from recovered men obtained 8–54 days after disappearance of symptoms, 14 from control subjects, and 2 from patients with an active COVID-19 infection. The study found that while moderate viral infection could affect semen parameters, there was no evidence of its presence in semen and hence its sexual transmission. This is the first study showing an actual impact of the SARS-CoV-2 infection on semen parameters. The investigators could not detect the virus in semen samples of nine Italian Covid-19 patients despite prolonged nasopharyngeal swab positivity. These studies have largely cleared the air with respect to the presence of the virus in the semen samples.

It is noteworthy that the preparation of the semen samples for IVF consists of washing in 2-3 steps, which would not leave any virus particle attached to sperm, further reducing the possibility of sexual transmission. Hence assisted reproduction need not take a back seat amid COVID-19 pandemic. Infertility is a serious personal, psychological and societal problem. While several other critical illnesses may need attention during the COVID-19 pandemic, infertility treatment cannot be ignored or delayed either. A delay in the treatment could leave several infertile individuals in a more despaired state, including faster deterioration of semen quality, further limiting the possibility of assisted reproduction using their own sperm. Stress makes a vicious cycle with infertility and individuals undergoing infertility care are already under significant stress, hence any further delay in the availability of treatment could incite deeper stress clock and render them more prone to losing their remote fertility. In infertile individuals, a delay of 6 months to 2 years could take a significant toll as the clock in these individuals is ticking faster in comparison to all others.

Reproduction is at the core of the survival of a species. Given that spermatogenesis is at the core of reproduction, testicular privilege to contain the entry of viruses and other infectious agents adds to the robustness of the reproductive system. It is because of the tight regulation in these tiny organs that we often talk about the infections of accessory glands in infertility without infection right inside the testicular compartments. It is not just about the presence of various receptors in the testis, further layers that provide immunological privilege to these special organs make penetration impossible. High vulnerability of the testis to various infections would have rendered the species prone to extinction by new challenging infections that may evolve and swipe a species. While the overall health state of an individual, overtly spillage of the immune response to distant organs, and the impact on the hypothalamic-pituitary-gonadal axis render the reproductive organs vulnerable to the indirect effects of COVID-19, a direct access to the virus in the organs no less critical than the vital organs could not be considered by the nature. ***(Singh Rajender, Fertility Sterility 2021)***.

7.2 Compound heterozygous mutations in the *SRD5A2* gene in ambiguous genitalia

The disorders of sexual development (DSD) represent an array of phenotypes with ambiguous genitalia. The present case had microphallus and fused and bifid scrotum, and was initially assigned as androgen insensitivity syndrome; however, sequencing of the complete coding region of the androgen receptor gene failed to identify a causative mutation. We undertook whole exome sequencing for identification of the pathogenic mutation. The most promising pathogenic variants were genotyped using Sanger sequencing to confirm the genotypes. Sequencing in 96 control samples was undertaken to rule out the presence of the mutation in the population. We found compound heterozygous mutations,

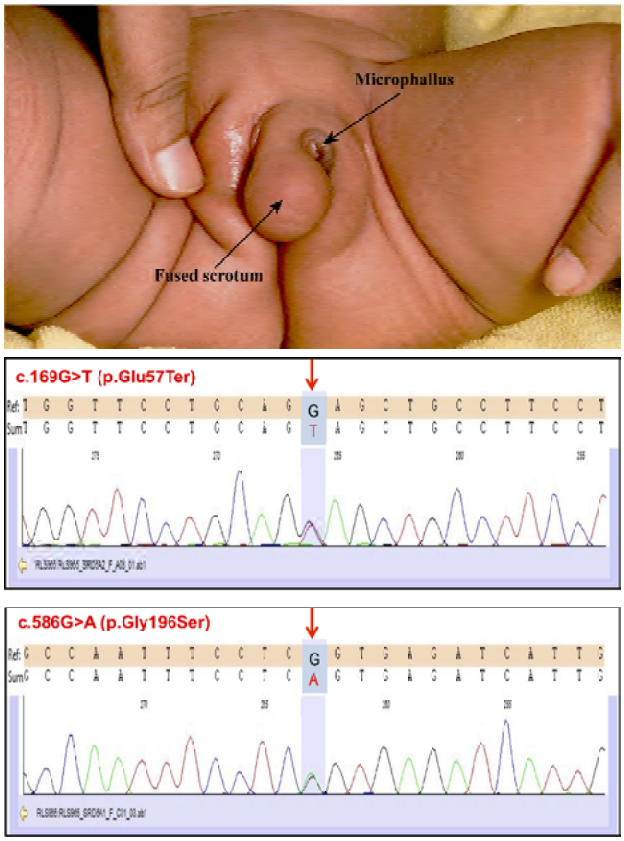


Figure showing abnormal genitalia in the child and the causative mutations.

c.169G>T and c.586G>A in the *SRD5A2* gene in this case, resulting in a non-sense (p.Glu57Ter) and a non-synonymous substitution (p.Gly196Ser), respectively. While the non-sense mutation would result in a truncated protein, p.Gly196Ser substitution has been previously reported to be pathogenic. The mutations were confirmed by Sanger sequencing. Sequencing of 96 normal male individuals did not show the above mutations, suggesting their pathogenic nature. In conclusion, we identified compound heterozygous pathogenic mutations, c.169G>T (p.Glu57Ter) and c.586G>A (p.Gly196Ser), in the *SRD5A2* gene in a case of ambiguous genitalia. p.Glu57Ter is a novel mutation, which in compound heterozygote combination with Gly196Ser causes 5a reductase deficiency ***(Andrologia, 2020, doi.org/10..1111/and.13937).***

7.3 COQ10 is a good choice for treatment of asthenozoospermic infertility

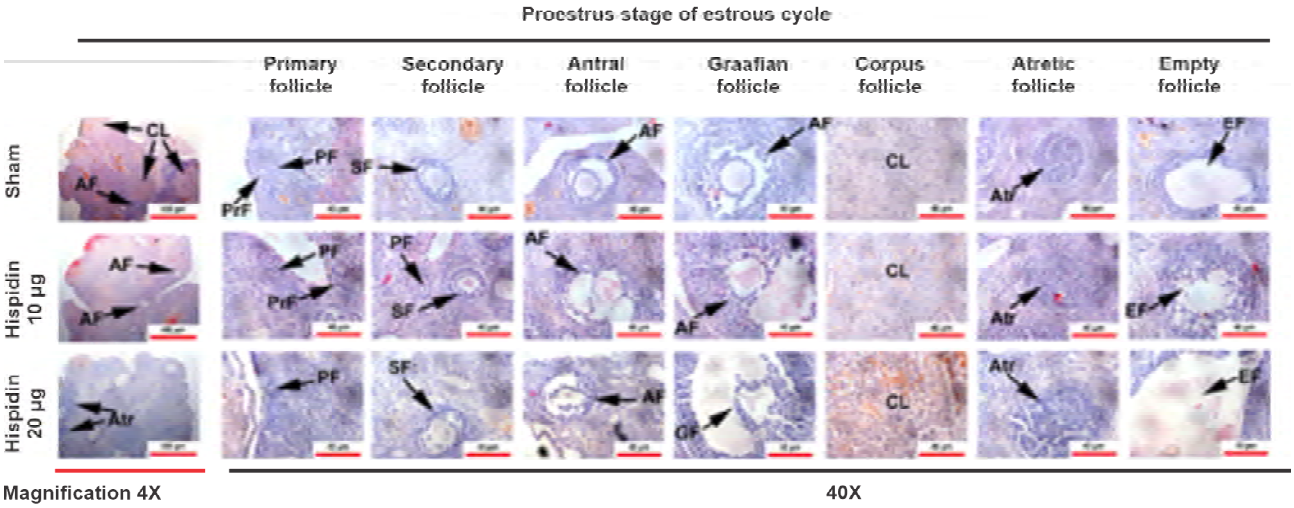
Coenzyme Q10 has shown promise in treating male infertility; however, there are inconsistencies across the published data. We undertook a quantitative meta-analysis by pooling data from three placebo controlled randomized clinical trials (RCTs) in order to evaluate the efficacy of CoQ10 in improving semen parameters. Sperm count, sperm motility, sperm forward motility, sperm morphology, CoQ10 level in the seminal plasma were measured and quantitatively correlated with CoQ10 oral administration. Pooled analysis showed a significant impact of CoQ10 in improving sperm motility and forward motility, without a significant impact on sperm count, sperm morphology, ejaculate volume or seminal plasma level of CoQ10. Efficacy assessment suggested that CoQ10 shows better results at higher doses and when administered for a period of more than three months but not longer than six months. We conclude that CoQ10 has a profound effect on sperm motility and a meager effect on all other parameters. Therefore, CoQ10 can be used for treating asthenozoospermic infertility with the dosage and duration depending upon the severity of the disorder and the patient's response to the treatment ***(Andrologia 2020 PMID: 33368459)***.

7.4 Ovarian follicles are controlled by PKC-RAC1 signaling.

Ovarian follicular development is a multifactorial process and in the premature ovarian failure (POF), early menopause, leads to infertility. Protein kinase C (PKC) isoforms are reported in the oocyte lutenization and meiotic resumption. We previously reported that RHOGTPase, RAC1, and RHOG are associated with ovarian functions. We investigated the role of RAC1 GTPase and its plausible activator PKC in ovarian follicular dynamics and the pathological condition, POF. We observed augmented expression and activity of PKC-± during the estrus (ovulatory stage) and metestrus stage (luteal stage) of the estrous cycle. The other PKC isoform, PKC-² was uregulated during the diestrus, proestrus, and estrus stages. Further, in cultured primary theca and granulosa cells of antral follicle, PKC activity modulation resulted in alteration of RAC1 expression and GTPase activity. During the proestrus stage of estrous cycle, RAC1-GTPase activity was higher than other stages of the estrous cycle. In the VCD-induced POF model of SD rats, the activity of PKC and RAC1-GTPase was increased and in contrary, the expression levels of PKC-±, phosphorylated-RAC1, and total RAC1 were downregulated. RAC1 and PKC-± were ubiquitously present in the ovary during the estrous cycle. We confirmed that PKC activity is essential during proestrus stage for antral follicles and corpus luteum maintenance.

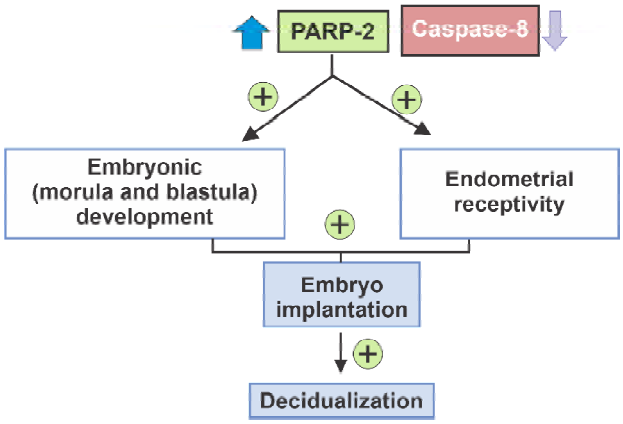
7.5 Poly(ADP-ribose) polymerase -2 is essential in the acquisition of the endometrial receptivity in mouse model

Embryo implantation is intricately controlled by various local and systemic factors originating from the embryo as well as endometrium. Failure at the uterine receptivity level derails the blastocyst implantation in consequence the pregnancy is failed and even a miscarriage can take place. The studies are on to explore



PF; Primary Follicle, SF; Secondary Follicle, AF; Antral Follilce, GF; Graafian Follicle, CL; Corpus luteum, Atr; Atretic Follicle, EF; Empty Follicle

the endometrial receptivity controlling factors. In our earlier finding in the receptive endometrial biology, we have found important role of PARP-1 in the acquisition of endometrial receptivity for the embryo implantation. It has been noticed that PARP isoform 2 also coordinates the function of PARP-1; hence, we evaluated the PARP-2 role in the endometrial receptivity for blastocyst implantation in a mouse model. We found upregulated PARP-2 at the receptive stages implantation region and was localized in the endometrial stromal region; however, downregulated during pregnancy failure and pseudopregnancy. Further, to know the necessity of PARP-2 for embryo implantation, we pharmacologically inhibited PARP-2 'before' & 'after' embryo arrival in the endometrium. Interestingly, we observed a reduction in blastocyst implantation suggesting PARP-2 crucial role for blastocyst implantation by promoting the endometrial receptivity. As PARPs are know, to be controlled by caspases, so does PARP-2 by caspase-8. In contrary to PARP-2 upregulation in the implantation sites during peri-implantation stage, caspase-8 was downregulated. Indeed, elevated caspase-8 expression and activity was noticed during pseudopregnancy, delayed implantation, and embryo implantation failure conditions. Further, decreased levels of caspase-8 in the decidualization exhibited an inverse pattern with PARP-2, suggesting caspase-8 as a negative regulator of blastocyst implantation. We confirmed under *in vitro* conditions that caspase-8 is one of the regulators of PARP-2 activity in the mouse endometrial epithelial and stromal cells. Interestingly, the uterine expression level of PARP-2 is downregulated whereas the caspase-8 is upregulates during embryo implantation. Collectively, PARP-2 facilitates the endometrial receptivity for blastocyst implantation for pregnancy establishment and caspase-8 constituted a crucial step as check-point in embryo implantation.



7.6 Inflammation driven tumor-like signaling in prostatic epithelial cells by sexually transmitted Trichomonas vaginalis

Trichomonas vaginalis, a flagellated parasitic protozoan, causes the most prevalent, non-viral, sexually transmitted disease called trichomoniasis in humans, with more than 250 million new cases added annually worldwide. Although well investigated in females, not much is known about its virulence in the male population, where it is mostly asymptomatic. T. vaginalis infects the prostate gland, which serves as its reservoir, and the parasite is found in prostatic glandular, submucosal and stromal tissues. Recently, Trichomoniasis has been corroborated with the manifestation of prostate-related pathologies, such as prostatitis, BPH and prostate cancer. Identification of the sequence of inflammation-driven signaling cascades and other molecular events that might cause tumor-like transformation of prostatic cells was taken up. Cytokine array, Reactome and STRING analysis, immunoblotting, and immunocytochemistry were used to investigate the molecular mechanisms governing inflammation-driven adverse changes in human prostatic cells caused by the sexually transmitted infection, Trichomonas vaginalis, resulting in prostatitis, benign

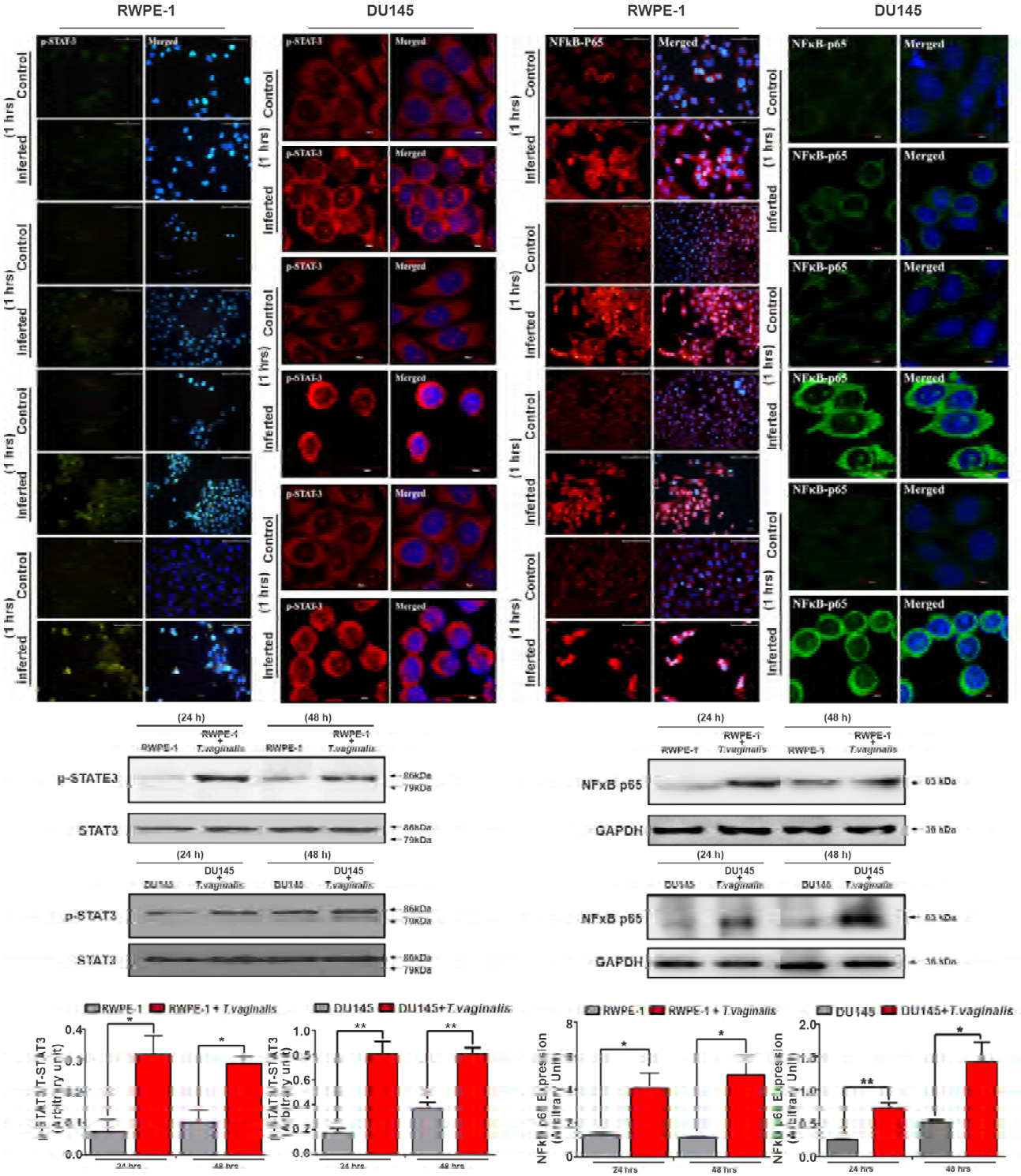


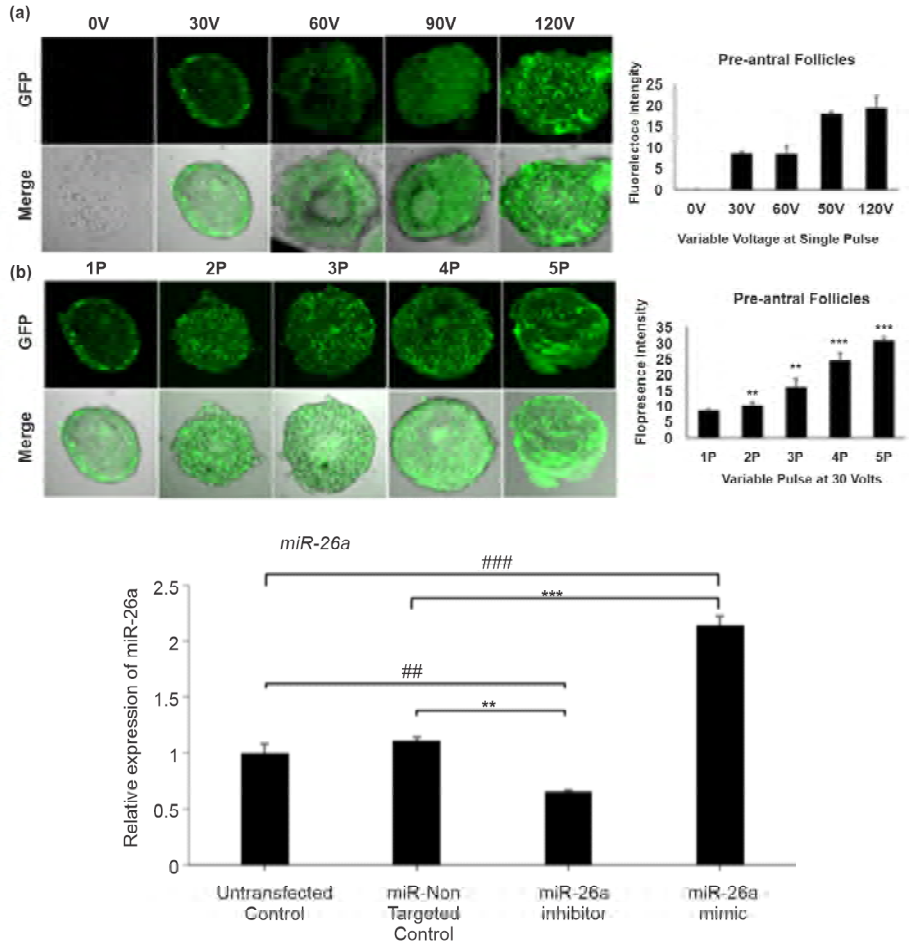
Figure: Immunofluorescent staining of STAT-3 and NFkB in RWPE-1 and DU145 cells after different durations of infection with *T.vaginalis* (upper panel); phosphorylation (activation) of STAT-3 and NFkB in infected RWPE-1 and DU145 cells by immunoblotting (middle panel); and statistical analysis of immunoblots (lower panel). (*P<0.05; **P<0.01) (Fluorescence tags – Alexafluor (red); FITC (green); nucleus staining by DAPI (blue)).

prostatic hyperplasia and prostate cancer. Array analysis showed upregulation of 23 cytokines within 24 h of infection of human prostatic epithelial cells with the parasite, *in vitro*. Reactome and STRING analysis of array data identified interleukin-6, interleukin-8, nuclear factor kappa B, signal transducer and activator of transcription 3 and cyclooxygenase-2 as the chief instigators of prostatic anomaly, which were found to be significantly upregulated by immunofluorescence and western blott analyses. STRING further connected these instigators with macrophage migration inhibitory factor, PIM-1 and prostate-specific antigen; which was confirmed by their marked stimulation in infected prostatic cells by immunoblotting and immunocytochemistry. Upregulated proliferation markers, such as Ki67, proliferating cell nuclear antigen and B-cell lymphoma 2, suggested tumor-

like signaling in infected RWPE-1 cells, which was further supported by downregulation of E-cadherin, upregulation of vimentin and activation of focal adhesion kinase. Prostate tumor DU145 cells were more sensitive to parasite invasion, and showed rapid upregulation with nuclear translocation of sensitive parameters, such as nuclear factor kappa B, signal transducer and activator of transcription 3, and macrophage migration inhibitory factor. The migration of DU145 cells augmented when incubated in spent media from parasite-infected RWPE-1 cells. The initiation of inflammation driven tumor-like cell signaling in parasite infected human prostatic epithelial cells is apparent, with the prostate tumor (DU145) cells being more sensitive to T. vaginalis than normal (RWPE-1) prostatic cells. ***[Int J Urol, 2020; PMID: 33251708].***

7.7 Developmental Competency of Electroporated Oocytes to Manipulate their miRNA

Electroporation is an effective technique of transfection; but its efficiency depends on the optimization of various parameters. In this study; a simplified and efficient method of gene manipulation has been standardized through electroporation to introduce a recombinant Green Fluorescent Protein (GFP) construct as well as RNA inhibitors in intact mouse follicles, mature oocytes and early embryos; where various electroporation parameters like voltage, pulse number and pulse duration were standardized. Electroporated preantral follicles were cultured further *in-vitro* to obtain mature oocytes and their viability was confirmed through the localization of a known oocyte maturation marker Ovastacin; which appeared to be similar with the *in-vivo* derived mature oocytes and thus proved the viability of the *in-vitro* matured oocytes after electroporation. Standardized electroporation parameters i.e., three pulses of 1 millisecond, each of 30 V at an interval of 10 seconds were applied to manipulate the expression of mmu-miR-26a in preantral follicles through the electroporation of miR inhibitors and mimics. Further TUNEL apoptosis assay confirmed the normal development of the electroporated embryos when compared to the normal embryos. Conclusively, this study paves the way for delivery of exogenous oligonucleotides into intact mouse follicles, oocytes and embryos without hampering their normal function and development.



8

ANTI-VIRAL RESEARCH, DIAGNOSTICS, AND THERAPEUTICS DEVELOPMENT (ARTH)

Area Coordinators: Dr. R. Ravishankar, Dr. Raj Kamal Tripathi and Dr. C.B. Tripathi

Vision and Goal:

Viral diseases are often deadly, result in huge loss of productive working time, and can devastate families quickly. This has been underscored by the COVID19 pandemic where our shortcomings in effectively countering the disease scourge in terms of appropriate research facilities and a robust discovery program has been identified. The ARTH program has been conceived to effectively meet this shortcoming and deliver effective diagnostics and therapeutics to counter the present and future viral diseases, develop a deep understanding of the pathogen and host interactions and pathogenesis.

The global objectives of CSIR-CDRI program in the immediate future are:

i) Develop and use cutting edge platform technologies, facilities and drug repurposing approaches to identify therapeutic interventions, diagnostics and strategies against viral disease caused by SARS COV2, Japanese Encephalitis, Dengue and other viruses.

ii) Advancing Knowledge Frontiers through studies on viral drug targets, host-pathogen interactions, *in vitro* and *in vivo* assay development, coupled to rational identification of new inhibitors with therapeutic potential.

Core Competencies and Activities:

The ARTH team uses several cutting edge drug discovery platform technologies involving screening, molecular & structural biology, chemistry, computational biology and allied areas. The team has characterized several novel targets and has identified several new scaffolds through early target discovery and research that feeds into the drug discovery pipeline of the institute. Two process technologies for APIs have been transferred to the Industry and related patents have been filed. A Phase-III clinical trial against SARS COV2 is at an advanced stage presently and permission is being sought for another Phase-III trial.

Front row (L to R): Dr. Rajkamal Tripathi (Area Coordinator), Dr. Ajay Kumar Srivastava, Dr. Atul Goel, Dr. Ravishankar R. (Area Coordinator), Dr. Atul Kumar, Dr. Prabhat Ranjan Mishra & Dr. Sanjay Batra

Back Row (L to R): Dr. Niti Kumar, Dr. Damodara Reddy N., Dr. Ramesh Chintakunta, Dr. Kishor Mohanan, Dr. C. B. Tripathi (Area Coordinator), Dr. Malleswara Rao Kuram & Dr. Ravindra Kumar

8.1 Initial focus on COVID-19 pandemic

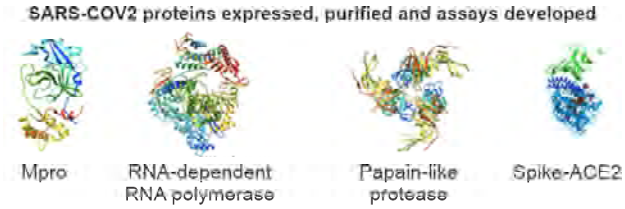
COVID-19 infection has become a pandemic as declared by World Health Organization (WHO). As on date more than 1.6 million known positive patients are there and several thousand have died. Over 25% of SARS-CoV-2 infected patients are asymptomatic and in one month about 400 people can be infected by a single COVID positive patient. CSIR and CSIR-CDRI are countering it with an emergency multi-pronged response against COVID-19 pandemic. With wide ranging meetings and discussions with the DG-CSIR and other teams, several objectives are being carried out.

8.1.1 Target-based screening involving the SARS-CoV-2 and related host proteins and assay development

(i) SARS-CoV-2 proteins like the mPro, PL-Pro, Spike-ACE2, RNA-dependent RNA polymerase have been chosen based on their importance in the pathogenesis. The FDA approved library of drugs and isolated natural product compounds from important plants like *Andrographis paniculata*, were screened against them computationally and the best hits were evaluated against them through *in vitro* inhibition assays and virus culture inhibition assays. The results are being exploited in drug-repurposing strategies as well as in new lead development.

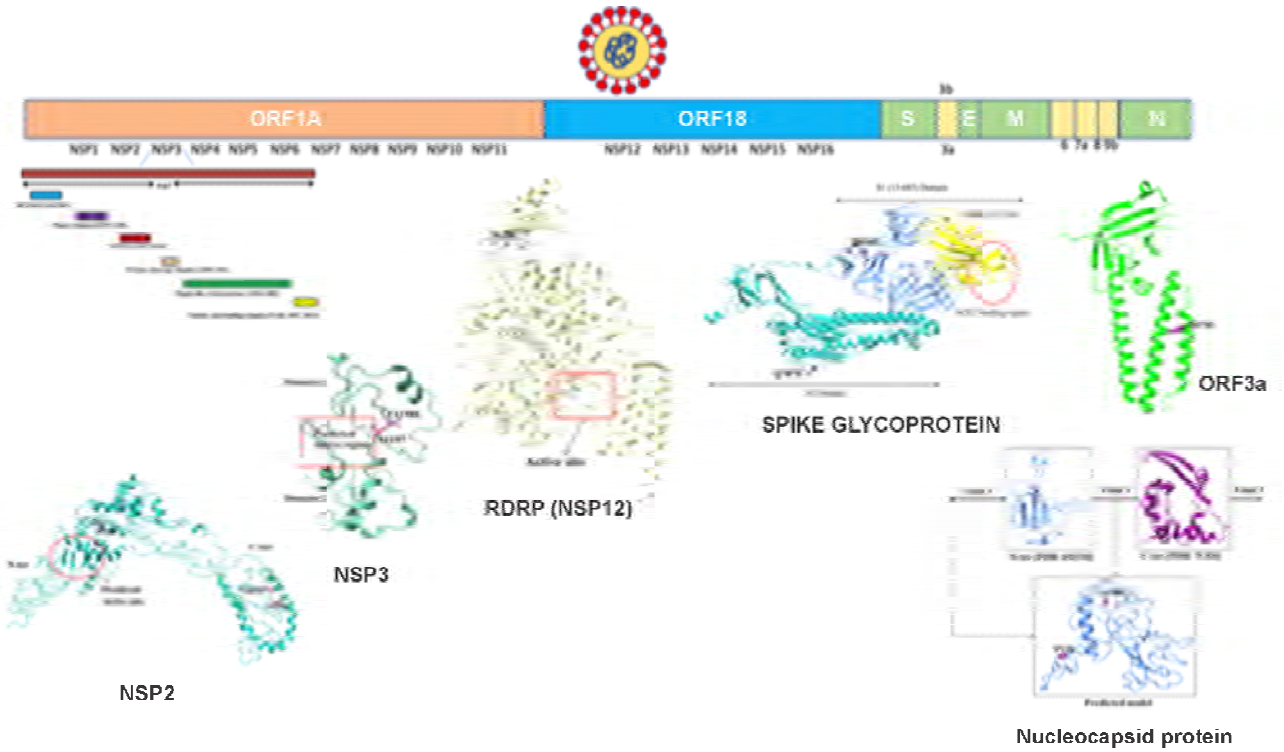
(ii) Assay for NETosis has been developed, and FDA approved drug library has been screened. The results have led to the identification of drug-repurposing candidates for repurposing against NETosis

(iii) A battery of assays to assess the immune system response and to counter / modulate excessive host immune response has been developed. Several interesting compounds have been identified through these assays.



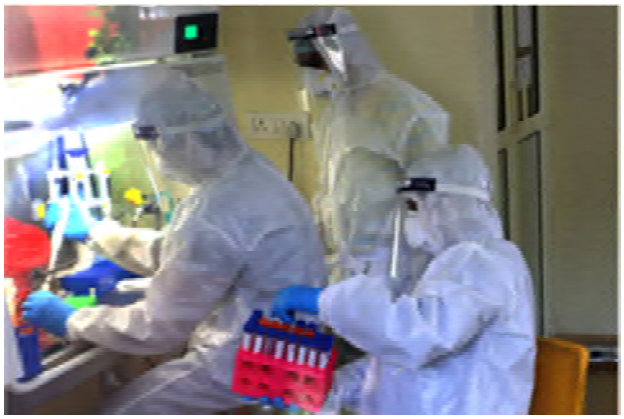
8.1.2 Sequencing of viral strains from patient samples to identify mutations and their implications for therapeutics

About 200 virus strains from patient samples predominantly from Uttar Pradesh have been sequenced. There are several interesting results and implications for the pathogenesis are being analyzed presently.



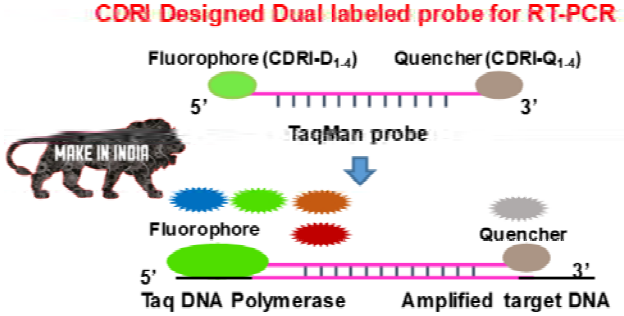
8.1.3 COVID19 testing of patient samples:

RT-PCR based SARS-CoV-2 screening laboratory with BSL2+ facility has been established at CSIR-CDRI. About 800-1000 samples are being tested daily. More than 1,25,000 patient samples have been tested in the testing lab till date.



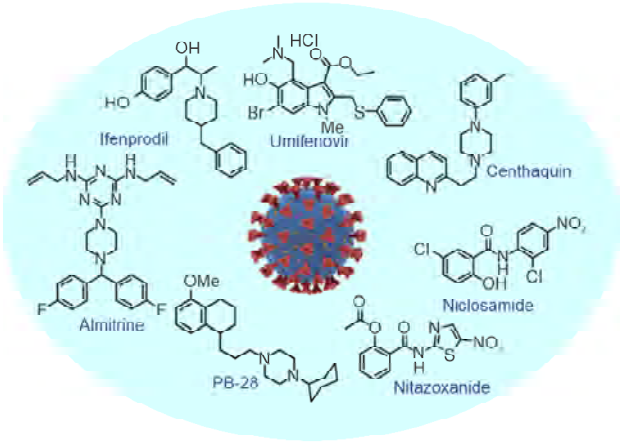
8.1.4 Diagnostics:

The cornerstone of COVID-19 containment is testing of the SARS-CoV-2 infection, followed by quarantine or treatment of the infected individuals. Currently, RT-PCR is the most robust and accurate method of testing for the SARS-CoV-2. Several fluorescent dyes and quenchers with a variety of excitation and emission characteristics were prepared for TAQMAN probes, which are used in qRT-PCR diagnostics of COVID-19. Our larger goal is a capacity building for India on the path to make India self-reliant without depending on the supply of key materials from foreign manufacturers. The technology of fluorescent dyes and quenchers has been licensed to a company for further development and commercialization.

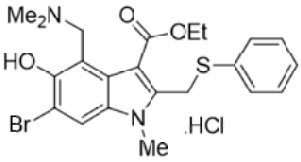


8.1.5 Drug repurposing and process technology development for API

Considering the pandemic situation due to COVID-19, enormous efforts have been made to identify lead drug candidates through repurposing route that could be the fastest way to find a cure for the deadly coronavirus. We shortlisted several drugs that were being investigated clinically towards nSARS-CoV-2 and prioritized 6-9 molecules for the development. The main criteria of the selection was efficacy, availability and speed to develop the viable process followed by clinical trials if necessary. Umifenovir, Niclosamide, Nitazoxanide, Almitrine, Ifenprodil, Centhaquin, PB-28 and Galidesivir are the drugs that were taken further for development. *Among above drugs, the process for the bulk scale preparation of Umifenovir (brand name Arbidol) was developed and the technology was transferred to the industrial partner, and a DCG(I) permission for the phase III clinical trial was received within the record period of three months*.



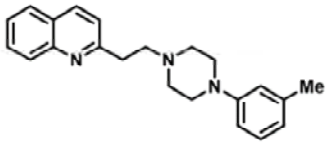
Umifenovir is an antiviral drug, which has been used for the treatment of influenza infection in Russia and China. This drug is presently unavailable to Indian patients. Umifenovir is being investigated as a potential treatment and prophylactic agent for COVID 19 caused by SARS-CoV-2 infections in combination with both currently available and investigational HIV therapies. At CSIR-CDRI we developed the improved and scalable process of Umifenovir on a multi-gram scale and this technology was transferred to our industrial partner Medizest Pharmaceuticals Pvt. Ltd., Goa.



Phase 3, Randomized, Double-blind, comparative trial of Efficacy, Safety and Tolerability of Umifenovir and

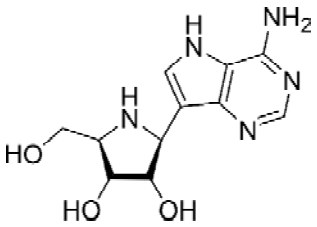
hydroxychloroquine combination therapy vs hydroxychloroquine therapy in non-severe COVID-19 patients is ongoing at 3 clinical trial sites.

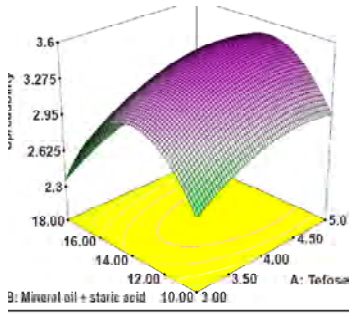
Centhaquin is another drug that was discovered at CSIR-CDRI for hypotensive response (US Patent No. US3983121A). The invention discloses synthesis of centhaquin and analogues, and its detailed pharmacological study in mice and cats. The molecule is safe [*LD50 in mice was 600 mg/kg. Intraperitoneally (i.p.)*], and *the compound produced dose dependent sustained fall of blood pressure starting from the dose of 10µg/kg to 0.5 mg/kg*. Very recently, a citrate salt of centhaquin is being pursued by different industries. The clinical study reports it to be immensely helpful *for the management of hypovolemic shock in critically ill COVID-19 patients* (US20150250782A1, WO2010127096A2, WO2019213558A1). The safety and tolerability of centhaquin was demonstrated in a human phase I study in 25 subjects (CTRI/2014/06/004647; NCT02408731). Clinical phase II results indicated that, centhaquin is potentially a novel first-in-class highly effective resuscitative agent for hypovolemic shock (CTRI/2017/03/008184; NCT04056065). Safety and highly significant efficacy in improving systolic and diastolic blood pressure, lactate levels and base-deficit in Phase III (CTRI/2019/01/017196; NCT04045327) studies in patients of hypovolemic shock was convincing to submit application of centhaquin for market approval for hypovolemic shock patients in India.). As per recent reports centhaquin is reported to be immensely helpful for managing hypovolemic shock in intubated patients in COVID-19. *Considering these findings, CSIR-CDRI further developed the improved process for the synthesis of centhaquin. Discussions with the industrial partners are currently underway for the marketing of this drug.*



PB-28 is a high affinity σ_2 receptor agonist with Ki values in range of 0.8 and 15.2 nM for σ_2 and σ_1 receptors respectively. A very recent study in nature (doi: 10.1038/s41586-020-2286-9) highlighted that ligands for σ_2 and σ_1 receptors can offer a solution in COVID-19. *Although there is no clinical data on patients however, in view of the recent data, the molecule was undertaken for the development at CSIR-CDRI. The team has developed the non-infringing route for the synthesis and required biological studies are currently underway.*

Galidesivir: Galidesivir (BCX4430) is a broad-spectrum investigational antiviral under consideration for the treatment of SARS-CoV-2 too. Galidesivir was safe and generally well tolerated in Phase 1 clinical safety and pharmacokinetics trials by both intravenous and intramuscular routes of administration in healthy subjects. In animal studies, galidesivir has demonstrated survival benefits against a variety of serious pathogens, including Ebola, Marburg, Yellow Fever and Zika viruses. Galidesivir has also demonstrated broad-spectrum activity *in vitro* against more than 20 ribonucleic acid (RNA) viruses in nine different families, including coronaviruses, filoviruses, togaviruses, bunyaviruses, arenaviruses, paramyxoviruses and flaviviruses. The drug is undergoing Phase II clinical trials for treating COVID-19. The synthesis of this drug involves more than 40 steps which makes its availability highly expensive. In a project directed towards building the capability of synthesizing antiviral drugs of significant importance, the synthesis of Galidesivir is being pursued using KSMs available within the country.





9

PRE-CLINICAL STUDIES & TRANSLATION

Area Coordinators: Dr. Sharad Sharma and Dr. Prabhat Mishra

Vision and Goal:

- Pre-clinical and clinical development of drug substances and drug products for diseases of national importance, international relevance and public health needs;
- Provision of services to the pharmaceutical industry, especially micro, small and medium enterprises and public sector manufacturers in areas of clinical trials, regulatory toxicology, safety pharmacology, pharmaceutics and pharmacokinetics;
- Continued engagement with drug regulation and pharmaceutical policy making in India as well as internationally

Core Competencies and Activities:

- Analytical and bio-analytical method development, quality assurance and stability studies on drug substances and drug products;
- Pre-clinical pharmacokinetics and metabolism of synthetic compounds and natural products in rodents, small animals and monkeys;
- Bio-analysis and pharmacokinetic modelling for clinical pharmacokinetics and metabolism including bioequivalence and bioavailability studies for generic medicines;
- Pre-formulation, 'Quality by Design' (QbD) formulation and process development for conventional and novel drug substances;
- Safety pharmacology of CSIR-CDRI candidate drugs under certified "Good Laboratory Practice" (GLP);
- Pre-clinical toxicology and toxicokinetics of candidate drugs as per international guidelines under GLP;
- Preparation of dossiers on new candidate drugs for regulatory filings;
- Protocol design, trial monitoring and coordination for Phase I to Phase IV clinical trials;
- Generation of information on mechanism of action, toxicity and metabolism of drugs and deployment of alternative model systems for assessing the efficacy of new chemical entities;
- Development of better and targeted drug delivery systems for CSIR-CDRI candidate drugs as well as existing drugs;

Front row (L to R): Dr. Amit Misra, Dr. Manoj K. Barthwal, Dr. Smrati Bhadauria, Dr. Prabhat Ranjan Mishra (Area Coordinator), Dr. Sharad Sharma (Area Coordinator), Dr. D.S. Upadhyay, Dr. S.K. Rath & Dr. Vivek Vidyadhar Bhosale

Middle row (L to R): Dr. Manish Kumar Chourasia, Dr. Jiaur Rahaman Gayen, Dr. Kashif Hanif, Dr. Prem N Yadav, Dr. Sachin Kumar, Dr. Anil Gaikwad, Dr. Kumaravelu Jagavelu, Dr. Wahajuddin, Dr. Sarika Singh, Dr. Baisakhi Mohrana & Dr. Shubha Shukla

Back Row (L to R): Dr. Rajdeep Guha, Dr. Rajkamal Tripathi, Dr. Rabi Sankar Bhatta, Dr. Madhav Nilakanth Mugale, Dr. Aamir Nazir & Dr. Dhananjoy Hansda

9.1 Pharmaceutics

9.1.1 Development, validation and deployment of methods of pharmaceutical analysis

Analytical methods were developed and validated according to the New Drugs and Clinical Trials Rules, 2019, for HPLC and LC-MS/MS analysis/bio-analysis of favipiravir.

9.1.2 Clinical formulation development for N020-001

N020-001 has exhibit anti-NETosis activity. Tablet formulation was developed with approved excipients. The formulation was found to be stable in accelerated stability testing condition and long term stability at room temperature is ongoing.

9.1.3 Clinical formulation development for S007-1500

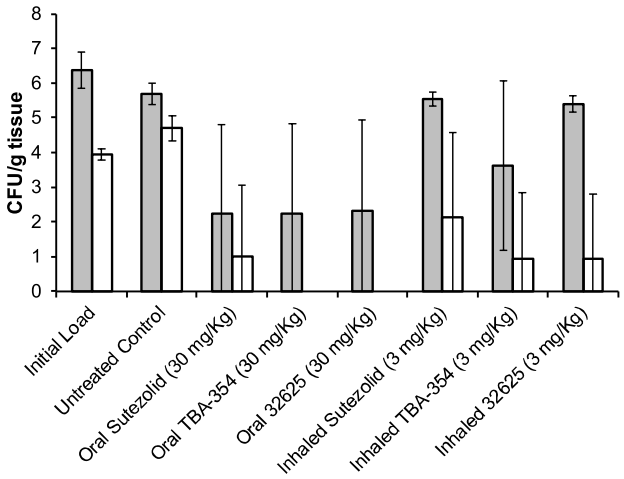
Tablet formulation of S007-1500 was developed for Phase-I clinical trial. The tablet formulation was developed at a strength of 1 mg, 10 mg and 40 mg to cover the dose escalation studies from 1 mg to 80 mg per individual. The formulation has completed six months of stability studies.

9.1.4 Inhalable particles containing anti-tuberculosis agents

The clinical testing plan has been submitted to the Institutional Ethics Committees of CSIR-CDRI and King George's Medical University. The trial has objectives of determining safety, pharmacokinetics and early measurement of drug activity.

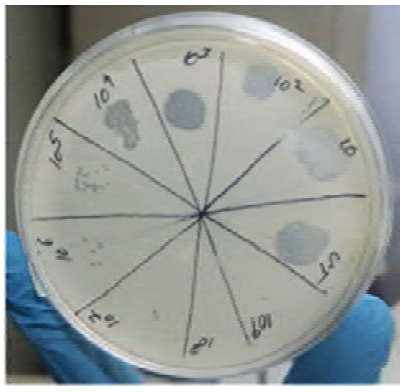
9.1.5 Inhalable particles containing drugs used in multi-drug resistant (MDR) tuberculosis

In collaboration with Prof. Gareth W Griffiths at the University of Oslo, inhalable particles containing sutezolid, TBA-354 and Compound 32625 provided by Prof. Andrew Thompson from The University of Auckland were evaluated in a mouse model of tuberculosis at the National JALMA Institute of Leprosy and Other Mycobacterial Diseases, Agra. The efficacy of the inhalable particles administered at 1/10th of the recommended oral dose was found to be comparable to the full oral dose in clearing bacterial from the lungs (*open bars in Figure below*), but not the spleen (*shaded bars*), as expected.



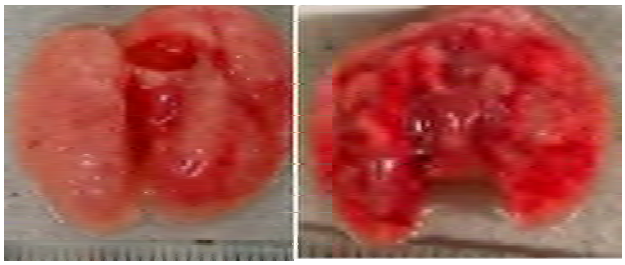
9.1.6 Inhaled mycobacteriophages for phage therapy of tuberculosis

Bacteriophages are viruses that kill bacteria. We received ICMR funding in collaboration with NJIL&OMD, IISER-Bhopal and AND College, University of Delhi to search for mycobacteriophages that kill *Mycobacterium tuberculosis* and could therefore be useful for treating tuberculosis (TB). Our primary responsibility in this collaboration is to prepare inhalable formulations of viable phages. In the reporting period, we and our colleagues isolated 28 phages and tested their ability to lyse TB bacteria. Only two of these were found capable of killing TB bacteria, and these are well-reported in the literature. We prepared dry powder inhalations using these phages. At this time, the phages are viable to the extent of 30% of the starting number used to prepare the formulation, and the formulation is stable only for 3 months. Efforts are underway to isolate more phages, and improve the viability and stability of the inhalable formulations. The Figure below shows plaques formed on a lawn of *Mycobacterium smegmatis* when different dilutions ranging from 1/10th to one billionth of the phage formulation were spotted in different sectors of the petri dish. If the phage preparation is diluted beyond 10 million times, the number of phages remaining is not detectable.



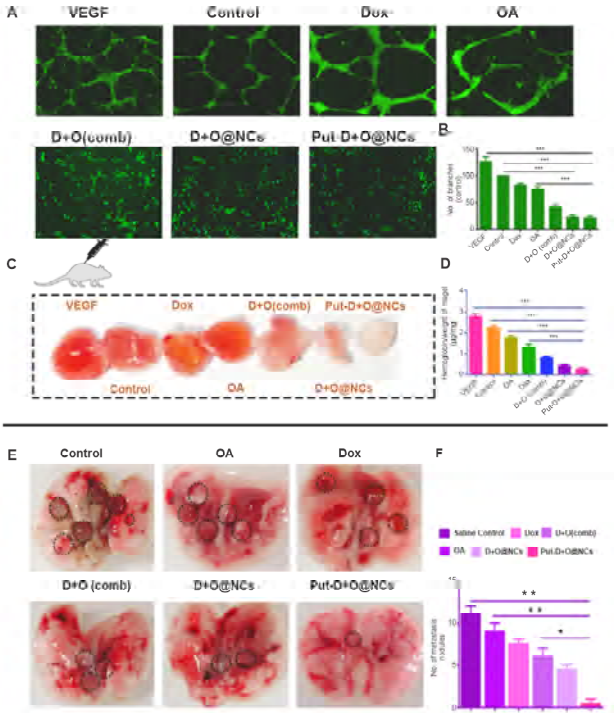
9.1.7 Transient transfection of the respiratory epithelium with gamma interferon to provide host-directed therapy in pulmonary tuberculosis

Pulmonary tuberculosis (PTB) is caused by intracellular pathogens like *Mycobacterium tuberculosis* (Mtb) and congeners in a fraction of the population that is infected by the bacteria. Nebulized gamma interferon (IFN-γ) has shown clinical efficacy against multiple drug resistant (MDR) PTB. Because IFN-γ protein is expensive, thermolabile and requires a cold chain for field deployment, it is not suitable for limited resource settings. We established preclinical proof of concept of the efficacy of inhaled plasmid DNA engineered to express IFN-γ protein in the mouse respiratory epithelium for host-directed therapy of PTB. The Figure below shows the healed lungs of a mouse that received 3 ng of DNA once a week for 3 weeks after being infected with Mtb 4 weeks in advance of treatment on the left, and the lungs of another mouse that had been infected at the same time but received no treatment (right). To our knowledge, this is the first report of transient gene therapy. The untreated animal's lungs bore several lesions, while the treated animal's lungs were free from lesions. When we cultured lung homogenates, we found that the average number of colony forming units (CFU)/gram of tissue was about 1 million in untreated animals and one hundred in treated animals. Thus, gene therapy reduced the bacterial load by four orders of magnitude in just 3 weeks. ***(Molecular Therapy- Nucleic Acids, 2020;22: 1121-1128).***



9.1.8 Development of Putrescine anchored nano-crystalsomes bearing Doxorubicin and Oleanolic acid-Deciphering its role in inhibiting metastatic breast cancer

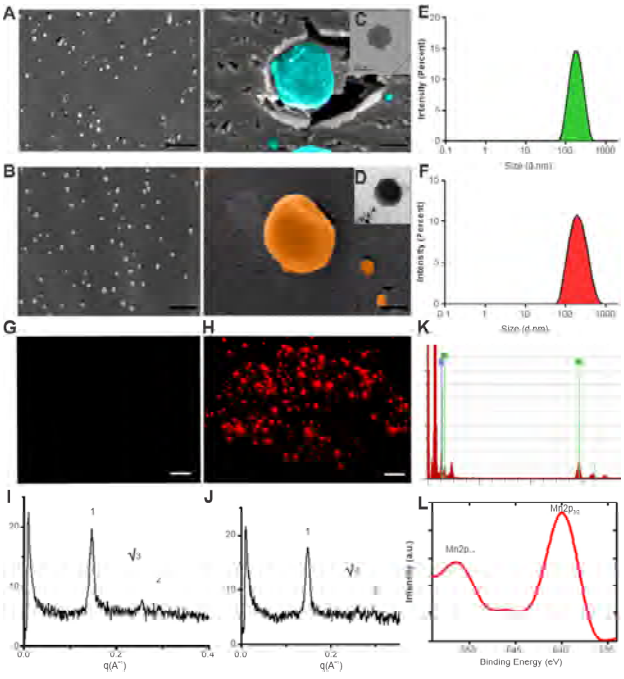
Angiogenesis driven tumor initiation and progression calls for a targeted therapy. In the line of context, we envisaged to develop a targeted crystalosomes delineating the tumor cells against the normal cells. A self-assembled crystalline monodispersed nanosized PE-PEGbased hollow crystalsomes has been modified with pluronylated putrescine (Put-PF) and loaded with Doxorubicin (Dox) synergistically in combination with Oleanolic Acid (OA) to target the glypican-1 (gp-1) receptor on tumor cells. The developed crystalsomes (PutD+O@NCs) showed an increased intracellular accumulation of Dox and OA in synergistic combination inside the MDA-MB-231 cell lines. The developed crystalsomes marked an enhanced depolarization of mitochondrial membrane potential and cell cycle arrest leading to apoptosis. Furthermore, the proposed therapy has greater anti-angiogenesis activity with VEGF dependent modulation in proliferation, invasion, migration and tube formation of HUVECs *in vitro* and *in vivo* on Balb/c mice model. Interestingly, the perseverance of the tumor boundary by inhibiting the expression and activity of the matrix metalloproteinase (MMPs) (>5.2-fold) with suppressed degradation of the extracellular matrix pave for significant inhibition of metastases. However, an intravenously administered Put-D+O@NCs showed an improved pharmacokinetic profile and exquisite inhibition of 4T1 induced tumor with significantly lower toxicity. In a nutshell, these finding highlights the important role of Put for gp-1 receptor for specific targeting and synergistic delivery of Dox and OA through crystalsomes as a potential approach for metastatic breast cancer using combined chemotherapy ***(Biomaterial Science 2020 dio.org/ 10.1039/DOBM01033B)***.



9.1.9 Theranostic lyotropic liquid crystalline nanostructures for selective breast cancer imaging and therapy

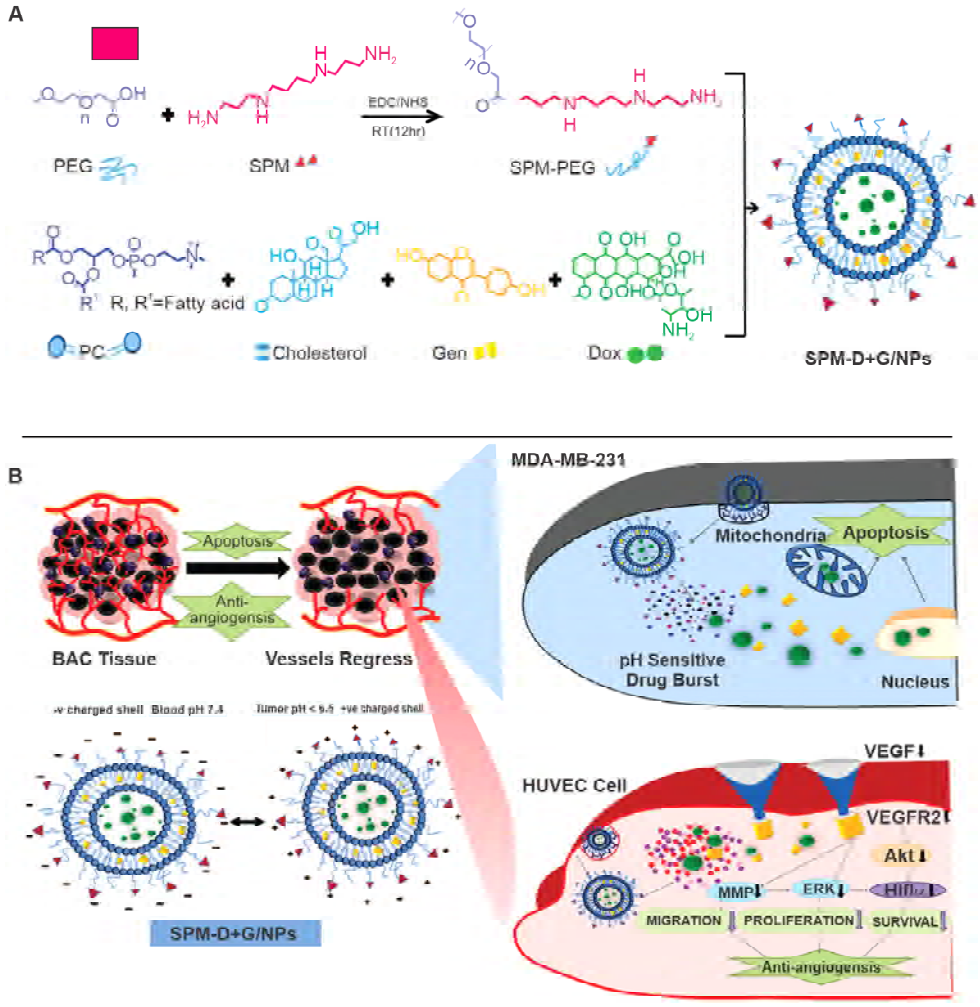
We have developed a theranostic lyotropic liquid crystalline with chemodynamic approach and fluorescent diagnostic capabilities for the first time in a cancer

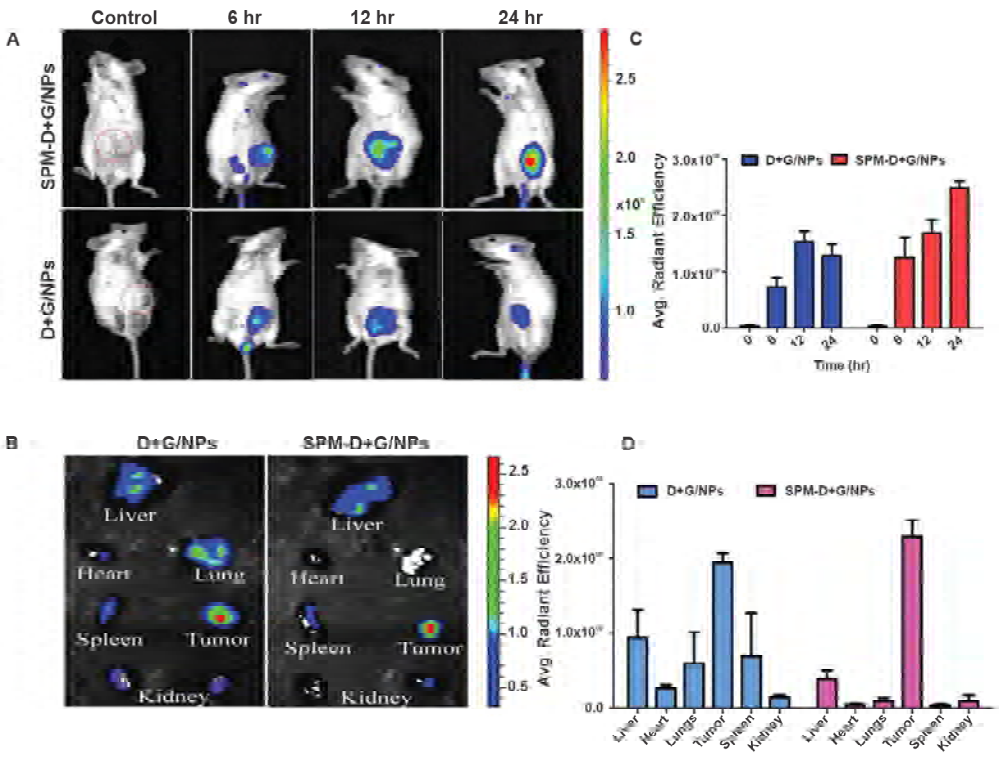
prevention perspective. Mn^{2+} generates free OH • radicals in the presence of H_2O_2 and, unlike Fe^{2+}, catalyzes a Fenton reaction even in mild acid pH. This was confirmed by the detection of free OH • radical generation by HPF and TA-based fluorescence test in a cancer extra-cellular environment (pH 6.4) and endosomal / lysosomal pH (pH 5.5). In LCN's, MO complex also served as a gateway for drug release. A clear picture of pH-dependent ionization and decent release of Mn^{2+} ions and BA was observed in the *in vitro* release study. Chemo- dynamic therapy strategy used in this investigation employs Mn^{2+} generated reactive oxygen species (ROS) as a weapon to annihilate cancer cells with oxidative stress. Results showed that LCN's not only inhibited the growth of cancerous cell lines (MDA-MB-231 and 4T1 cells) but also ensured the safety of normal cells (HEK cells) due to slow drug release and substantially suppressed Fenton reaction in the normal cell microenvironment. BA was loaded into LCN's (LCN@Mn-BA) to synergize the anti-cancer activity of Fenton's reactant-Mn. The cell viability of MDA-MB-231 has been reduced to 40 % for Mn + BA cocktail and 17% for LCN@Mn-BA treated cells compared to control. In addition to having anticancer activity, the LCN@Mn-BA had the ability to diagnose it, MNPs loaded in it possessed the tunable excitation-dependent fluorescence emission over the entire visible spectral region. In cellular uptake studies, this intrinsic fluorescence helped to track nanoparticles without further conjugation or encapsulation of secondary fluorescent nanoprobe. Additionally, LCN@Mn-BA's optical imaging property was used *in vivo* and *ex vivo* imaging studies to study nanoparticles distribution in tumor-bearing mice model. *In vivo* tumor suppression studies on the 4T1 xenograft mice model, a reasonable effect of tumor regression was observed in both LCN@Mn-BA and Mn + BA cocktail treated groups. According to the quantitative tumor growth inhibition index (TIX), LCN@Mn-BA's TIX rate was 97±3% and for Mn + BA cocktail 75±4% as compared to control. Overall, the fluorescent and Fenton-type catalyst loaded LCN's developed in this study could be a comprehensive nano-theranostics for breast cancer bio-imaging and chemodynamic therapy ***(Acta Biomaterialia 2020, 113, 522-540)***.



9.1.10 Multifunctional hybrid nanoconstructs facilitate intracellular localization of doxorubicin and genistein to enhance apoptotic and antiangiogenic efficacy in breast adenocarcinoma

The progressive development of tumors leading to angiogenesis marks the advancement of cancer which requires specific targeted treatment preferably with combination chemotherapy. However, there is still a long way to go to develop an efficient delivery system that could overcome the tumor microenvironment to achieve efficient delivery. Therefore, we have developed spermine (SPM) tethered lipo-polymeric hybrid nanoconstructs with cell surface heparan sulfate proteoglycan (HSPG) specificity for higher intracellular localization and pH dependent charge reversal in the tumor microenvironment (below pH 5.8) to facilitate Doxorubicin (Dox) and Genistein (Gen) release in a synergistic combination. We have observed the specific uptake of SPM anchored hybrid nanoconstructs by receptor-mediated endocytosis in human breast cancer cells (MDA-MB-231) through the HSPG receptor. The SPM-D + G/NPs induced a higher rate of apoptosis in MDA-MB-231 cells via disruption of the mitochondrial membrane potential and also exhibited a stronger anti-angiogenic effect governing the inhibition of VEGF pathway modulation, proliferation, invasion and migration of HUVECs in *in vitro* and *in vivo* Balb/c mouse models. The involvement of Akt/Hif1α/VEGF dependent signal cascading and its down-regulation with a pro-apoptotic drug Dox and an anti-angiogenic agent Gen was evident as demonstrated by an in silico docking study and subsequently proven by RT-PCR and western blotting. The tumor regression studies confirm that the treatment with SPM-D + G/NPs led to a significant decrease in tumor growth, and angiogenesis by directing the Akt/Hif1α/VEGF axis as compared to that with Dox and Gen alone and their combination. Interestingly, the findings show the efficient co-delivery of Dox and Gen using HSPG-targeted NPs, and *in silico* docking results show direct binding of Dox and Gen to key proteins (Akt, Hif1á and VEGFR2) leading to a significant decrease in mRNA and protein levels of Akt, ERK, Hif1α, VEGF-A, VEGFR2, MMP-2 and MMP-9 in human breast cancer cell lines (MDA-MB231) and a xenograft mouse model system.

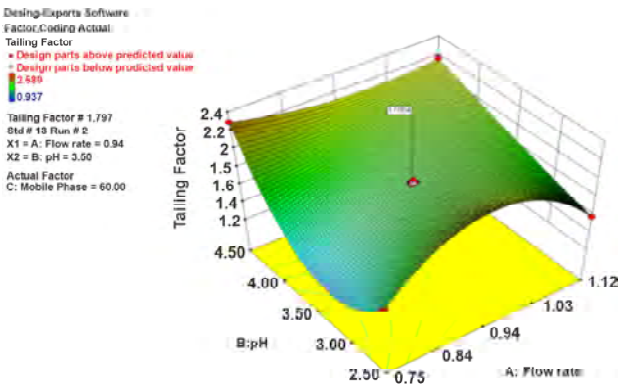

A
PEG
SPM
EDC/NHS
RT(12hr)
SPM-PEG
R, R'=Fatty acid
PC
Cholesterol
Gen
Dox
SPM-D+G/NPs
B
Apoptosis
Anti-angiogenesis
BAC Tissue
Vessels Regress
MDA-MB-231
Mitochondria
Apoptosis
pH Sensitive Drug Burst
Nucleus
SPM-D+G/NPs
HUVEC Cell
VEGF
VEGFR2
Akt
MMP
ERK
MIGRATION
PROLIFERATION
SURVIVAL
Anti-angiogenesis


A
Control
6 hr
12 hr
24 hr
SPM-D+G/NPs
D+G/NPs
C
Avg. Radiant Efficiency
D+G/NPs
SPM-D+G/NPs
Time (hr)
B
D+G/NPs
SPM-D+G/NPs
Liver
Heart
Lung
Spleen
Tumor
Kidney
D
Avg. Radiant Efficiency
D+G/NPs
SPM-D+G/NPs
Liver
Heart
Lungs
Tumor
Spleen
Kidney

Altogether this study highlights the potential role of SPM in targeting HSPG receptors and synergistic delivery of Dox and Gen as a promising strategy to effectively inhibit BAC progression and these findings could open a new window to deliver combinations of chemotherapeutic agents along with anti-angiogenic ligands using hybrid nanoparticles ***(Biomaterial Science, 2020, 8, 1298-1315)***.

9.1.11 Bioavailability enhancement of bortezomib

Poor water solubility and low intestinal permeability of bortezomib restricts its bioavailability and therapeutic uses. In the present study we have developed and characterized BTZ loaded oral nanoemulsion by high energy emulsification method, well optimized by DoE software (version 8.0.4) using central composite design (CCD) for the amount of Solutol® HS-15 (6.2%) propylene glycol (6.2%) Caproyl 90 (3.7%). Furthermore, RP-HPLC method was also developed by applying Box-Behnken design (BBD) to quantitate the bortezomib entrapped in oral nanoemulsion as per ICH Q2R1 guidelines with r^2 value 0.999, LoD (0.014 µg/ml), LoQ (0.045 µg/ml) and recovery 100± 2%. *In vitro* drug release (48% in PBS pH 6.8) and cytotoxicity study (IC_{50} value = 72 nM after treatment of 72 hrs) on MDA-MB-231 cell line was performed. 3D model graph for tailing factor is presented in the following figure.

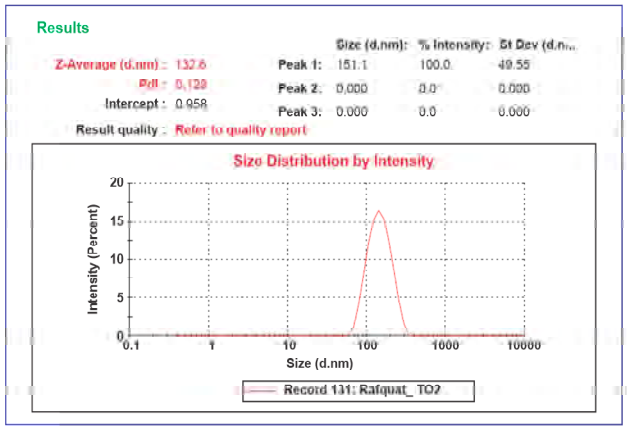


9.1.12 Oral sustained released formulation to control alcohol induced dose dumping

The purpose of this work was to control the alcohol-induced dose dumping through proposed delivery system. A successful sustained released (SR) matrix tablets has been developed by using different kind of polymers like HPMC, HPMC K 100M, HPMC K-4, PVP-K30, talc, lactose, xantham gum, microcrystalline cellulose, and methylcellulose. The SR matrix tablet has been prepared using wet granulation technique and characterized on the basis of pre-compression and post-compression quality control parameters. For the estimation of proposed formulation, a simple and sensitive analytical method has been developed by applying QbD approach and the method has been validated as per ICH Q2 R1 guideline.

9.1.13 Mitochondria targeted thyme nanoemulsion: Therapy for breast cancer

In the proposed work we have envisaged fabricating a surface modified thyme oil nanoemulsion with dequalinium, incorporating bortezomib. A mitochondria-specific nanocarrier system has been prepared from the amphiphilic quinolinium derivative dequalinium chloride to deliver bortezomib to mitochondria in cells to improve the pro-apoptotic action of bortezomib. The electrostatic interaction between adjacent dequalinium molecules at periphery conserves the size of nanoemulsion in the core even after modification, hence shall prolong its circulation time. The core nanoemulsion loaded with bortezomib has been prepared and characterized for size and surface zeta potential using Malvern zetasizer. Conjugation of dequalinium on to the periphery of thyme nanoemulsion and its characterization will be further studied. Representative histogram showing size and zeta potential of formulation is shown in the following figure.



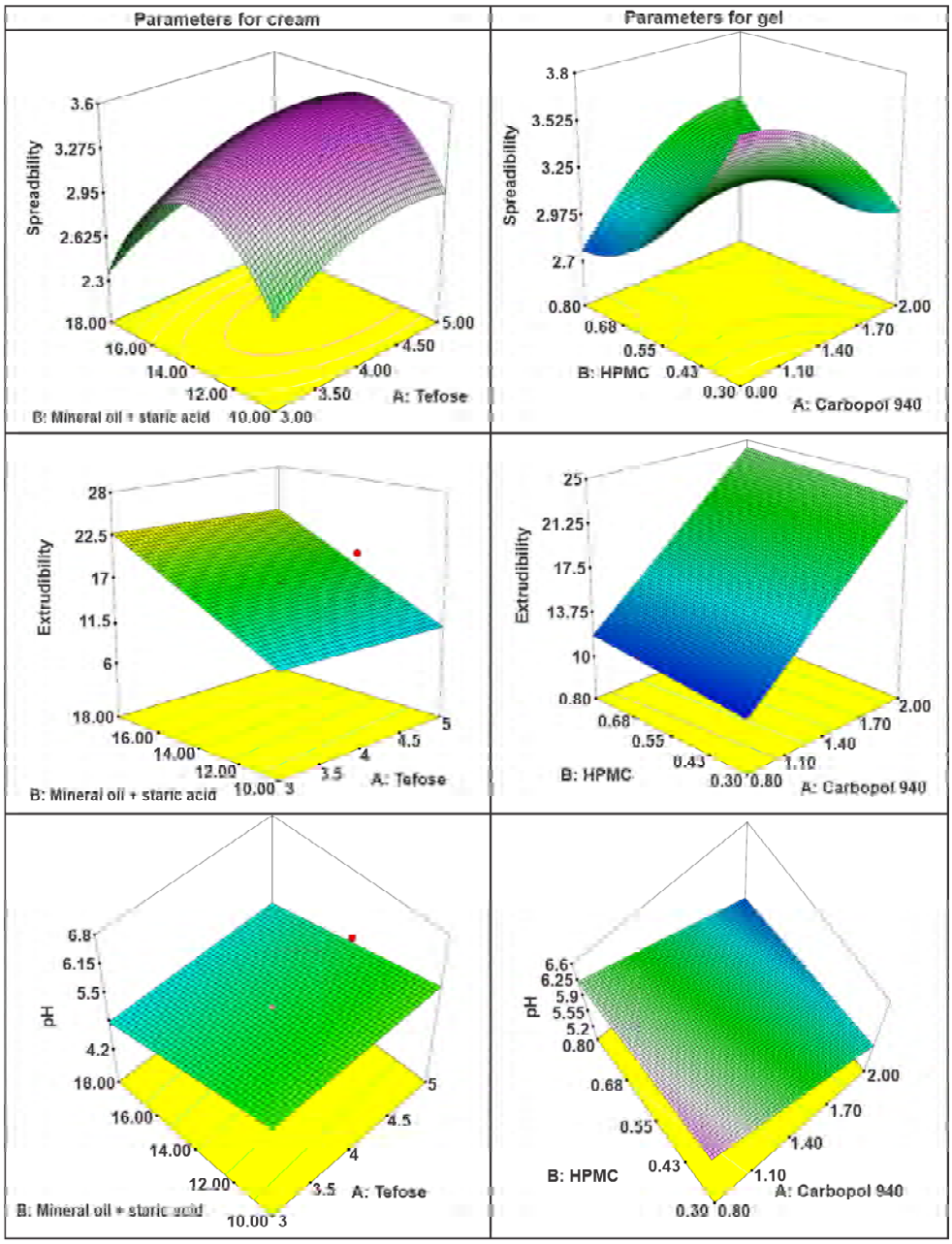
9.1.14 Analytical method development for estimation of levofloxacin: Application in estimation of drug in nano-formulations and pharmacokinetic studies

A simple, robust, selective and sensitive HPLC analytical method has been developed, optimized through DoE and validated as per ICH Q2R1 used for the determination of levofloxacin encapsulated inside

nanocarrier as well as in plasma. Levofloxacin was extracted from plasma using liquid-liquid extraction using validated HPLC method at 295 nm. The developed method can be used for rapid estimation of levofloxacin in nano-formulations without shift in retention time. Development of a method that uses minimal solvents with least preparation time also helps in reducing the errors generated by the analyst during processing.

9.1.15 Development of topical formulations bearing phytochemicals for wound healing

The topical gel and cream formulations were intended to be prepared to enhance the administerability and permeability of hydroalcoholic extract with wound healing capacity. Initially the excipients were subjected to solubility, compatibility, and optimization investigation. For solubility and compatibility various excipients were mixed together in the proportion to be used in topical formulations i.e. gel and cream and kept for 2 weeks for observation. For optimization were done using quality by design approach applying central composite design from response surface methodology. Moreover, surfactant component, oil phase, buffering agent and water component were set as independent variables for the characterization of spreadability, extrudability, pH as dependent variables. The placebo systems with the most appropriate characterization results have been optimized and shall be used to prepare the polyherbal formulations incorporating plant extracts. Figure representing the optimized composition-response parameters based on the central composite design as follows.



9.1.16 Optimization and development of analytical method for Donepezil through Quality based Design approach

The present work is focused on development of a simple, precise, rapid and cost effective analytical method for donepezil using QbD approach. The RP-HPLC method has been optimized through response surface methodology using BBD design with 17 runs and 3 independent variables as well as 3 dependent variables. Mobile phase composition, flow rate and column oven temperature has been varied to optimize the AUC, NTP and tailing factor. In conclusion, a method with MilliQ (pH-3): methanol (60:40) as mobile phase, flow rate (0.63 mL/min) and column oven temperature (39.92 °C) has been optimized. It has been validated for various parameters including linearity, LoD and LoQ, system suitability, recovery, robustness, method precision, intermediate precision, solution stability, specificity, filter paper interference as per regulatory Q2 R1 guidelines. Thus, the present study entails a robust analytical method with low cost solvents in minimal amount, least run time and rapid estimation for donepezil.

9.2 Pharmacokinetic studies

9.2.1 Topical corneal targeted sustained release amphotericin B liposomal formulation for the treatment of fungal keratitis and its PK-PD evaluation

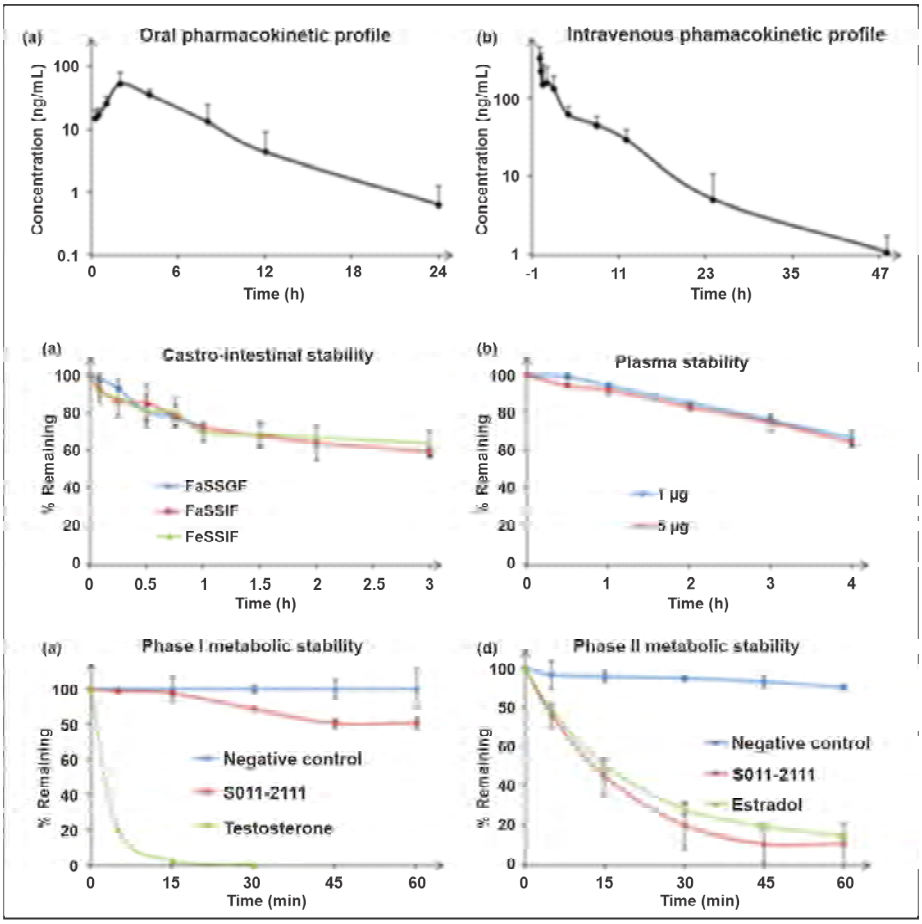
The present study reports topical ocular prolong residence amphotericin B (AB) liposomal formulation. The AB was entrapped within liposome (AB-liposome) with a size range of 142 ± 0.11 nm. The AB-liposomes powder was prepared by an optimized freeze-drying process with cryoprotectant for reconstitution before use. Liposomes showed biphasic release, initial fast release followed by sustained release. AB-loaded liposomes significantly increase $t_{1/2}$ (half-life), MRT (mean residence time) and AUC (area under the curve) in comparison to the current clinically available formulation. The formulation has significantly increased corneal bioavailability of AB.

9.2.2 Rapid and simultaneous analysis of multiple classes of antimicrobial drugs by Liquid Chromatography-Tandem Mass Spectrometry and its application to routine biomedical, food, and soil analyses

Antimicrobial agents (AMAs) are widely exploited nowadays to meet the high demand for animal-derived food. It has a significant impact on the food chain whose end consumers are human beings. The burden of AMAs on humans comes from either meat or crops cultivated on soil containing high residual antibiotics, which are responsible for the global crisis of antibiotic resistance. Thus, the objective of this study was to design a selective and sensitive liquid chromatography–mass spectrometry (LC-MS)/MS-based simultaneous bioanalytical method for estimation of twenty AMAs in human plasma, raw meat, and soil samples. The selective extraction of all analytes from the above matrices was performed by the solid-phase extraction clean-up method to overcome the interferences. Analytes were separated on a Waters Symmetry Shield C18 (150 × 4.6 mm2, 5 µm) column, using an isocratic solvent system of methanol–0.5% formic acid (80:20, v/v) with 0.75 mL/min flow rate. The average extraction recoveries for all analytes in plasma were ranged from 42.0 to 94.0% with relative standard deviations (RSDs) below ±15%. All of the validation parameters are in accordance with the United State Food and Drug Administration guidelines. Moreover, the method was also valid for a broad plasma concentration range and can be proposed as an excellent method for routine pharmacokinetic studies, therapeutic drug monitoring, clinical analysis, and detection and quantitation of AMA remnants in raw meat as a standard quality control test for human consumption.

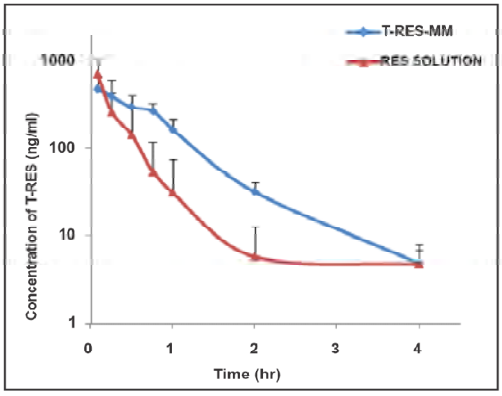
9.2.3 Pharmacokinetic studies of anticancer compound S011-2111

S011-2111 is a semicarbazone and chalcone hybrid demonstrating antiproliferative tumor cell-selective effects along with unique antimetastatic potential by mitigating PP2A-β-catenin signaling pathway. The present study envisaged to explore the *in vitro* and *in vivo* pharmacokinetics of S011-2111. A sensitive and selective liquid chromatography-tandem mass spectrometry bioanalytical method was developed and validated to determine S011-2111. It has high permeability across intestinal membrane as observed in *in situ* single-pass intestinal perfusion study. It has high plasma protein binding and poor aqueous solubility. It was rapidly partitioning into plasma of blood, where it was moderately stable. In mice liver microsomal stability study, S011-2111 was stable against cytochrome P450 enzymes but undergoes rapid glucuronidation with intrinsic clearance of 148.6 ± 48.3 µL/min/mg. Following 100 mg/kg oral dosing of S011-2111, the compound was detectable in the plasma samples up to 24 h with a maximum plasma concentration of 45 ± 16.5 ng/mL at 2.4 ± 0.1 h and absolute bioavailability of 1.68%. Knowledge from this research will assist in further development of S011-2111 as an anti-cancer agent.

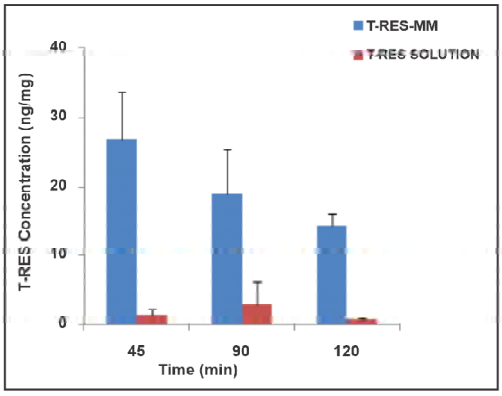


9.2.4 Pharmacokinetics and Brain targeting of Trans-Resveratrol

Trans-Resveratrol (T-RES) is compound with wide therapeutic applications shows low bioavailability and distribution across blood-brain barrier. The purpose of our study was to develop T-RES loaded mixed micelle (T-RES-MM) for its enhanced systemic availability and targeting to the brain. T-RES-MMs were formulated using Pluronic F-127 (PF-127) and d-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) by using film hydration process. Formulations were characterized for size of particles, zeta potential, drug efficiency of entrapment, drug loading, and haemolytic study. Further *in vivo* pharmacokinetic and brain distribution study carried out in Sprague Dawley rats. The nano ranged size for drug loaded mixed micelles was 21.55±2.15 nm for optimized formulation with PF-127:TPGS (4:1). Formulation with maximum drug loading and entrapment efficiency of 8.4±0.37% and 94.37±1.01%, respectively were further used for *in vivo* study. Percent haemolysis by micelles at all concentrations indicates the biocompatibility and safety for administration by i.v. route. The AUC_{0-t} for T-RES-MM was 460.98±158.99 hr*ng/mL while for T-RES it was 276.27±174.05 hr*ng/mL. Drug targeting index suggests successful targeting of T-RES to the brain. From the overall findings it was concluded that prepared T-RES-



(a)

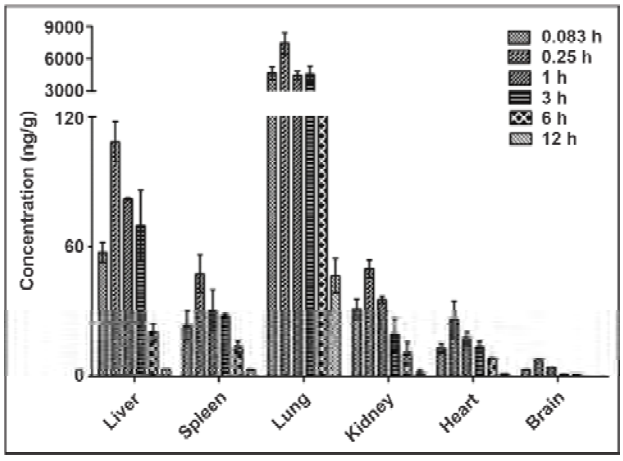


(b)

MM exhibit superiority of formulation as compared to T-RES solution.

9.2.5 Pharmacokinetics and tissue distribution of Withanolide A in rats: A neuroprotective steroidal lactone

Withanolide A (WA), a steroidal lactone is a major bioactive constituent of *Withania somnifera* (L.) with remarkable neuropharmacological activity. In the present study, we investigated the permeability, plasma protein binding, blood partitioning, intravenous (i.v.) and oral pharmacokinetics as well as i.v. tissue-distribution (TD) of pure WA in a rat model. The plasma protein binding, RBCs partitioning, and permeability of WA were determined by UPLC method. However, the pharmacokinetics and TD of WA were evaluated by validated and sensitive liquid chromatography coupled tandem mass spectrometry (LC-ESI-MS/MS) method. The plasma protein binding and permeability of WA were determined by equilibrium dialysis and parallel artificial membrane permeability assay (PAMPA) method, respectively. The results demonstrated that WA has high plasma protein binding and passive permeability. Furthermore, WA was found to have fast equilibration between RBCs and plasma. Following i.v. (2 mg/kg) and per-oral (25 mg/kg) administration of WA, the max concentration (Cmax) in plasma was found as 85.53±6.54 and 48.04±5.78 ng/mL, respectively. The tissue-distribution study results indicated that WA has a rapid and wide tissue distribution. The maximum concentration in various tissues was found in following order: Clung > Cliver > Ckidney ≈ Cspleen > Cheart > Cbrain. The preclinical *in vitro*, as well as pharmacokinetics and tissue-distribution results, are anticipated to support the future preclinical and clinical application of WA.



9.3 Regulatory Toxicology Science

9.3.1 14 Days Repeat Dose Toxicity study of S011-1793 in SD Rats by Oral Route with 7 days reversal.

We have completed the 14 days toxicity studies of antimalarial S011-1793 in SD rats by oral route with 7 days reversal in GLP mode. Report submitted to PI and archived in the CADC of CDRI.

9.3.2 90 Days Repeat Dose toxicity studies of *Cassia occidentalis* Lin. Extract (219/C003) in SD Rats by oral route.

We have completed the 90 days toxicity studies of phytopharmaceutical (219/C003) for bone health (corticosteroid induced osteoporosis) in SD rats by oral route with 14 and 28 days reversal in GLP mode. No toxicity was observed, report submitted to PI and archived in the CADC of CDRI. Toxicity study in non-rodent is required.

9.3.3 S007-1500: *In vitro* Chromosomal Aberration Study in Human Peripheral Blood Lymphocytes

In vitro chromosomal aberration study in human peripheral blood lymphocytes has been performed for assessing aberration of chromosomes following exposure to **S007-1500** in three doses. One hundred metaphases per sample are being evaluated. The results will be compiled by the end of January.

9.3.4 S007-1500: Male fertility study in SD rat by oral route

Fertility of males are being evaluated in three doses of test item **S007-1500.** Male SD rats were subjected to treatment for 54 days and then exposed to females in 1:2 ratio for three cycles. Three doses were checked and the compound is found to be not affecting the fertility of males.

9.3.5 28 days repeat dose toxicity study of DIBER-1: herbal health supplement (HHS C-8) in SD rats by oral route.

We evaluated an Ayurvedic mixture of herbal health supplement (HHS C-8) of DRDO supplied by DIBER coded as DIBER-1in SD rats by oral route. 28 days repeat dose toxicity studies did not show any significant alteration.

9.4 Clinical and Experimental Medicine

9.4.1 Phase 3 clinical trial of antiviral drug Umifenovir for COVID-19:

The WHO has declared COVID-19 as pandemic. There is no approved therapy for corona virus disease. Umifenovir (also known as Arbidol) is another antiviral agent that has been approved in China and Russia for treating influenza, SARS, and Lassa viruses. A limited number of case reports showed that patients with COVID-19 successfully recovered after receiving Umifenovir treatment. CSIR-CDRI received IND permission form Drugs Controller General of India to conduct phase 3 clinical trial of antiviral drug Umifenovir for treatment of COVID-19. This multicentric trial is ongoing at three centers at King George Medical University, Lucknow, RML Institute of Medical Sciences, Lucknow, and Era's Lucknow Medical College & Hospital, Lucknow. More than 50% recruitment is over.

9.4.2 Phase 1 clinical trial of antiplatelet drug S007-867

As per recent WHO report, cardiovascular diseases (CVD) are the number 1 cause of death globally: more people die annually from CVDs than from any other cause. The heart attacks and strokes are usually acute events and are mainly caused by a blockage that prevents blood from flowing to the heart or brain. An antiplatelet drug reduces blood aggregation and reduces thrombus formation to reduce morbidity and mortality. S007-867 is a novel antiplatelet agent discovered and developed by CSIR-CDRI Lucknow. It selectively inhibits collagen mediated platelet activation resulting in reduced bleeding risk than existing therapies. The permission for conducting phase 1 clinical trial in healthy volunteers has been received from Drugs Controller General of India. The trial has been planned at Seth G.S. Medical College & KEM hospital Mumbai.

9.4.3 Phase 1 clinical trial of fracture healing drug S007-1500.

According to the World Health Organization, road traffic injuries are the sixth leading cause of death in India. Diseases like osteoporosis also pre-dispose populations to increased fracture risk. Presently, there is no FDA approved orally active drug available in the market worldwide for fracture healing. There is unmet medical need to develop fracture healing drugs. S007-1500 is a bone fracture healing agent developed by CDRI Lucknow. It is a synthetic pterocarpan. It has potential osteogenic property and shows accelerated fracture repairing. New bone formation at the fracture site is increased by ~40% in rats treated with S007-1500. The preclinical experiments and toxicity studies in rodents and Dogs has been completed. The IND application has been filed for conducting phase 1 clinical trial in healthy volunteers. The study is planned at King George Medical University, Lucknow and will start after permission from DCGI.

9.4.4 Phase 3 multi-centric clinical trial of Immunobooster polyherbal formulation.

"Immune boosting" is a trending topic during the COVID-19 pandemic. This immunity booster formulation use power of Ayurveda – a 5000 year old Indian science. It may increase immunity and defend against multiple viral and bacterial diseases. The Immunity builder (Immune system booster) uses aqueous extracts of multiple herbs. A phase 3 clinical trial of this polyherbal formulation for COVID-19 has been planned and will start after its marketing approval by FDA.

9.4.5 Phase 3 Clinical trial of Picroliv for non alcoholic fatty liver disease (NAFLD) by ICMR

The picroliv herb has been standardized at CSIR-CDRI. It has been tested in animal models of NAFLD and found effective. The phase 3 clinical trial has been planned in collaboration with ICMR. The IND application preparation is in process. The trial will begin after approval from DCGI in phytopharmaceutical mode.

9.4.6 A case control clinical study to assess the early risk of complications in young patients of metabolic syndrome by genetic, biochemical and biomarker estimation methods.

The study is ongoing in collaboration with King George Medical University. The three groups are under investigation. Young and middle aged individuals with metabolic syndrome, and complication are compared with healthy individuals of same age groups. Hematology and biochemical parameters are being compared. There are significant changes in hematology and biochemical parameters. It is advisable to do have preventive checkup for healthy adults for early identification of complications.

9.4.7 NABL accreditation from Quality Council of India: Received accreditation from QCI in this year for clinical laboratory.

9.4.8 Extension of scope of GLP facility: Repeat dose toxicity study is added to the Scope of our GLP facility of preclinical studies.

9.5 NABL Accreditation for Medical Testing Laboratory

CSIR-CDRI received NABL accreditation for Medical testing laboratory from Quality Council, Government of India. The laboratory work involves Hematology and Biochemistry testing of Human samples. The facility was recognized and received certificate no. QAS-BC-Entry Level-00063 dated 6.6.2020. The certificate is valid for three years. The NABL accreditation increases confidence in Testing/ Calibration Reports issued by the laboratory. The NABL accreditation is mandatory for testing done in clinical trials. The supervision of NABL activities and contact person for NABL is medical professional Dr. Vivek Bhosale M.D. The consultant pathologist is Dr. Sharad Sharma. The other staff involves Dr. Shail Singh, Mr. M.P.S. Negi, Mr. Umesh Kumar and Mr. Ravi with support from department of Toxicology and Experimental Medicine, SAIF division and others.

National Accreditation Board for Testing and Calibration Laboratories
(A Constituent Board of Quality Council of India)

CERTIFICATE

Criteria: NABL 128 (Quality Assurance Scheme for Basic Composite Medical Laboratories - Entry Level)

Certificate No.: QAS-BC-Entry Level-00063

Issue Date: 06-06-2020

Valid till: 05-06-2023

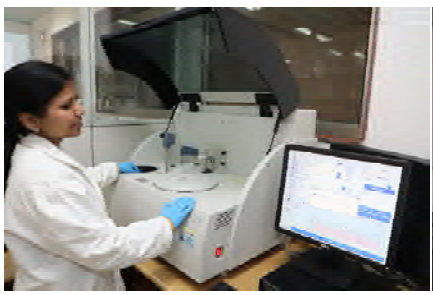
This certificate is valid for the scope as specified in annexure for fulfilment to the requirements of NABL 128.

CSIR-Central Drug Research Institute

Sector 10, Jankipuram Extension, Sitapur Road, Lucknow 226031, UP India , LUCKNOW, Uttar Pradesh 226031, India

Signed for and on behalf of NABL

N.Venkateswaran
CEO



Section II:
Technical Services and Facilities

National Good Laboratory Practice Compliance Monitoring Authority

Certificate of GLP Compliance

सत्यमेव जयते

GOVERNMENT OF INDIA
Department of Science and Technology
Technology Bhawan, New Mehrauli Road, New Delhi-110016
www.dst.gov.in/ngcma

राष्ट्रीय उत्तम प्रयोगशाला पद्धति (जी एल पी) अनुपालन निगरानी प्राधिकरण (एन जी पी एम ए)
विज्ञान और प्रौद्योगिकी विभाग
भारत सरकार

जी एल पी अनुपालन प्रमाण-पत्र

प्रमाणित किया जाता है कि

सीएसआईआर– केंद्रीय औषधि अनुसंधान संस्थान
सेक्टर 10, जानकीपुरम एक्सटेंशन
लखनऊ– 226031, उत्तरप्रदेश (भारत)

एनजीसीएमए की प्रवेश संख्या जीएलपी–160 "जैव सुविधा केंद्र द्वारा जीएलपी प्रमाणीकरण की प्राप्ति एवं अनुरक्षण से संबंधित एनजीसीएमए के नियमन एवं शर्तों" और जीएलपी के ओईसीडी के सिद्धांतों का अनुपालन करने वाला जीएलपी प्रमाणित जांच सुविधा केंद्र है।

यह जैव सुविधा केंद्र निम्नलिखित जांच/अध्ययन संचालित करता है:

- **विषाक्तता अध्ययन**
- **उत्परिवर्तनीयता अध्ययन**
- **अन्य**

विशेषज्ञता के विशिष्ट क्षेत्रों, जांच मद और जांच प्रणालियों की सूची अनुलग्नक में दी गई है।

वैधता की अवधि : 18 अक्टूबर, 2020 – 17 अक्टूबर, 2023

प्रमाण पत्र सं.: जी एल पी/सी–160/2021
जारी करने की तारीख: 14-01-2021

(डॉ. नीरज शर्मा)
प्रमुख, एनजीसीएमए

National Good Laboratory Practice (GLP) Compliance Monitoring Authority (NGCMA)
Department of Science and Technology
GOVERNMENT OF INDIA

Certificate of GLP Compliance

This is to certify that

CSIR-Central Drug Research Institute
Sector 10, Jankipuram Extension, Sitapur Road
Lucknow – 226031, Uttar Pradesh (India)

is a GLP certified test facility in compliance with the NGCMA's Document No. GLP-101 "Terms & Conditions of NGCMA for obtaining and maintaining GLP certification by a test facility" and OECD Principles of GLP.

The test facility conducts the below-mentioned tests/ studies:

- **Toxicity Studies**
- **Mutagenicity Studies**
- **Others**

The specific areas of expertise, test item and test systems are listed in the annexure overleaf.

Validity: October 18, 2020 – October 17, 2023

Certificate No : GLP/C-160/2021
Issue Date : 14-01-2020

(Dr. Neeraj Sharma)
Head, NGCMA

National GLP Compliance Monitoring Authority (NGCMA)

Annexure to Certificate of GLP Compliance No. GLP/C-160/2021

Areas of Expertise:

- **Toxicity Studies**
  - Acute Toxicity
  - Repeated Dose Toxicity
- **Mutagenicity Studies**
  - Bacterial Reverse Mutation (AMES) Test
  - Micronucleus Test (in vivo)
- **Others**
  - Safety Pharmacology

Test Item (s) : Pharmaceuticals (Human).

Test System (s) : Mouse, Rat and *Salmonella typhimurium*

(Dr. Neeraj Sharma)
Head, NGCMA

Unique R & D Facilities and Services Group

1. Good laboratory practice in non-clinical studies

More than fifty studies have been conducted at our GLP certified facility since certification in 2017. These studies include safety pharmacology and regulatory Toxicity studies as per requirements of Drug Controller General of India. The safety Pharmacology studies include, CNS, CVS and respiratory parameters including Oxygen saturation levels in rodents. In Toxicology mutagenicity is studied using AMES assay, clastogenicity using formation of micronuclei and chromosomal aberration. Acute, sub-acute, sub chronic and chronic studies are carried out using rats. The scope of facility will be increased soon with the addition of a battery of tests in reproductive performances in rodents more specifically in Rat. Following the Certification, we will work on including more Test systems like Rabbits and Monkeys. We also helped other CSIR laboratories and government sector laboratories to evaluate their health products. The facility has one hundred thirty-one active standard operating procedures. Sixty-one study personals from Pharmaceutics & Pharmacokinetics, Pharmacology, Toxicology animal facility chemistry and engineering. The following studies have been conducted this year and archived.

- 14 Days Repeat Dose Toxicity study of S011-1793 in SD Rats by oral route with 7 days reversal.
- 28 days repeat dose toxicity study of DIBER-1: Herbal health supplement (HHS C-8) in SD rats by oral route.
- 90 Days Repeat Dose toxicity studies of *Cassia occidentalis* Lin. Extract (219/C003) in SD Rats by oral route.
- S007-1500: *In vitro* Chromosomal Aberration Study in Human Peripheral Blood Lymphocytes
- S007-1500: Male fertility study in SD rat by oral route.

Recently we have filed the IND at DCGI S007-1500 for the fracture healing and preparing IND for of *Cassia occidentalis extract* (219/C003) which is meant for Bone health. We have completed the first cycle of the GLP certification and applied for the second cycle of the certification.

Front row (L to R): Dr. Aamir Nazir, Dr. Rajdeep Guha, Dr. Rajkamal Tripathi, Dr. Sarika Singh, Dr. Sharad Sharma, Prof. Tapas K. Kundu (Director, CSIR-CDRI), Dr. S.K. Rath, Dr. Smrati Bhadauria, Dr. Jayanta Sarkar, Er. Manoj Kumar Rawat, Dr. Mukesh Pasupuleti, Dr. Prem N. Yadav, Ms. Neha Topno, Dr. Shubha Shukla & Dr. D.S. Upadhyay

Back Row (L to R): Dr. Prabhat Ranjan Mishra, Dr. Durga Prasad Mishra, Dr. Manish Kumar Chourasia, Dr. Jiaur Rahaman Gayen, Dr. Sachin Kumar, Dr. Madhav Nilakanth Mugale, Er. Ranvir Singh, Dr. Rabi Sankar Bhatta, Dr. Dhananjoy Hansda, Dr. Manoj K. Barthwal, Dr. Anil Gaikwad & Dr. Kashif Hanif

2. DSIR Common Research and Technology Development Hub (CRTDH)

R&D Scale Formulations Manufacturing Facility, Drug Testing Lab (DTL), and Bioanalytical Facility for Preclinical and Clinical Pharmacokinetics'

To undertake GMP manufacturing and regulatory-compliant testing of formulations at CSIR-CDRI, the DSIR and CSIR have jointly granted `14 crore to develop the necessary infrastructure and human resources. This facility will also be accessible by academia, MSME and large corporations. It is to be inaugurated within the current financial year.

This Unit will undertake the following activities:

a) *Generation of chemical and pharmaceutical information on API and formulations* physicochemical, analytical and validation data;

b) *Quality Assurance, Monograph and Final/Batch Release Specifications including Stability Studies:* Real-time and accelerated, per Schedule Y and ICH Q1A(R2) through Q1E.

c) *In vitro pharmacokinetics and metabolism*: Solubility, pKa, logP and stability in simulated biological fluids, PAMPA/CaCo2 permeation, plasma stability and protein binding, whole blood partitioning; Rat S9 and human microsomal stability, CYP regulation/ reaction phenotyping using recombinant human CYPs.

d) *Preclinical pharmacokinetics, absorption, distribution, metabolism and excretion:* PK, Metabolite identification, and toxicokinetics in blood using rodents, other efficacy models, caninesor non-human primates; biodistribution, allometric scaling, PK modeling and population PK.

e) *Bioanalysis for clinical pharmacokinetics, including bioavailability and bioequivalence.* (Liaison with CSIR-CDRI's Clinical Pharmacology sites at KGMU, Lucknow; PGI, Chandigarh and KEM Hospital, Mumbai.)

Application to the CDSCO for a License to operate a Drug Testing Facility (DTL)

The application was submitted in January 2021 in the prescribed format. If the License is granted, the CRTDH will be able to undertake testing activities like specifying expiry dates, verifying Label Claims on batches of commercial drug products, issuing valid Certificates of Analysis, developing Drug Monographs and Batch Release Specifications for commercial drug products. Because the intent is to provide services to MSME, these activities will be performed with tiered-tariff business model. Thus, the DTL in the CRTDH

Front row (L to R): Mr. Deepak, Dr. Wahajuddin, Dr. Manish Kumar Chourasia, Dr. Amit Misra, Dr. Prabhat Ranjan Mishra, Dr. Jiaur Rahaman Gayen
Second and Third Row: Research Scholars & Project Staff of Division of Pharmaceutics & Pharmacokinetics

will work as a self-sustaining, but not-for-profit entity, passing off costs to large firms while working in a "break-even" mode for MSME, academia and in-house projects.

Equipment for accelerated stability and photostability studies as per Appendix IX of The Drugs and Cosmetics Rules, 1945/2016 for assigning expiry date to commercial drug products

Dissolution test apparatus for carrying out tests per the Indian Pharmacopoeia method 2.5.2 and other compendia.

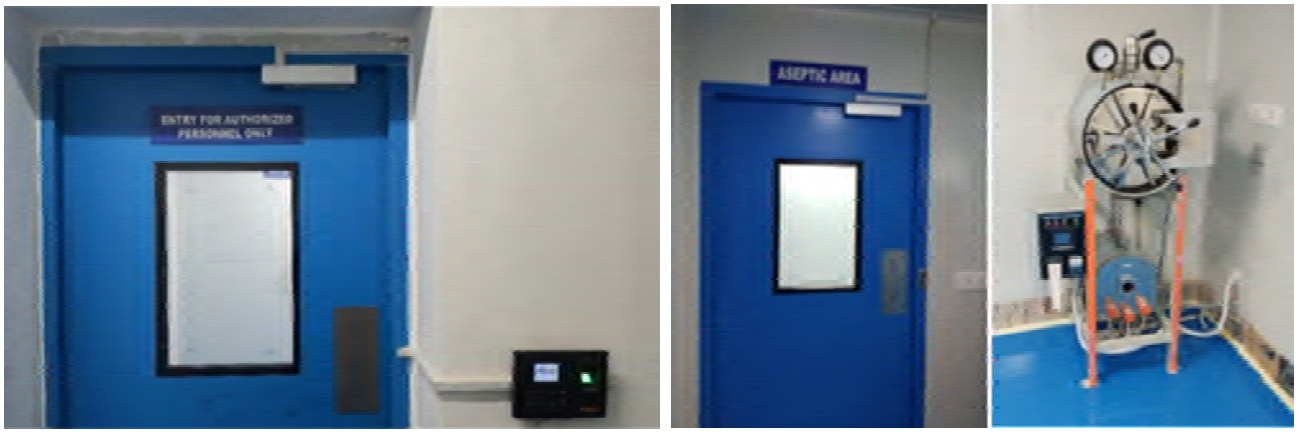
Disintegration test apparatus for the same.

HPLC systems for carrying out tests and bioanalysis per the Indian Pharmacopoeia method 2.4.14 and other compendia in GLP-certified environment.

LC-MS/MS system for pharmaceutical and biomedical analysis for preclinical and clinical pharmacokinetics including bioavailability/ bioequivalence (BA/BE) studies

Commissioning of the Manufacturing Facility

The floor plan of the manufacturing area was developed in consultation with several experts. It was decided that the facility would not have dedicated "lines" as used in large-scale manufacture, separated from each other. Instead, we would use the principle of "separate in real time." Thus, at any one time, only one product would be processed, whether a tablet, capsule, oral liquid or sterile preparation, etc.



Views of the manufacturing area, awaiting final commissioning as on date of reporting. Entrance to the manufacturing area is biometrically controlled. The main entrance to the facility (*left*) is a Class C foyer, leading to a Change Room where operators will don PPE to enter a Class B area. The room for Asceptic Processing (manufacture of injectables) is preceded by a Class B area. Class A conditions for the actual manufacturing operations will be achieved by the use of an isolator placed in the Aseptic Area (*right*).

3. Sophisticated Analytical Instrument Facility (SAIF)

Sophisticated Analytical Instrument Facility and Research (SAIF&R) has highly sophisticated and modern analytical equipment. The facility offers a wide range of analytical services viz. analytical testing/ method development / qualitative and quantitative analysis/ elemental analysis/ structure determination of small and large molecules/TEM/SEM specimen preparation and characterization of nanoparticles, APIs, nano-drug delivery systems, nanostructures like proteins, macromolecular assemblies and viruses / confocal microscopy for sub-cellular localization of macromolecules of biological interest. SAIF services are offered to both internal and external users. The services are availed by about 250 internal and 500 external users annually. More than 90% of the external users comprise researchers from universities and colleges. Researchers from national laboratories and industries constitute the rest.

Besides providing analytical service, the division scientists contribute significantly to all disease areas of the institute and are involved in R&D activities of the institute with several ongoing institutional and extramural projects. Research fellows at SAIF&R are working for their Ph.D. degrees utilizing modern analytical equipment in line with the institute's mandate. In addition to the above, division also offers contract/collaborative research options.

Short term Trainings: SAIF offers training programs to motivate interested postgraduate students and research fellows with an opportunity to spend valuable time in gaining practical experience in the field chemical and biological sciences.

Workshops: Awareness programmes on various techniques are held every year at SAIF-CDRI to keep the users informed about the scientific advancements in above areas.

Project: SAIF Supported by Department of Science & Technology (Govt. of India) to division of Sophisticated Analytical Instrument Facility & Research

Sample analyzed during Dec 2019 to Nov 2020

Name of Laboratory	External	Internal	Total
Mass spectrometry	689	20394	21083
NMR spectroscopy	719	23994	24713
Electron & Confocal Microscopy	32	1500	1532
IR & UV-Vis spectroscopy	277	1199	1476
Flow Cytometer	69	10497	10566
HPLC & OR	79	2860	2939
Micro Analysis	00	119	119
Total	**1865**	**60563**	**62428**

Front row (L to R): N.K. Agarwal, Dr. Ravi Sankar Ampapathi, Dr. Ravishankar R (In-charge) & Dr. Sanjeev Kanojiya.
Back Row (L to R): Dr. Kalyan Mitra, Er. Manoj Kumar Rawat & Sanjeev Kumar Shukla.

4. Tissue & Cell Culture Facility

The Tissue & Cell Culture Laboratory is mandated to maintain and propagate the various kinds of mammalian Cell lines and make its provision to user scientist of this institute on demand basis round the year. Presently the laboratory has 42 mammalian cell lines in our repository and some of them are actively being maintained and propagated for the user scientists to meet out the demand for their various research projects and rest of them are maintained in frozen state. In addition, we also provide training in cell culture and its related techniques to the students / research scholar time to time.

Task carried out/service rendered during reporting period: Provision of 176 cell culture of various cell lines including Vero, MDA MB 231, MCF-7, J774 A.1, A 549, C6, SHSY 5Y, Hep G2, DLD 1, HEK 293, HT 29, Neuro-2A, C33A etc. to user scientist required for their different research projects.

Dr. Neena Goyal, In-charge

5. National Laboratory Animal Facility

5.1. Objectives:

The Laboratory Animal Facility of CSIR-Central Drug Research Institute, Lucknow which is also recognized as the National Laboratory Animal Center (NLAC), is a CPCSEA-registered (Reg. no. **34/GO/ReBiBt-S/Re-L/ 99 CPCSEA**), Institutional Animal Ethics Committee (IAEC) monitored and GLP certified test facility (No.: GLP/C-108/2017, DOI: 18.10.2017) and R&D support facility of the institute engaged in breeding , care and management of different laboratory animal species including rodents (rat, mouse, hamster, gerbil, mastomys, guinea pigs) and rabbits required for in-house biomedical research and experimentation programs as per mandate of the institute. This facility also serves as one of the national resource center for sale & supply of surplus healthy experimental animals for research purposes to other valid CPCSEA registered and functional IAEC research and academic institutions across the country. The facility possesses approximately twenty thousand animals of about 8 species with their more than 20 nos strains of inbred, out-bred, immunodeficient and transgenic models.

Major objectives of the center are as follows:

- Breeding, care, management and supply of healthy laboratory animals for IAEC approved in-house biomedical studies and research programs.
- Supply of healthy animal models to other valid CPCSEA-approved private/government research and academic organizations having functional IAEC.

(L to R): Dr. Prem N Yadav, Dr. Rajdeep Guha, Dr. Sharad Sharma, S. Raja Kumar, Dr. D.S. Upadhyay, Dr. Dhananjoy Hansda, Dr. Shishir Kumar Gupta

- Monitoring and maintaining animal health and quality parameters through genetic, microbial, viral, pathological, and parasitological screening of various animal colonies maintained in the facility.
- Acting as Referral Center for scientific and technical advisory/consultancy services for developing and establishing research animal facility in accordance with the guidelines of the CPCSEA.
- Conducting human resource development programs like Skill development programme etc including organizing symposium/ workshop/seminar on various aspects of laboratory animal science and hands-on training for fresher/advanced practical training in the area of "Care, breeding and management of laboratory animals"
- Publication and dissemination of scientific literature on contemporary issues of laboratory animal science and animal experimentation.

5.2. Animal species and strains maintained:

Sl. No	Species	Strains	Opening stock (as on 01.01.2020)	Closing stock (as on 21.12.2020)
1	Mice	Out bred: Swiss, PS and Inbred: C57BL/6, CBA , AJ, BALB/c, DBA1J, DBA2J, db/db	6624	10062
		Transgenic: NOS1,NOS2,ApoE,	1290	1090
2	Rat	Outbred: SD, CF, DR and Inbred: Wister, Lew, SHR	5543	4541
3	Hamster	Syrian golden	2250	1436
4	Gerbil	Mangolian	344	404
5	Mastomys	Coucha	539	331
6	G. pig	Duncan Hartley	510	458
7	Rabbit	NZW & Belgian	536	484
8	Monkey	Rhesus	44	42
9	Sheep	Marino(Non-descript)	1	Nil
Grand total of animals			**17681**	**18848**

5.3. Animal issued for IAEC approved projects of in-house R&D divisions and supplies of surplus animals towards other IAEC approved, valid CPCSEA registered institutions:

Animal Species	In-house supply Nos.	Out-side sale and supply Nos.	Total Animals Supplied
Mouse	9508	1528	11,036
Rat	4664	1205	5869
Hamster	1174	247	1421
Mastomys	88	04	92
Gerbil	55	04	59
Guinea pig	-	02	02
Rabbit	68	107	175
Total	**15557**	**3097**	**18654**

5.4. Experimentation on Non-Human Primates (NHPs):

The primate facility of the institute LAF is also approved by the CPCSEA for the purpose of research and experimentation on monkeys in the area of regulatory toxicology, pharmacology, anti-malarial and anti-leishmanial screening of novel compounds and vaccines. The eco-friendly NHP rehabilitation unit has been developed according to the norms of the CPCSEA to rehabilitate the monkeys surviving after termination of the experiments. Proper management and due veterinary care is extended to these animals round the clock by the expert veterinarians. Recently, the primate facility has been renovated and upgraded in view to comply with the GLP and other regulatory guidelines enabling the institute to perform experiments on NHPs as per global standards.

Status of animals in NHP facility

Species maintained	Brought forward	Animals under experiment	Animals procured	Animals in rehabilitation unit	Animals euthanized as per protocol	Current stock position
Rhesus monkey	44	18	0	24	0	42

Nonhuman primates maintained in the units were periodically examined physically and clinically for their physical and physiological wellbeing. Tuberculin testing and chest radiography were done for screening of tuberculosis during quarantine period of newly received NHP. Post mortem examinations were carried out for the animals sacrificed /died during the course of experimentation as well as kept under rehabilitation.

5.5. Parasitological monitoring of animals:

In rodents, for detection of ecto-parasites, like mites, lice etc living in the skin, samples of the piece of the hair or deep skin scrapping were collected and examined microscopically. Fecal samples were collected for detection of endo-parasites or their eggs/ ova by means of microscopic examination. Direct smear technique was performed to detect the infection. The detailed observations and findings are as follows:

Species	Total number of samples examined	Observation/Findings
Rat	320	*Hymenolepis nana* (27)
Mice	230	*Hymenolepis nana* (07) ,*Shypheshia* (03)
G.Hamster	50	*Hymenolapis nana* (10)
Mastomys	70	Nil
Gerbil	80	Nil
Rabbit	100	Nil
G. Pig	50	Nil

5.6. Pathological monitoring of animals:

Diseased or moribund animals from the breeding colonies showing clinical symptoms were subjected to necropsy and their gross pathologies were recorded. Representative tissue samples were also collected and preserved for further confirmative histopathological diagnosis as per details given below.

Species	Number of Samples	Observation/Gross Pathology
Mice	5	Generalized vascular degenerative changes, emphysema of lungs and enteritis in 2 animals, others shows NAD*
Rat	6	Abscess in 2 rats, splenomegaly in 1 rats, others showed NAD*
G. Hamster	2	NAD*

*NAD: No Abnormality Detected

5.7. Microbial monitoring of animals:

Rodent and non-rodent animal colonies were observed for potential infections that affect biomedical research outcome and can have adverse effects on health of the animals. Bacterial load was assessed in individual strains on periodic basis, floor swabs and an air sample was assessed for bacterial load in GLP test facility as per the SOP.

The microbial screening was performed at regular intervals to determine the microbial presence in laboratory research animals. Animals were screened for the following microorganisms at regular intervals:

Helicobacter pylori

Corynebacterium sp.

Streptococcus pneumoniae

Pasteurella multocida / P. pneumotropica

Pseudomonas aeruginosa

Salmonella sp.

Klebsiella pneumoniae

Group B-Streptococci

Staphylococcus aureus

Bordetella bronchiseptica

The animal colonies of C57BL/6, BALB/c, Swiss mice, Wistar and SD rats and Golden Hamsters were screened for the potential infections that might have adverse effects on the health of the animals and affect biomedical research outcome. Most of the animal colonies were observed to be free from any disease symptoms. No outbreak of any disease was reported during the period. The screened laboratory rodents showed presence of opportunistic pathogens. Measures such pest control, proper cleaning and sterilization were taken up strictly as per SOP accordingly. Animals showing clinical signs of disease were immediately separated and euthanized.

5.8. Genetic monitoring of animals:

A panel of twenty SSLP markers was used as primary genetic screen to genetically monitor the common inbred mice strains and twenty markers were analyzed for Rats. Genetic profiling of the animals examined confirmed the homozygous state of the inbred strains of the animals being bred and heterozygosity of outbred strains maintained in the animal facility of the institute.

Animal Species	Sample No.	Marker Panel
Mice-Balb/C	20	D1Mit17, D1Mit77, D1Mit171, D2Mit75, D3Mit54, D3Mit200, D4Mit15, D4Mit53, D5Mit10, D6Mit39, D6Mit102, D7Mit25, D7Mit222, D9Mit172, D16Mit5, D17Mit24, D17Mit28, D18Mit14, D18Mit49, D18Mit87
Mice-C57Bl/6	20	
Rat-SD	10	D1Rat169, D2Rat255, D3Rat204, D4Rat107, D5Rat19, D5Ra34, D6Rat160, D7Rat10, D8Rat155, D9Rat33, D10Rat13, D11Rat52, D12Rat86, D13Rat129, D14Ra110, D15Rat6, D16Rat84, D17Rat75, D18Rat121, D20Rat37
Rat-Wistar	10	
Rat-SHR	10	

5.9. Ethics in animal experimentation programmes of the institute:

- During the year 2020 more than 150 fresh and ongoing animal research proposals were reviewed and granted approvals by IAEC.
- The students of the institute were regularly trained for justified use of animals in research in accordance with the principles of 3R and compliance of animal wellbeing issues as per guide line of CPCSEA.

6. Repository of Small Organic Compounds

Exploring the bioactivity in new chemical compounds as a prelude to discovering drugs against new, known or orphan diseases is a continuous process. The process owes its significance to the fact that even after the remarkable advances toward understanding the molecular biology, biochemical pathways and epigenetic factors for several diseases, the drug discovery and development remain challenging, labour and cost intensive effort. Perhaps the challenges became apparent during the current pandemic caused by nSARS-CoV-2, against which the chemotherapeutic efforts were mostly unsuccessful.

Although serendipity, hypothesis-driven or phenotypic approaches still hold their place in drug discovery, the paradigm has shifted towards target-based discovery approaches. The success of the target driven drug discovery relies on bioinformatics and computational approaches, which allow drug designers to visualize ligands bound to different targets providing a wealth of details concerning the non-bonded or covalent interactions that control the binding process and their implications. Various techniques including molecular docking, virtual screening, molecular simulations, and machine learning are employed to study the ligand-protein interactions and discover or predict novel molecular architectures with selective pharmacological property. Besides these two approaches, the significance of Repurposing of known bioactives for different diseases gained pronounced significance due to lack of chemotherapy against the nSARS-CoV-2. Drugs such as Hydroxychloroquine (anti- rheumatoid arthritis), Ivermectin (antiparasitic), Favipravir (anti-influenza), Remdesivir (investigational drug for Ebola virus), Niclosamide (antiparasitic), Arbidol (anti-influenza) and several more were investigated in the in vitro assays and then used in clinics for treating COVID-19.

It is widely accepted that the two distinct discovery approaches viz. phenotypic and target driven require a large pool of diverse chemical prototypes for *in silico*, biochemical or cell-based screening to identify the bioactive molecules. On the other hand, the Repurposing too underscores the need for a collection of bioactive compounds. Being premier institute of the country involved in drug discovery and development, the institute is sensitive towards the requirement of such diverse collection of compounds. In this context, the institute commissioned the state of the art facility since 2012 for archiving the compounds which are generated regularly within the Medicinal and Process Chemistry Division of the institute. In addition to these compounds, the institute acquired commercial chemical libraries of organic compounds and pure natural compounds to boost the efforts for identifying the leads. Moreover, the institute is forthcoming to recruiting compounds from all academic resources including Universities, IITs, IISERs, or elsewhere for

Robotic compound library

Dr. Sanjay Batra, In-charge

enhancing the diversity of the chemical prototypes. Presently the CDRI Repository comprises of more than 90,000 small organic compounds and 225 pure natural compounds. The Repository at this institute is equipped with state of the art Liquid Handling Platform that is effectively utilized for preparing stock solutions of compounds and their distribution for bioassays towards identifying bioactives under different diseases areas being pursued at the institute. There is a battery of more than 30 primary screens which is often employed for identification of hits. Needless to mention that SOPs and cut offs for all bioassays as per the global standards are maintained. In order to maintain proper record of all compounds being distributed and archived in the Repository, an Online Chemical and Biological Assay Reporting System popularly acronymed as CBRS was developed inhouse by the Computer division. This not only assist in archiving the spectral records and purity parameters of all compounds present in the repository but also allow to keep record of all assays together with results of biological investigations a compound has undergone.

The Institute is forthcoming in establishing linkages with other research institutions so as to utilize compounds from the library for identifying bioactives for diseases of national significance and orphan diseases. A collaborative project with Regional Centre for Biotechnology Faridabad funded by DBT, New Delhi was secured for screening the compounds of the library for their effectiveness against Dengue and Japanese Encephalitis viruses.

7. Knowledge Resource Centre

The well-equipped Knowledge Resource Centre (KRC/Library) provides information support to the scientific staff, students of the laboratory, visitors using both archival print resources and contemporary digital resources. It is situated in a beautiful building measuring 8000 sq. feet (approx), full air conditioning building located in the main campus of CSIR-Central Drug Research Institute.

The primary objective of Knowledge Resource Centre (KRC) is to support the educational and research programs of the Institute by providing physical and online access to information, consistent with the present and the anticipated educational and research functions of the Institute. In accordance with the objectives of the Institute, over the years, KRC has been developing a comprehensive collection of peer-reviewed scholarly literature useful for the research community of the Institute. The secondary objective is to serve as a resource centre for the scholars and scientific community of the country. Besides this to promote Hindi, KRC procures Hindi books literature of common interest.

Resource Type	Collection Size
Books	23000
Bound Volumes of Journals	73969
Gratis/Donations	275
eJournals	4700 approx
Reference/ Serials	2863 +
CDRI Theses & Dissertations	1527
Hindi Books	927 +

Knowledge Resource Centre is serving the mission and purpose of the Institute by providing the literary services with a collection of books, bound volumes of journals, theses, annual reports of various scientific Institutions & many more e-version of resources. This facility is available to the entire scientists, technical staff, students and guests. Resources received on gratis and donations are also housed in the KRC.

Services

- **Online Catalogue** (OPAC: http://172.16.0.44/ (Intranet) Online Public Access Catalogue (OPAC) available for document search.
- **KRC Management** (through KOHA packages): The KRC/Library is fully computerized using Koha software for day to day operations. Web Online Public Access Catalogue (OPAC) is available on the Internet. KRC/Library is part of KNOWGATE project initiated by CSIR where KRC moved its data from proprietary software (Libsys) to open source software Koha.
- **Language Editing and Plagiarism Check:** Appox. 850 Number of thesis and publications language improved with the tools such as Grammarly and Anti-plagiarism tools i.e. iThenticate (Turnitin).
- **S & T Reference Service Using Online Digital Resources:** Many Online databases are subscribed by the KRC such as SciFinder, Science direct, Clarivate Analytics/ Web of Science and detailed Patent information database Orbit etc. for imparting knowledge and training to the entire scientific, technical and academic researchers of the Institute.

Mr. Prem Prakash, Mr. Vinay Tripathi, In-charge

- **Document Delivery Service:** Provide 97 document delivery service for from our print & archival and subscribed resources as and when requested by the user via email, fax etc.
- **Scientometric Analysis:** Carried out citation analysis of publications of individual scientists and organization using scientometric tools such as Web of Science of Clarivate Analytics.
- **Reprographic Services:** The CDRI KRC offers photocopying service to all its members, and this service is for all the faculty members and students on nominal charges.
- **Archiving/Institutional Repositories:** To provide better access to the recently published literature as pre-prints of publications and theses are archived using D-Space Software.
- **Reference Service:** Reference service helps users to make full use of the resources available in the KRC. It guides the use of KRC resources and services, assists in accessing e-journals, e-books, databases, multimedia sources etc. It also maintains a collection of reference books consisting of encyclopedias, dictionaries, directories, technical reports, scientific reports, pharmacopoeia (s), current protocols, methods, and globes, etc.
- **Awareness Programme:** The KRC takes an active part in the orientation programme to familiarize users with various resources and services available for them and also whenever a new product or service is introduced. Orientation programmes-8 (Web of Science-21.04.2020, 04.05.2020, 10.08.2020, 05.10.2020, 02.11.2020, 07.12.2020, Adis Insight - 03.09.2020, Orbit Intelligence - 24.08.2020)
- **News Clipping:** News and reports appearing in the media, especially in newspapers, relevant to S& T in general use to be uploaded on Intranet.
- **Electronic access** to the databases & journals hosted on the CDRI Intranet. KRC provides access to several electronic journals through the web for students and faculty members of CSIR-CDRI.

8. Herbarium and Horticulture Activities

During the year, twenty-two important medicinal plants have been introduced at "Dr. Nitya Anand Drug Discovery Park". The total number of plants are more than one hundred now. The list of newly introduced plants are mentioned below:

1. *Cissus quadrangularis* L.
2. *Rauvolfia serpentina* (L.) Benth. ex Kurz
3. *Centella asiatica* (L.) Urb.
4. *Bixa orellana* L.
5. *Gymnema sylvestre* (Retz.) R.Br. ex Sm.
6. *Acorus calamus* L.
7. *Andrographis paniculata* (Burm.f.) Nees
8. *Asparagus racemosus* Willd.
9. *Bacopa monnieri* (L.) Wettst.
10. *Boerhavia diffusa* L.
11. *Guilandina bonduc* L.
12. *Hellenia speciosa* (J.Koenig) S.R.Dutta
13. *Pleurolobus gangeticus* (L.) J.St.-Hil. ex H.Ohashi & K.Ohashi
14. *Nyctanthes arbor-tristis* L.
15. *Phyllanthus amarus* Schumach. & Thonn.
16. *Pithecellobium dulce* (Roxb.) Benth.
17. *Putranjiva roxburghii* Wall.
18. *Sapindus mukorossi* Gaertn.
19. *Sesbania grandiflora* (L.) Poir.
20. *Solanum nigrum* L.
21. *Solanum virginianum* L.
22. *Withania somnifera* (L.) Dunal

Dr. D.K. Mishra, In-Charge

Photographs of some important newly introduced plants:

Cissus quadrangularis

Rauvolfia serpentina

Centella asiatica

Gymnema sylvestre

Sesbania grandiflora

Bacopa monnier

Guilandina bonduc

Acorus calamus

Bixa orellana

Knowledge Management Group

1. Business Development & Intellectual Property

Business Development & Intellectual Property Group aims to establish a stronger link between the Institute and Industry, Stakeholders and Society. The overall objectives of the group:

- To promote the technologies developed at CSIR-CDRI and facilitate the R&D divisions of CSIR-CDRI to have a better interaction with industries to develop novel technologies.
- Management of Intellectual Property Rights of the Institute.
- Coordination of the technical services based on immense expertise available with CSIR-CDRI to various users.
- Representing CSIR-CDRI in the exhibitions and expo to exhibit accomplishments of the Institute and opportunities available for industry, academia and society to collaborate with CSIR-CDRI.
- Coordination of the International S&T Affairs activities at CSIR-CDRI.

Label : (L to R): Dr. S.R. Kulkarni, IP Coordinator & Mr. N.A. Siddiqui, Head BD

During the reporting period, The Business Development group continued to explore the business development opportunities by establishing liaison with national and international organizations and industries in order to have more public–private partnership at early stage of the development and to have collaborations for new leads. Several new contracts / assignments were signed / undertaken by the Institute during reporting period.

Number of Agreements Signed

(Details given in the Research Output Section)

Demonstration of Technology (Know-how)	01
License Agreements	01
Collaborative Research Agreements	04
Sponsored Agreements	02
Consultancy Agreements	02
Testing Services	03
Memorandum of Understanding signed for joint R & D	10
Memorandum of Agreements	05
Secrecy Agreements	15
Material Transfer Agreements	11

Number of Patents Processed:

(Details given in the Research Output Section)

- Patents Filed in India 8
- Patents Granted in India 8
- Patents Granted Abroad 5

2. Scientific Directorate

The Scientific Directorate is looking after three major portfolios viz. Director Secretariat, PME, and Technical Information, apart from Coordination with agencies, and other crucial management activities. Significant work carried out during the year are as follows:

2.1 PME

- Revised budget estimates 2020-21 and Budget estimates 2021-22
- 164 project proposals vetted and processed for approval of the competent authorities.
- Monitoring of funds in more than 250 projects and day to day clearance of indent through the Real Time
- Budget Monitoring Tool raised by the scientists & other staff members in various projects.

Dr. Ananad P. Kulkarni, PME Head

- Co-ordination with Finance & Accounts and Stores & Purchase
- Maintenance of all kind of project folders (more than 250 numbers) and record keeping at central place
- Vetting of expenditure statements, utilization certificates for more than 150 projects and processing for approval of the competent authorities.
- Digitized information management
- Coordination with Audit
- Management of R & D Portal of the ERPS
- Research Council Meeting coordination, preparation of Executive Summary and Presentation.
- Project Monitoring Meetings

2.2 Director Secretariat

- Support in overall R & D planning activity with inputs from concerned stake holders
- Implementation & follow up reports on policy decisions taken by the Director from time to time
- Preparation of background papers/documents and policy drafts
- Collation and analysis of information pool for informed decisions
- Preparation of reports/documents sought by the CSIR from time to time
- Periodic performance mapping and reports to the Director
- Monthly/ Quarterly Reports
- Processing of scientific matters & budgetary requests for Director approval
- Any other activity as assigned by the Director from time to time
- Background work for recruitment of Technical & Scientific Staff
- Nominations for training programs
- Processing of staff nominations for honours & awards and fellowships
- Instrumental support in organizing visits of important delegations, VIPs, Industry personnel, etc
- Popular Health Talk and Nobel Symposium organization
- Coordinating organization Faculty Colloquium
- Coordination of CDRI Awards for Excellence in Drug Research

2.3 Dissemination of Technical Information

- Response to queries from various corners (Govt./ Non-Govt. agencies)
- Replies to Parliament Queries
- Communication within and outside the institute
- Management of database on Projects, Staff, Budget, ECF, Awards, etc.

2.4 Institutional Publications

- CSIR-CDRI Annual Report 2019-20 (Hindi)
- CSIR-CDRI Annual Report 2019-20 (English)
- CDRI Newsletters (Bi-annual)
- Banners, Brochures and publicity material
- CSIR-CDRI Advertisements

2.5 Institutional Photography and Design Work

Scientific Directorate is the core of institutional photography and all designing work. It undertakes given activities under its domain

- Scientific Digital Photography for all publications, Scientific Journals and Research papers
- CSIR-CDRI Advertisements
- Photography coverage of all institutional events namely, seminars, symposiums, agreements, conferences, lectures, farewells, colloquiums, and many such events
- Designing of Institute publications including Invitation Cards, Posters, banners, certificate, Brochures, Mementos.
- Allied services under photography and designing like Poster designing for conferences, computerized graphic diagrams, drawings and charts, editing and processing of digital images for publications, etc.
- Maintenance and update of central Institutional Digital Photo repository.

3. Academic Affairs Unit

3.1 Academic Activities

Coordination of the academic activities related to PhD Programs of Jawaharlal Nehru University (JNU) New Delhi and Academy of Scientific and Innovative Research (AcSIR), Ghaziabad starting from admission, organization of course works, seminars, comprehensive, Research/Doctoral Advisory Committee (RAC/DAC) Meetings to Thesis submission, Viva-voce examination and finally award of Doctoral Degree. In the reporting period nearly 445 (298 from AcSIR and 146 from JNU) research scholars are registered for PhD.

(L to R) : Dr. Ajay Kumar Srivastava, Dr. Ritu Trivedi, In-charge, and Dr. Sanjeev Yadav

3.1.1 Coordination of admission process of ~166 (72+94) PhD positions in reporting period under CSIR-CDRI PhD Program (JNU & AcSIR):

- Drafting and designing and processing for publication of advertisement for CSIR-CDRI PhD Programs
- Collection, compilation and approval of JRF requirement from scientists as per norms Constitution and getting approval of screening committee and coordination with screening committee for screening of more than 500-600 admission forms in each session and selection committee for Interview.
- Compilation, preparation of result proceedings, declaration & communication of results.
- Facilitated the interaction with scientists and completion of documental requirements for admission
- Newly admitted research fellows (Number of Research Students registered in AcSIR in August 2020: **~35** and in AcSIR in January 2021: **~21** and in JNU in January 2021 batch: **~55**)

3.1.2 Coordination of Pre-PhD Corse work of CSIR-CDRI PhD Programs:

- Preparation, display & distribution of academic calendar for Pre-PhD course work including notification of Examination Schedule for each Semester (Four exams per semester i.e., Ist sessional, Mid Term, IInd Sessional & End Term Examinations)
- Organization and coordination of meeting of course coordinators to discuss syllabus for smooth conductance of pre Ph.D. course work
- Compilation of Optional subjects collected from students and coordination with course coordinator and HRMS for proper attendance
- Coordination with faculty and course coordinators for smooth conduction of classes, seminars and other activities related with Pre PhD course work, exams and evaluation of answer sheets, question paper formatting & printing
- Compiling results, result sheet with SGPA and display of results.

3.1.3 Coordination with Doctoral/Research Advisory Committee (DAC/RAC) for CSIR-CDRI PhD Programs:

- Coordination with supervisors for constitution of Doctoral/Research Advisory Committee (DAC/RAC) for each student
- Coordination for Comprehensive for candidates registered with AcSIR
- Formalities regarding issue of Enrolment number and confirmation and registration process of students for PhD Program
- Collection of RAC/DAC reports periodically
- Collection of synopsis for the approval of Academic committee
- Coordination with supervisors for Panel of examiners for thesis evaluation
- Thesis submission along with all the documents related to thesis & viva voce, scanned & send to JNU and AcSIR

3.1.4 Coordination for conducting Viva-voce Examination:

- Formalities related to Ph.D. thesis submission (Total **45** Thesis (JNU: 36 & AcSIR: 09) submitted in the reporting period)
- Organizing viva-voce examinations of JNU/AcSIR students of previous batches (**40** viva-voce examinations were conducted during reporting period)

- To promote Digital India, many viva-voce examinations were done through Inline mode MS Teams/SKYPE (**37** viva-voce examinations were conducted during reporting period)
- Follow up of thesis in case of delay in viva-voce
- Coordination with AcSIR/JNU for awards of provisional degree and degree and related issues.

3.1.5 Issue of Transcripts and certificates and verifications thereof:

- Issue of certificate of completion of PhD Course work as per the UGC norm
- Issue of Transcripts, verification of Degree, current and previous students as and when required by the employer or by third party academic record verifying agencies.
- Maintaining record of Ph.D. certificates received from JNU and issued to students.

3.1.6 Formalities regarding other financial remittance to JNU/AcSIR according to commitments

- Coordination with JNU and CDRI administration for submission of affiliation fee to JNU as per the MoU for continuation and smooth running of CSIR-CDRI-JNU PhD Program.
- Process the payments of TA/DA and Honorarium for the evaluator of thesis and examiners of viva-voce.
- Handling of AcSIR budget (P-92-205) for AcSIR related activities.

3.1.7 Coordination and organization of Academic Council (Institutional, JNU & AcSIR)/ JNU Scrutiny committee meetings

- Coordination for JNU-CDRI Academic Council meeting (twice in a year) from constitution of committee to preparation of minutes of meeting
- Coordination for Scrutiny Committee Meeting for scrutiny of the results of course work of CSIR-CDRI-JNU PhD Program (This year we did it first time)
- Coordination for CDRI Academic Committee meeting (twice in a year) for formulating the guidelines to implementing the existing guidelines.

3.1.8 Initiative taken towards connecting stakeholders (Research /Academic Institutes/ University/ Medical Colleges) for enriching the academic environment and knowledge sharing

In reporting period connected more than **90** Research Institute/ Academic Institutes/ University/ Medical Colleges for enriching the academic environment and knowledge sharing for academic/scientific uplift through our PhD programs. It helps for knowledge sharing and academic/scientific uplift through value addition and providing intellectual inputs. This also provides the opportunity to others to collaborate with Institute and finally both the can mutually help in betterment of Science.

3.2 Administrative Activities

Beside academic activities, Unit is also involved on other activities to support the science and technology management and administrative work.

3.2.1 Financial approval of Monthly Fellowship, HRA and Contingency of UGC Fellows

In the reporting period, for regular disbursement of Monthly Fellowship, HRA and Contingency of UGC JRF & SRF of CSIR-CDRI; Unit perform the following activities for more than **120** UGC JRF & SRF as a "Maker" on UGC-portal as financial administrator on the basis of records available in Establishment-I section.

3.2.2 Processing of applications for attending the conference/ seminar/ workshop/symposium

In the reporting period, Total only **22** applications were processed for the research scholars (JRF, SRF, RA, N-PDF and Women Scientists) who have attended various national and international conference/ seminar/ symposium/workshops.

3.2.3 Processing of application of SRFs and RAs for various funding agencies

In the reporting period total **26** applications including, 02 applications for ICMR-Research Associate (RA), 02 DST NPDF, 02 DST-TARE Fellowship, 02 ICMR JRF, 17 ICMR-Senior Research Fellow (SRF), 01-Newton Bhabha PhD Program. 02 DST

3.2.4 Coordination of Online interviews of CSIR-SRFs and CSIR-RAs of CSIR-HRDG, New Delhi

The selection committee meeting for CSIR-SRF/RA in the area of Life Sciences (Biochemistry, Biophysics, Immunology, Microbiology & Physiology of Living Systems, Subject code LIFE-12) was coordinated by Academic Affairs Unit at CSIR-Central Drug Research Institute, Lucknow during 26-27 November on behalf of CSIR-HRDG, New Delhi. Total 215 CSIR-SRF applicants and 195 CSIR-RA applicants were interviewed.

3.2.5 Coordination of Physical Entrance Examination of M.Sc. (Food Technology) by CFTRI-Mysuru

Due to Covid-19 pandemic, CSIR-CFTRI, Mysuru has conducting its M.Sc. (Food Technology) All India Entrance Exam on November 22, 2020 (Sunday) at various twelve centers across the nation. Academic Affairs Unit has conducted the physical entrance examination as per the Covid-19 guideline at CSIR-CDRI, Lucknow center.

3.3 Science Communication and Dissemination Activities

Organization's brand image can be as important as the goods or services it produces. A strong brand image is a powerful asset. A recognized and trusted brand identity makes people confident that the organization is dependable. Hence, the image building of Institute is very crucial part for any organization it showcases the achievements and relevance of organization to society nationally and internationally and attracts the other stakeholders. Regular inputs were provided to SCDD, CSIR-HQ New Delhi, Vigyan Prasar, Print, Electronic and Social Media including Twitter & Facebook for science communication and dissemination of information and achievements of Institute.

3.3.1 Science Communication and Dissemination through Vigyan Prasar & SCDD, CSIR-HQ

During the reporting period, regular inputs were provided to Science Communication and Dissemination Directorate (SCDD), CSIR-HQ, New Delhi, CSIR-NISCAIR, New Delhi and Vigyan Prasar, DBT, Govt. of Indi, New Delhi to showcases the achievements and success stories of Institute to society, nationally and internationally. Since June 2020 Daily reports of activities and achievement is being sent to SCDD, CSIR-HQ, New Delhi.

3.3.2 Science Communication and Dissemination through Print and Electronic Media

During the reporting period more than **50** bilingual (English & Hindi) stories (press releases) were communicated to Press & Media by which Institute was in limelight for **60** days with **197** news articles in local and national print and electronic media (Including TV Channels and Web Portals).

3.3.3 Science Communication and Dissemination through Social Media (Twitter & Facebook)

During the reporting period on twitter handle of CSIR-CDRI, followers increased from **6330 to 10507** with the help of more than **2578** tweets from our handle. The average tweet impression increased from **13.4K** per day to **51.7K** per day during reporting period. During the reporting period, on Facebook account of CSIR-CDRI, number of followers increased up to maximum allowed number i.e. **5000** with more than friend **4950** followers during the reporting period.

3.4 Activities under the aegis of Scientific Social Responsibility (SSR) of Institute

Scientific Social Responsibility (SSR) is the confluence of scientific knowledge with visionary leadership and social conscience. SSR is about building synergies among all stakeholders in our scientific knowledge community and also about developing linkages between science and society.

3.4.1 CSIR-800 Program (Health Awareness and Outreach Projects by PhD Students)

The major objective of the CSIR-800 project is to create and nurture a sense of social consciousness and responsibility by participation in Science & Technology activities relevant to the nation. In the reporting period, we have coordinated total **12** outreach projects which were undertaken in the focus area for improve the quality of life through enhancing the awareness related to affordable healthcare. The objective of these CSIR-800 programs were to sensitize the research scholars to address the issues at grass root level for the benefit of last man of the society and to create and nurture a sense of social consciousness and responsibility by participation in Science & Technology activities relevant to the nation.

3.4.2 Other Societal programs

To initiate and promote experimentation and innovativeness in education and bringing confidence to society about the relevance of Institute in terms of Social Impact, various other societal programs including, Online Health Awareness Outreach Program, Outreach Program for Women Health, Vigyan Jyoti Program for Girls in STEM, JIGYASA and Students Motivation Programs for various Schools & Colleges were conducted/coordinated in collaboration with HRD unit (details mentioned in that section).

S.No.	Title of Health Awareness and Outreach Projects	Outreach Project by
1.	Survey on concerning Cervical cancer factors among women at King George's Medical University	Ms. Pragya Yadav (Student of Dr. T Narender)
2.	Awareness Programme about Tuberculosis treatment in women at Naya Khera Village, Jankipuram Vistar, Lucknow	Ms. Sapna Pandey (Student of Dr. Kishore K Srivastava)
3.	Cardiovascular health and associated risks: A silent killer. Does the youth actually bother?	Mr. Amit Manhas (Student of Dr. Kumaravelu J)
4.	Awareness of tuberculosis and challenges towards multidrug-resistant tuberculosis (MDR-TB) in India	Mr. Ratnakar Dutt Shukla (Student of Dr. Atul Kumar)
5.	Survey to create awareness against smoking in rural population of Lucknow district (Naya Khera Village)	Ms. Priya Pathak (Student of Dr. Kumaravelu J)
6.	Knowledge, attitude and practices on healthy lifestyle among students: A questionnaire based online survey	Ms. Nagode Savita Babasaheb (Student of Dr. Namrata Rastogi)
7.	Diabetes: Awareness Status in Rural and Suburban People	Mr. Sourav Chattopadhyay (Student of Dr. Sabyasachi Sanyal)
8.	Assessment of the cardiovascular risk among the urban and rural population	Mr. Sukka Santosh Reddy (Student of Dr. Manoj K Barthwal)
9.	Online Survey on factors associated with depression and anxiety among Research Scholar	Mr. Rohit Singh (Student of Dr. T Narender)
10.	A survey on knowledge and awareness of Tuberculosis in rural population of Nawa Khera, Lucknow	Ms. Jyoti Vishwakarma (Student of Dr. R. Ravishankar)
11.	Creating awareness of vaccination amongst pregnant women in village Nawa Khera of Lucknow district	Ms. Shikha Dubey (Student of Dr. R. Ravishankar)
12.	A survey on knowledge and awareness of 'Leishmaniasis' in rural population of Tiwaripur, Lucknow	Ms. Rekha Sangwan (Student of Dr. Pintu K. Mandal)

4. Human Resource Development

4.1 Skill Development Program (Healthcare & Life Science)

Skill India is an initiative launched to empower the youth of our country with skill sets which make them more employable and productive in their work environment. Skill shortage remains one of the major constraints to the continued growth of the Indian economy. We wish to address this knowledge-gap by professionally trained youth of India. The courses have been designed to meet the aspirations of students, young researchers and industry-sponsored personnel looking for training. We offer six certificate courses under the CSIR-CDRI, Skill Development Program. These courses provide an opportunity for skill development and hands-on experience in the area of healthcare and life science.

(L to R): Mr. Vinay Tripathi, In-charge & Mr. Prem Prakash

4.2 Skill Development Program for Postgraduate Students

The course meets the aspirations of students/young researchers looking for training and hands-on experience in the chosen area. Students pursuing their post-graduation course from universities/ colleges in any of the relevant areas can develop skills through these courses. Candidates have taken training for a duration of 4 months to 1 year depending upon the recommendations from their HOD. During the period of report 15 post graduate students received training at CSIR-CDRI.

4.3 Advance Training Courses for the employees of R & D Institutions/Pharmaceutical Industry/Government Laboratories etc.

Institute conducts different kinds of training of short duration in various disciplines against payment. These courses comprise both lectures and practicals by our experienced scientists with emphasis on practical R & D aspects in a particular domain. During the period of report 03 aspirants received training at CSIR-CDRI.

4.4 Training for Scholarship Awardees

Under this category candidates getting scholarships/selected/nominated from some of the prestigious institutions of India are provided training. The training comprises of both lectures and practical by our scientists and technical staff.

A. Indian Academy of Sciences, INSA-IASc-NASI Summer Research Fellowship

B. INSPIRE Fellowship

C. UPCST Fellowship:

D. AcSIR–Dr APJ Abdul Kalam Summer Training Program

4.5 Biological Activity Screening (BAS):

Over the years CSIR-CDRI has developed a large number of Biological Assays and Screening Protocols to carry out biological activity studies of compounds against various diseases. Disease areas for which the assays are available on payment basis are CNS-CVS, reproductive health, malaria and other parasitic diseases, cancer, tuberculosis, microbial infections and regulatory/ experimental toxicity studies.

During the period we have received 153 samples through Biological Activity Screening (BAS) during the year from 25 beneficiaries. External Cash Flow (ECF) generated Rs. 2,95,350/

4.6 RTI

Centre is responsible implementation of Right to Information Act-2005 in the Institute related with scientific, technical and academic matters to promote transparency and accountability in the working and appeals related with all types of RTI related matters. During the period of CPIO (S&T) responded to 33 RTI queries and the Appellate Authority disposed of 9 appeals.

4.7 Activities under the aegis of Scientific Social Responsibility (SSR) of Institute

Scientific Social Responsibility (SSR) is the confluence of scientific knowledge with visionary leadership and social conscience. SSR is about building synergies among all stakeholders in our scientific knowledge community and also about developing linkages between science and society. Since independence, India's development in the scientific field is praiseworthy; however, the transfer of scientific knowledge and its benefits to society at large is still an area of concern. Thus, apart from deploying more resources on human and social development, building a strong connection between science and society is essential. One way could be through the translation of scientific knowledge in achieving social goals which could be institutionalized through a policy on "Scientific Social Responsibility". The relationship between science and society being a two-way engagement, SSR is not only about the scientific impact upon society but also about the social implications upon science. SSR would, therefore strengthen the knowledge ecosystem and bring efficiencies in harnessing science for the benefit of society. It will also bring change in attitudinal, mindset and work style of the scientific community, thereby enhancing the social reputation of our scientific organization. Thus, SSR has the potential to fundamentally transform society by improving the lives of our citizens while helping the nation to achieve its goals for sustainable development. In view of the above, CSIR-CDRI has organized various programs to connect science with society in the reporting period towards fulfilling its scientific, social responsibilities, viz. JIGYASA, Student motivation program, Health Awareness & Outreach program & IISF 2020:

4.8 JIGYASA – Quest for Curiosity

JIGYASA, a student-scientist connect programme, initiated by Council of Scientific and Industrial Research (CSIR) and Kendriya Vidyalaya Sangathan (KVS) in the year 2017, however now Navoday Vidyalaya and other Government Schools have also been added in it. The objective of the programme is to expose students with practical activities to get a flavour of research in CSIR-CDRI by extending classroom learning to research and laboratory-based learning at an early age.

The program promotes Science education among children and develops conceptual clarity amongst children, establishes linkage between the classroom and real-life experience, interaction with scientists and research scholars will motivate students for careers in science, promote science education by nurturing the potential talent of students, creation of scientific temper amongst students and teachers by "doing science", encourage students towards experimentation and innovativeness to create positive perceptions towards science, create a positive image of scientists by showcasing the pride for the passion, enhancing the scientific approach of children by explaining simple science concepts around them, play a key role in the emergence of new student entrepreneurs, awareness on emerging global/country issues, training and development of teachers is important and will be improved and science model exhibition and quiz competitions.

4.9 Students Motivation Programs for various Schools & Colleges

To initiate and promote experimentation and innovativeness in education and bringing confidence to society about the relevance of Institute in terms of Social Impact, various student motivation programs were organized to inculcate the scientific temperament. During the reporting period, Total 05 Student Motivation Programs (SMP) for 05 Schools and Colleges other than Kendriya Vidyalaya were organized in which total 427 faculties and 272 students get benefitted with these programs.

04.02.2010	CK Thakur ACS College, New Panvel, Mubai	52	2
11.02.2020	"Vigyan Jyoti Program" for Navoday Vidyalay Samiti (NVS), Piparsand	50	5
27.02.2020	Govt. Upper Primary School Chapar Hardaun, Koraon, Prayagraj (Allahabad)	40	11
28.02.2020	Meet the Role Model program during National Science Day Celebrations at Navoday Vidyalay Piparsand	100	10
28.02.2020	Popular lecture on National Science Day Celebrations at SR Group of Institutions	200	20

1.7.3 Health Awareness and Outreach Program

To fulfil the Scientific Social Responsibility of Institute, CSIR-CDRI regularly organizes Health awareness programs in villages on different disease areas related to health as per its mandate. During the reporting period, Due to Covid-19 pandemic outreach programs were restricted, though following programs were organized:

Online Mental Health awarenss program

Coordinating an ongoing online survey (research study) for Mental Health Awareness to sensitize the students and other general public for stress management and other mental health related disorders including depression, mood disorders, OCD and generalized anxiety disorders, etc. (https://cdri.res.in/surveymha).

Outreach program for women health

An outreach program about the Women Health was organised on 26 November 2020 as a pre-event activity of IISF-2020 in Hanuman Prasad Rastogi Girls Inter College, Lucknow. The program was coordinated by Dr Namrata Rastogi, Sr Scientist. There were two lectures, one by Dr Ritu Trivedi Principal Scientist on "Menstrual Health & Hygiene" and another by Dr Monika Sachdeva Principal Scientist on "Women Reproductive Health" followed by a poster session by students on women health which was managed and judged by Dr Namrata and Dr Vineeta Tripathi. The program was followed by an interactive session in which with about 50 students, around 15 teachers and all the four scientists participated. Four of the winners were felicitated for the poster competition among students. Several of students and teachers showed interest and willingness to visit CDRI in future.

4.10 IISF 2020

The series of India International Science Festival (IISF) is an integral part of India's long term vision in developing and widening the spectrum of scientific temper in India and abroad. To display India's contribution in the field of S&T and to motivate the young scientists to find solutions to the burning issues of our society; So far, the festival was organized six times which were a grand success. CSIR-CDRI participated in the sixth IISF with following online programs:

- In the Curtain Raiser Ceremony at CSIR-CDRI, Dr V.P. Kamboj, Former Director, CSIR-CDRI, Lucknow delivered a lecture on "Atmanirbhar Bharat for Covid-19" on 27 November 2020.
- An outreach program about the Women Health was organised on 26 November 2020 as a pre-event activity of IISF-2020 in Hanuman Prasad Rastogi Girls Inter College, Lucknow.
- Mr Vinay Tripathi delivered a lecture through webinar on "Science & Career" on December 15, 2020 at IISF, Press Information Bureau, Ministry of Information & Broadcasting Government of India, Lucknow
- Mt Pankaj Prasun participated in Multilingual Vigyan Kavi Sammelan in IISF 2020 and recited his poems

Infrastructure Management Group

1. Information Technology Services

(L to R) : Er. Kural, In-charge & Mr. Santosh Shukla

A) Software Development/Maintenance: Computer Center has developed, implemented and maintained the following software systems during the reporting period:

1. Software enhancement, maintenance and support for old and new SnP
2. Compound Submission and Bio-Assay Reporting (CBRS) System
3. CDRI internet and intranet website.
4. Requisition for Bio-evaluation of compounds from CDRI Repository
5. Online Request / Reporting for Small Molecule X-ray Diffraction Facility
6. Online Sample Submission/Analysis and Equipment Booking software for SAIF
7. Maintenance of MoES database Application
8. Operation and maintenance of HRMS system for students
9. Enhancement of Software for online Digital Herbarium
10. Online Electrical/Civil/Refrigeration/Other Lab Services Job cards
11. Software for dispensary automation (under-implementation)
12. Instrument online pre-booking system
13. Implementation of latest DSPACE software
14. Animal Issue Software
15. Co-operative Society Database
16. Database for GPF Statement
17. Online Budget Monitoring System
18. Online Guest House Booking System (under-implementation)
19. Vendor Registration Software for CSIR-HQ, its security audit and hosting
20. Online Skill Development Program (SDP) registration for CSIR-CDRI Courses
21. Online Gate Pass application for visitors
22. Management & hosting of *plantmetabolome. cdri.res.in* Plant Metabolites database and Tendem Mass Spectrum Database
23. Software for Wireless Controller log
24. Web application for seeking nominations for awards for Annual day etc.
25. Design and development of new institutional website
26. Website for Survey on Mental health awareness
27. Web application for Canteen requisitions
28. Scientist & Technical Recruitment software and reporting

B) ICT Infrastructure Management and Services

1. Operation and Management of LAN/WAN System comprising of 1500 wired nodes and campus-wide Wireless network and NKN link of 1 Gbps bandwidth.
2. Operation and Management of servers and SAN systems
3. Comprehensive IT support to institute wide users comprising of approximately 1000 clients.
4. Web hosting services for several publicly accessible websites including institute's internet website (www.cdri.res.in)
5. Provisioning for NIC e-mail services

6. Maintenance of PCs as per Standard Operation Procedure(SOP) for Protection and validation of Hardware and Software under GLP
7. Routine backup for GLP related data
8. Hosting of CDRI tenders on website Portal
9. Helpdesk for ERP & AEBAS user support
10. Skype & Videoconferencing facility
11. ICT support for Audiovisual arrangements
12. Bulk procurement of ICT items (Desktop, Laptops, Printers etc.) for institute wide users
13. ICT support for adoption of GeM software
14. Implementation of SnP & e-Dak module of ONECSIR ERP.

2. Auditorium Management

Auditorium Management Unit under Scientific Directorate looks after the audio visual and related facility of auditorium and meeting rooms/halls for institutional scientific lectures, conferences, seminars, workshops, project meetings, selection committee meetings, RC meetings, Virtual Video Conferencing and other general events. The major activities of this unit are:

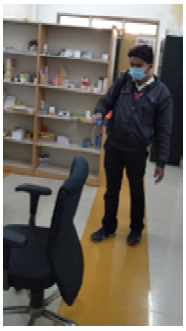
(L to R) : Dr. Ananad P. Kulkarni, Supervising Scientist In-charge & Mr. Arbind Kumar, Unit In-charge

- Operation and maintenance of high end audio and visual systems to ensure smooth functioning during events.
- Operation and Management of Auditorium Complex.
- Co-ordination with other facility/section for smooth organisation of events.
- Preventive maintenance of amplifiers switchers, feedback suppresser, microphones, portable sound systems, speakers and projection systems.
- Up-gradation of audio and visual system to make it compatible with available latest technology.
- Virtual Conferencing through Skype, MS Team, Zoom, Google Meet etc.
- Live Broadcast Facility.
- ICT Support for Seminar, Symposium and Virtual Conference meetings.
- Audio visual support for Online Interviews, Assessments and Recruitments.

3. Centralized Utility Services

Environmental Health & safety carries utmost importance in research laboratory; Compliances of various statuary and government agencies i.e. Ministry of Environment & Forest, UP Pollution control board, Good Laboratory practice for rigorous monitoring the experimental and environmental parameters has been followed by the CSIR-CDRI. Our lab core facilities at CSIR-CDRI provide very important services in terms of operation and maintaining various centralized gas supply i.e. LPG, Nitrogen, Compressed air, vacuum and pharmaceutical buffer grade water to the work bench in chemical and biological research labs. The centralized services optimize the recurring expenditure and maintenance cost of the institute where the quality at centralized point can be assessed / analysed. Presently following services are effectively functional and maintained under Institute Centralised Utility services at the CSIR-CDRI, Lucknow.

L to R Mr. Ranvir Singh, Unit In-charge E-Dr. Atual Kumar supervising scientist In-charge



1) Centralized Gas Supply & Utility Generation services

Centralized Gas supply and utility services under other lab services at CSIR-CDRI provide crucial technical services in terms of operation and maintaining various centralized Services. Presently following services are effectively functional and maintained under ICF Division at CSIR-CDRI, Lucknow

- Onsite generation of **Liquid Nitrogen (LN_2).**
- Operation & maintenance of nitrogen gas generation and onsite supply in approx. 500 distribution points in 120 labs.
- Onsite supply and maintenance of LPG gas at work bench.
- Operation & maintenance of vacuum generation services, air compressor and onsite supply at work bench at approx. 500 distribution points.
- In House operation and maintenance of Glass Blowing Unit to manufacture glass capillaries repair of glassware equipment's etc.
- Operation & Maintenance of pharmaceutical grade (ASTM D1193 Grade-III) specification De-ionized water supply at work bench.
- Operation, up keeping of fire alarm, fire-fighting, fire hydrant system, public announcement (PA) system, fire pumps and Safety stations as per statuary guidelines of Department of Fire services, Uttar Pradesh Government.
- Maintaining of various housekeeping services i.e. Pest & rodent control, termite control, fogging, specialized cleaning in Animal care lab, Horticulture services etc. Environmental & Waste management as per statuary /Good Laboratory Practices (GLP) guidelines.

2) Guest House

The division is maintaining Guesthouse facility at main Campus Jankipuram and Sec K Aliganj Guest House of the CSIR-CDRI to cater our guest from different government organizations, institutions, universities, colleges, industries coming for official meetings, workshops, conferences, seminars etc. We have accommodation for about 25 rooms including AC and Non-AC rooms and VIP rooms. As per the request for booking received from guest, we process it for approval by the competent authorities and inform within 3

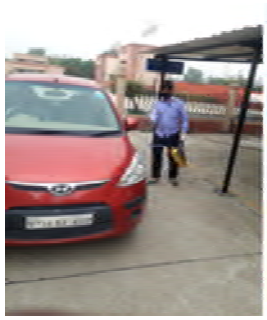
working days from the date of receipt of the request. We do not serve delicious dishes, we serve good memories.

3) Disaster Management: Fire Fighting Unit

CDRI laboratory fulfil compliances of "National Building Code-2005"; there is dedicated team for operation and up keeping of fire alarm system which has main control unit along with the modular control and repeater panel system. The fire detection devices i.e. Refractive indication, Optical detector, Manual calls point and speaker system and fire fighting devices i.e. Fire Extinguishers, Fire Hydrants, hose reels, hose pipes etc. installed as per approved design from Fire Department. Demonstration of fire fighting system and safety management done to all the scientific and administrative staff at every month. The building is inspected by Fire & safety officers of UP Government and consent/ no objection issued by them time to time. Further, in case of fire in nearby areas of CDRI, Fire tender on emergency basis also recharged with water in case of Fire incidents in nearby area/as per request made by Fire Officer, Police Fire Station by CDRI time to time.

Due to medical Health emergency and national pandemic COVID-19, the Centralised Utility services department carried out Sanitisation of Laboratory, working area, vehicles and dispensary and student residential premises.






Fogging & sanitisation drive in CDRI Campus during COVID Pandemic

4) Environmental, Health & safety Services:

The division coordinates and maintain Housekeeping services, specialized cleaning in Animal care labs, environmental & Waste management as per statuary /Good Laboratory Practices (GLP) guidelines. The divisional activity includes:

1. Operation and maintenance of Effluent Treatment Plant (ETP), Sewage Treatment Plant (STP) and Biomedical waste Incinerator etc.
2. In House Operation & maintenance of Sewage Treatment Plant (STP) & Effluent Treatment Plant (ETP), Biomedical waste disposal through Incineration unit and statuary compliances of UPPCB and Ministry of Environment & Forest.
3. Pest & rodent control, fogging for mosquito removal, termite control etc.
4. Operation and up keeping of fire alarm, fire-fighting, fire hydrant system and public announcement (PA) system and Safety stations.
5. Cleaning & maintenance of drinking water purification system & maintenance of common facilities and Rain water Harvesting system.
6. Miscellaneous work on waste solvent /chemical recycle; horticulture & preparation of sports ground, play grounds in campus.
7. Director CDRI took initiative to provide clean drinking water facility for commuters and road passer-by peoples and school children's.
8. To carry out cleanliness drive in CDRI Campus under"Swachh Bharat" mission of Government of India.

Effluent treatment plant at CSIR-CDRI; Lucknow


Sewage Treatment plant at CSIR-CDRI, Lucknow


Rain water Harvesting | Drug Discovery Park

4. Instrumentation Section

Management of Good Laboratory Practice (GLP) Facility

SAIF Division maintaining the Institutional GLP Facility as per the OECD Guidelines to comply the statutory requirements of NGCMA, New Delhi.

- Technical specification verification, installation and commissioning of GLP equipment.
- Calibration/validation of 101 nos. of GLP equipment as per OECD guidelines.
- Troubleshooting/repair of sophisticated GLP equipment.
- Performance check/preventive maintenance and report preparation of 87 nos. of GLP equipment on quarterly basis.
- Standard Environmental Parameter Monitoring, controlling and monthly report preparation of analysed environmental data of experimental rooms and other GLP labs (TICO, CADC, Geno Toxicology & Histopathology).
- Updating and maintaining 7 nos. of Standard Operating Procedure (SOP) related to GLP equipment and environmental parameters control.
- Preparing and Updating the unique identity tag and log book of GLP equipment.
- Providing training to user on GLP equipment use and performance check.
- Under Updating and maintaining following controlled GLP documents
- Mater equipment List (112 Nos. of GLP equipment)
- Calibration/Validation record (101 Nos. of GLP equipment)
- Minor equipment List ((7 Nos. of GLP equipment)
- Withdrawn/Replaced equipment list (19 Nos. of GLP equipment)
- Unique Identity Tag (112 Nos. of GLP equipment)

Facility Management

- As common facility management coordinating AMC of water purification systems (26 nos.) installed at common places of the Institute.

Management of Instruments

Instrumentation section provide efficient and economical repair, maintenance and upkeep of different sophisticated Analytical, Biomedical, Electronics and Laboratory equipment in CSIR-CDRI and CDRI-SAIF. Due to non-availability of imported components/ spares, indigenous substitute was used to ensure the smooth functioning of equipment. Tracing of part of circuit were carried out whenever circuit diagram/service manual is not available.

- Technical specification verification was carried out for the procurement of state of the art new equipment.
- Unit helped the user scientists to prepare broad based technical specification and to choose right equipment to suit their application.
- Laboratory equipment of different divisions of institute are calibrated as per GLP guidelines as per user requirement.
- Training provided on instrumentation technique and hardware to students from different academic institute under Skill development program.
- To identify the instruments either for their retention or disposal off.

(L to R): Mr. N. K. Agarwal, Dr. Ravishankar R., In-charge & Er. Manoj Kumar Rawat

5. Engineering Services

Laboratory Engineering Services Division, comprising of Civil, Electrical, & HVAC sections continued to provide Engineering Services to the Institute to maintain the existing infrastructure & services for R & D works and create new infrastructure. The major works carried out during reporting period are as follows:

(L to R) : Er. Parvez Mahmood & Er. Kamal Jain

Completed civil works:

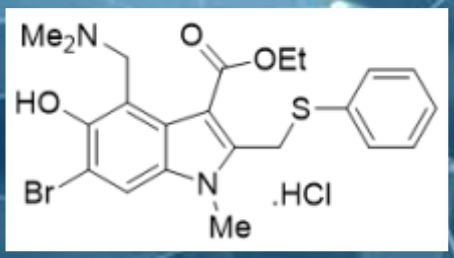
- Additional works for creation of COVID-19 Labs in lockdown period.
- Strengthening of (i) separation fencing wall between CDRI Chattar Manzil premises and ASI and (ii) provision of concertine wire fencing at river side upto Incinerator in Old Campus of CDRI, Lucknow.
- Renovation and upgradation of Guest House Canteen at CDRI New Campus, Sitapur Road, Lucknow.
- Repairing and painting work of existing boundary wall at CDRI, New Campus, Sitapur Road, Lucknow.
- Construction of Radio isotope Laboratory at CDRI New Campus, at Sitapur Road, Lucknow.
- Repair, Painting, and Fencing of boundary wall of CFTRI resource center, Deva Road, Lucknow.

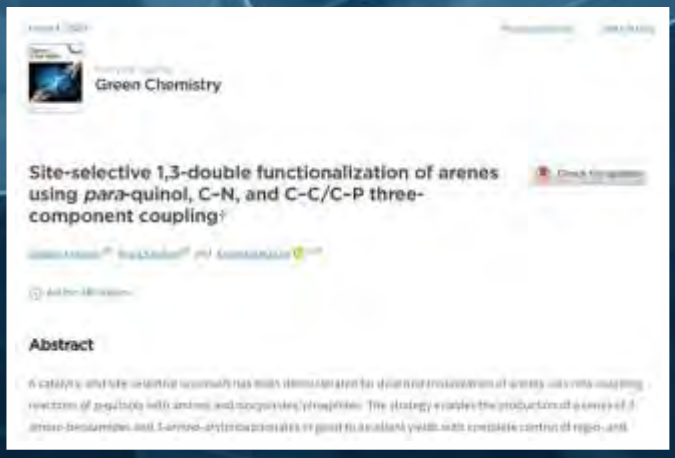
Ongoing works:

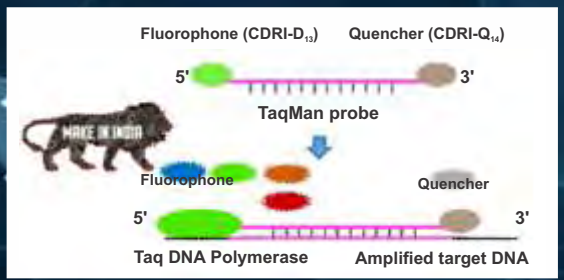
- Proposal for creation of BSL-3 Facility at CDRI, Lucknow.
- Proposal for International Guest House at CSIR Scientist Apartment, Sector K, Aliganj, Lucknow.
- Creation and re-organizing of the Neurobehavioral Animal Facility.
- Construction of garbage pits near ETP and temporary shed for existing walk way at Main canteen CDRI New Campus, Sitapur Road Lucknow.
- Supply and Fixing of Welded mesh in CSIR Scientist Apartment and Provision of Guard room and shade at CSIR Dispensary, Niralanagar, Lucknow.
- Annual item rate contract (ARC) for Civil and allied works for Institute area of CDRI Campus at Sitapur Road and Old Campus at Chattar Manzil Palace, Lucknow during 2020-21 & 2021-22.
    - Renovation of Director's Secretariat.
    - Provision of Aluminium grill ACP sheeing and replacement of Auditorium gutter etc.
    - Flooring in CDRI Crech Facility.
    - Epoxy flooring in GLP area of Animal House.
    - Miscellaneous repairs/painting, sheds, steel fabrication etc. works.
- Repairing and painting work of Process Development Building at Old CDRI, Lucknow.
- Upkeep of GLP Facility.
- Upkeep of Water supply to the Institute and residential colony.

Notes

Section III: Research Output








THE CHEMICAL RECORD
The Bestmann-Ohira Reagent and Related Diazo Compounds for the Synthesis of Azaheterocycles
Abstract
Chemical Communications
Synthesis of β- and γ-lactam fused dihydropyrazinones from Ugi adducts via a sequential ring construction strategy†
ACS Publications
LETTER
Pd-Catalyzed C–H Halogenation of Indolines and Tetrahydroquin with Removable Directing Group
1331
SUBJECTS:
Green Chemistry
Site-selective 1,3-double functionalization of arenes using para-quinol, C–N, and C–C/C–P three-
Chemical Communications
Metal-free α-arylation of α-fluoro-α-nitroacetamides employing diaryliodonium salts†
Abstract
Herein, we present a mild and efficient metal-free arylation of α-fluoro-α-nitroacetami
salts. A broad range of diaryliodonium salts and α-fluoro-α-nitroacetamides containing
was successfully employed in this protocol to yield the arylated products in good yields.
novel protocol was further highlighted by extending the α-arylation to α-cyano-α-fluoroa
Chemical Communications
Substrate-controlled, PBu3-catalyzed annulation of phenacylmalononitriles with allenoates enables tunable access to cyclopentenes†
ACS Publications
My Activity
Publications
LETTER
Cu(II)-Catalyzed Ortho C(sp2)–H Diarylaminati
Synthesize Triarylamines
1427
PDF (1 MB)
ACS Publications
My Activity
Publications
LETTER
Intramolecular 6-exo-dig Post-Ugi Cyclization of N-Substituted 2-Alkynamides: Direct Access to Functionalized Morpholinone Glycoconjugates
713
PDF (2 MB)
SUBJECTS:
Organic Letters
ACS Publications
LETTER
Hydrogen-Bond-Guided Reaction of Cyclohexadienone-aldehydes with
Amines: Synthesis of an Aminal Group Containing a Fused Tetracyclic
Framework
913
PDF (2 MB)
SUBJECTS:
Advanced Synthesis & Catalysis
Ruthenium(II)-Catalyzed Synthesis of Indolo[2,1-a]isoquinolines through Double Oxidative Annulation Reaction of Phenyl Isocyanates with Di(hetero)aryl Alkynes
BRITISH ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

1. Publications

2019

(Not included in the previous year Annual Report due to incomplete Citation)

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2. Dewaker V, Srivastava PN, Verma S, Prabhakar YS. Molecular dynamics study of HDAC8-largazole analogues co-crystals for designing potential anticancer compounds. **Journal of Biomolecular Structure and Dynamics 38(4), 1197-1213**
3. Kumar N and Kumar A. Amino acid-catalyzed direct synthesis of beta-Keto sulfones via aerobic difunctionalization of terminal alkynes in an aqueous medium. **ACS Sustainable Chemistry & Engineering 7(10), 9182-9188**
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6. Thopate Y, Singh R, Rastogi SK and Sinha AK. A highly regioselective and practical synthesis of alpha-Aryl ketones under a cooperative cascade effect of an ionic liquid and tetrabutylammonium fluoride. **Asian Journal of Organic Chemistry 8(11), 2017-2022**

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5. Ahmad S, Bhagwati S, Kumar S, Banerjee D and Siddiqi MI. Molecular modeling assisted identification and biological evaluation of potent cathepsin S inhibitors. **Journal of Molecular Graphics & Modelling 96, 107512**
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7. Ansari MY, Swarnkar S and Kumar A. Stereoselective aminosulfonylation of alkynes: An approach to access (Z)-beta-amino vinylsulfones. **Chemical Communications 56(66), 9561-9564**
8. Azmi S, Verma NK, Tripathi JK, Srivastava S, Verma DP and Ghosh JK. Introduction of cell-selectivity in bovine cathelicidin BMAP-28 by exchanging heptadic isoleucine with the adjacent proline at a non-heptadic position. **Peptide Science, e24207**
9. Balaji SN, Sahasrabuddhe AA and Trivedi V. Insulin signalling in RBC is responsible for growth stimulation of malaria parasite in diabetes patients. **Biochemical and Biophysical Research Communications 528(3), 531-537**
10. Barak DS, Dahatonde DJ, Dighe SU, Kant R and Batra S. Decarboxylative/Oxidative Amidation of Aryl α-Ketocarboxylic Acids with Nitroarenes and Nitroso Compounds in Aqueous Medium. **Organic Letters 23, 9381-9385**
11. Bharti R, Srivastava A, Roy T, Verma K, Reddy DVS, Shafi H, Verma S, Raman SK, Singh AK, Singh J, Ray L and Misra A. Transient transfection of the respiratory epithelium with gamma interferon for host-directed therapy in pulmonary tuberculosis. **Molecular Therapy — Nucleic Acids 22, 1121-1128**
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19. Chahwala FD, Singh D, Kumar R V, Rathore S, Yadav BK, Singh B and Singh AK. A novel monopartite begomovirus and satellites associated with yellow mosaic disease of Sida spp. in India. **Archives of Virology 166, 299-302**
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22. Chandrakar P, Parmar N, Descoteaux A and Kar S. Differential induction of SOCS isoforms by *Leishmania donovani* impairs macrophage-T cell cross-talk and host defense. **Journal of Immunology 204(3), 596-610**
23. Chaturvedi, Malik MY, Rashid M, Singh S, Tiwari V, Gupta P, Shukla S, Singh S and Wahajuddin M. Mechanistic exploration of quercetin against metronidazole induced neurotoxicity in rats: Possible role of nitric oxide isoforms and inflammatory cytokines. **Neurotoxicology 79, 1-10**
24. Chauhan A, Patel RK, Grellier M and Kumar R. Hydrogen-Bond-Guided reaction of Cyclohexadienone-aldehydes with amines: Synthesis of an aminal group containing a fused tetracyclic framework. **Organic Letters 22(15), 6177-6181**
25. Chauhan IS, Marwa S, Rao GS and Singh N. Antiparasitic dibenzalacetone inhibits the GTPase activity of Rab6 protein of *Leishmania donovani* (LdRab6), a potential target for its antileishmanial effect. **Parasitology Research 119(9), 2991-3003**
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29. Dubey A and Mandal PK. An efficient one-pot protocol for direct access to Diarylmethyl Thioglycosides with para-Quinone Methides via S-Glycosyl Isothiouronium salts. **Synlett 31(17), 1713-1719**
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curating the SIRT1 pathway in Parkinson's disease model. **ACS Chemical Neuroscience 11(24), 4416-4425**

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2. Patents

2.1 Patents Filed in India

Patent Application No.: 202011002577 **Date of Filing:** 21/Jan/2020

Title: FUNCTIONALIZED NEUTRAL PHOSPHORUS DENDRIMERS AND POLYCATIONIC PHOSPHORUS DENDRIMERS FOR THE TREATMENT OF *MYCOBACTERIUM TUBERCULOSIS*

Inventors: Serge Mignani, Kishore Kumar Srivastava, Rama Pati Tripathi, Dheeraj Soam, Sidharth Chopra, Arunava Dasgupta, Durga Prasad Mishra, Vishwa Deepak Tripathi, Jean Pierre Majoral, Caminade Anne-Marie

Patent Application No.: 202011002962 **Date of Filing:** 23/Jan/2020

Title: 4-HYDROXYISOLUCINE (4-HIL) ENRICHED FRACTION FROM *TRIGONELLA FOENUM-GRAECUM* (FENUGREEK) SEEDS FOR THE MANAGEMENT OF POLYCYSTIC OVARY SYNDROME (PCOS) AND ITS PROCESS OF PREPARATION THEREOF

Inventors: Narender Tadigoppula, Rajesh Kumar Jha, Rabi Shankar Bhatta, Srikanta Kumar Rath, Prabhat Ranjan Mishra, Brijesh Kumar, Vaibahve Ubba, Ashok Kumar, Ramanand Prajapati, Pratibha Singh, Vikash Kumar Gond, Vikas Bajpai, Sonam Kanchan, Nikhil Rai, Arun Agarwal, Sristi Agrawal, Anjali Mishra, Swati Rajpoot, Wahajuddin

Patent Application No.: 202011023422 **Date of Filing:** 04/Jun/2020

Title: AZIRINE CONTAINING COMPOUNDS AS ANTI-ANGIOGENESIS AGENTS AND PREPARATION THEREOF

Inventors: Gangarajula Sudhakar, Nagam Satish, Tella Ramesh Babu, Kumaravelu Jagavelu, Himalaya Singh, Mohammad Imran Siddiqi, Muhammad Wahajuddin, Sandeep Kumar Singh, Mamunur Rashid, Anil Kumar Karunakaran Sasikala (CSIR-CDRI + CSIR-IICT)

Patent Application No.: 202011028346 **Date of Filing:** 03/Jul/2020

Title: BETA CARBOLINES AS SELECTIVE AND BIASED KAPPA OPIOID RECEPTORS AGONISTS

Inventors: Sanjay Batra, Prem Narayan Yadav, Veena Devi Yadav, Lalan Kumar, Shalini Dogra, Poonam Kumari, Ajeet Kumar

Patent Application No.: 202031034400 **Date of Filing:** 11/Aug/2020

Title: POCT DEVICE TO DETECT CERVICAL CANCER SPECIFIC BIOMARKER

Inventors: Mitali Basak, Shirsendu Mitra, Ankita Jain, Saurabh Kumar Agnihotri, Akanksha Vyas, Madan Lal Brahma Bhatt, Rekha Sachan, Surjendu Maity, Nayanjyoti Kakati, Monika Sachdev, Dipankar Bandyopadhyay (CSIR-CDRI + IIT, Guwahati)

Patent Application No.: 202011039833 **Date of Filing:** 12/Sep/2020

Title: HESPERIDIN AS INHIBITOR OF NEUTROPHIL EXTRACELLULAR TRAP FORMATION AND PHARMACEUTICAL FORMULATION THEREOF

Inventors: Sachin Kumar, Anil Nilkanth Gaikwad, Naibedya Chattopadhyay, Sanjay Batra, Sanjeev Kanojiya, Narender Tadigoppula, Prabhat Ranjan Mishra, Jiaur R Gayen, Rabi Sankar Bhatta, Atul Goel, Vivek V. Bhosale, Apurwa Singhal, Ashok Kumar, Priyanka Rawat, Aritra Ghosh, Athar Husain, Chandra Prakash Sharma, Deepak Sharma, Anil Kumar K. S., Abhijit Deb Choudhury

Patent Application No.: 202011039625 **Date of Filing:** 12/Sep/2020

Title: CHEBULINIC ACID ENRICHED FRACTION FOR THE MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA (BPH) AND ITS PROCESS OF PREPARATION THEREOF

Inventors: Narender Tadigoppula, Monika Sachdev, Rabi Shankar Bhatta, Srikanta Kumar Rath, Prabhat Ranjan Mishra, Preeti Rastogi, Tripti Mishra, Ankit Kumar Agrawal, Deependra Singh, Saurabh Kumar, Bilal Ahmad Hakim, Sarvesh Kumar Verma, Arpon Biswas, Sandeep Urandur, Sonam Kanchan

Patent Application No.: 202011055682 **Date of Filing:** 17/Dec/2020

Title: NEW SMAC MIMETICS FOR CANCER THERAPY

Inventors: Wahajul Haq, Rafat Ali, Akhilesh Singh, Mushtaq Ahmad Nengroo, Roshan Katekar, Gajendra Singh, Jayanti Vaishnav, Mohammad Afsar, Manohar Singh, Srikanta Kumar Rath, Dipankar Koley, Durga Prasad Mishra, Ravishankar Ramachandran, Ravi Sankar Ampapathi, Jiaur Rahaman Gayen, Dipak Datta

2.2 Patents Granted in India

Patent No.: 341387 **Date of Grant:** 13/Jul/2020

Title: NEW RAPAMYCIN CONJUGATES AND PROCESS FOR PREPARATION

Inventors: Wahajul Haq, Rafat Ali, Dipak Datta, Rakesh Kumar Arya

Patent No.: 343268 **Date of Grant:** 04/Aug/2020

Title: 6/8 (DI(HETERO-2-YLMETHYL) MINO) METHYL)-7-HYDROXYL-4- (METHYLTHIO)-2-OXO-2H-CHROMENE-3-CARBONOTRILES USEFUL AS FLURESCENT PROBES.

Inventors: Atul Goel, Ajay Kumar Jha, Ashutosh Raghuvanshi, Rakesh Kumar Arya, Dipak Datta

Patent No.: 345265 **Date of Grant:** 27/Aug/2020

Title: PROTEASOMAL INHIBITORS USEFUL FOR OSTEOGENIC ACTIVITY AND PHARMACEUTICAL COMPOSITION THEREOF [osteo-HEAL]

Inventors: Prabhat Ranjan Mishra, Ritu Trivedi, Divya Singh, Priyanka Kushwaha, Vikram Khedgikar, Sulekha Adhikari, Dharmendra Choudhary, Jyoti Swarup, Avinash Kumar, Anirudha Karvande, Ashwni Verma, Shweta Sharma, Prabodh Trivedi, Neelam S Sangwan, Rajendra S Sangwan

Patent No.: 345995 **Date of Grant:** 03/Sep/2020

Title: SUBSTITUTED BIS QUINOLIN COMPOUNDS AND PROCESS FOR PREPARATION THEREOF

Inventors: Dinesh Kumar Dikshit, Vinita Chaturvedi, Manju Yasodha Krishnan, Shaheb Raj Khan, Sudhir Sinha, Bhupendra Narain Singh

Patent No.: 346806 **Date of Grant:** 15/Sep/2020

Title: AN IMPROVED PROCESS FOR PREPARATION OF 4-SUBSTITUTED AMINO-2,3-POLYMETHYLENEQUINOLINE HYDROCHLORIDE

Inventors: Mandalapu Dhanaraju, Rajesh Kumar Arigela, Tara Rawat, Vishnu Lal Sharma

Patent No.: 349025 **Date of Grant:** 12/Oct/2020

Title: NOVEL ARYL NAPHTHYL METHANONE OXIME DERIVATIVES FOR THE TREATMENT OF HEMATOLOGICAL MALIGNANCIES AND SOLID TUMORS

Inventors: Sabyasachi Sanyal, Atul Kumar, Naibedya Chattopadhyay, Jawahar Lal, Arun Kumar Trivedi, Dipak Datta, Srikanta Kumar Rath, Tahseen Akhtar, Shailendra Kumar Dhar Dwivedi, Manisha Yadav, Bandana Chakravarti, Abhishek Kumar Singh, Jay Sharan Mishra, Nidhi Singh, Anil Kumar Tripathi

Patent No.: 350680 **Date of Grant:** 02/Nov/2020

Title: CARBODITHIOATES AND PROCESS FOR PREPARATION THEREOF

Inventors: Sharma Vishanu Lal, Lal Nand, Sarswat Amit, Jangir Santosh, Bala Veenu, Kumar Lalit, Rawat Tara, Jain Ashish, Kumar Lokesh, Maikhuri Jagdamba Prasad, Gupta Gopal

Patent No.: 352311 **Date of Grant:** 26/Nov/2020

Title: SHORT ANTIMICROBIAL PEPTIDES WITH HIGH THERAPEUTIC VALUE AND ANTI-LEISHMANIA ACTIVITY

Inventors: Ghosh Jimut Kanti, Sarfuddin, Shukla Praveen Kumar, Mishra Nripendra Nath, Dungdung Sandhya Rekha, Aparna Gomes, Roy Syamal, Ghosh Prasanta, Bhattacharya Shamik

2.3 Patents Granted Abroad

Australian Patent No.: 2014291615 **Date of Grant:** 09/Jan/2020

Title: PROTEASOMAL INHIBITORS USEFUL FOR OSTEOGENIC ACTIVITY AND PHARMACEUTICAL COMPOSITION THEREOF [osteo-HEAL]

Inventors: Prabhat Ranjan Mishra, Ritu Trivedi, Divya Singh, Priyanka Kushwaha, Vikram Khedgikar, Sulekha Adhikari, Dharmendra Choudhary, Jyoti Swarup, Avinash Kumar, Anirudha Karvande, Ashwni Verma, Shweta Sharma, Prabodh Trivedi, Neelam S Sangwan, Rajendra S Sangwan

European Patent No.: 3027633 **Date of Grant:** 22/Jan/2020

Title: ULMOSIDE-A-DERIVED COMPOUND FROM *ULMUS WALLICHIANA* PLANCHON USEFUL FOR PREVENTION OR CURE OF METABOLIC DISEASES

Inventors: Sanyal Sabyasachi, Chattopadhyay Naibedhyay, Maurya Rakesh, Gayen Jiaur Rahaman, Bhadauria Smrati, Trivedi Arun Kumar, Singh Abhishek Kumar, Mishra Jay Sharan, Kumari Rashmi, Sharan Kunal, Khan Parvez Mohammad, Khan Kainat, Singh Nidhi, Dwivedi Shailendra Kumar Dhar, Yadav Manisha, Dixit Preety, Mishra Devendra Pratap, Sharma Sharad, Arya Kamal Ram

Great Britain Patent No.: 3027633 **Date of Grant:** 22/Jan/2020

Title: ULMOSIDE-A-DERIVED COMPOUND FROM *ULMUS WALLICHIANA* PLANCHON USEFUL FOR PREVENTION OR CURE OF METABOLIC DISEASES

Inventors: Sanyal Sabyasachi, Chattopadhyay Naibedhyay, Maurya Rakesh, Gayen Jiaur Rahaman, Bhadauria Smrati, Trivedi Arun Kumar, Singh Abhishek Kumar, Mishra Jay Sharan, Kumari Rashmi, Sharan Kunal, Khan Parvez Mohammad, Khan Kainat, Singh Nidhi, Dwivedi Shailendra Kumar Dhar, Yadav Manisha, Dixit Preety, Mishra Devendra Pratap, Sharma Sharad, Arya Kamal Ram

United States Patent No.: 10576078 **Date of Grant:** 03/Mar/2020

Title: COMBINATION OF CLOFAZIMINE AND IMATINIB FOR EFFECTIVE THERAPY OF DRUG-RESISTANT MYELOID LEUKEMIA

Inventors: Sabyasachi Sanyal, Harish Kumar, Naibedya Chattopadhyay, Ravishankar Ramachandran, Arun Kumarv Trivedi, Sonal Shree, Anagha Ashok Gurjar, Sourav Chattopadhyay, Sapana Kushwaha, Abhishek Kumar Singh, Shikha Dubey, Kiran Lata, Riyazuddin Mohammed, Jiaur Rahaman Gayen, Anil Kumar Tripathi

United States Patent No.: 10596115 **Date of Grant:** 24/Mar/2020

Title: PROTEASOMAL INHIBITORS USEFUL FOR OSTEOGENIC ACTIVITY AND PHARMACEUTICAL COMPOSITION THEREOF [osteo-HEAL]

Inventors: Prabhat Ranjan Mishra, Ritu Trivedi, Divya Singh, Priyanka Kushwaha, Vikram Khedgikar, Sulekha Adhikari, Dharmendra Choudhary, Jyoti Swarup, Avinash Kumar, Anirudha Karvande, Ashwni Verma, Shweta Sharma, Prabodh Trivedi, Neelam S Sangwan, Rajendra S Sangwan

3. Papers Presented in Scientific Conventions

107th Indian Science Congress, University of Agricultural Sciences, GKVK Campus, Bangalore, Karnataka, 3rd-7th January, 2020

- Synthesis of Fluorescent Carbon Quantum Dots from *Manilkara Zapota* (Chiku) Pulp for Bio-Medical Applications. *Kundan Singh Rawat and Atul Goel.*

26th ISCB International Conference, Ahmedabad, 22th-24th January, 2020

- Hantzsch Ester Mediated Reactions under Visible Light Irradiation. *Namrata Rastogi.*

12th Asia-Pacific Microscopy Conference (APMC-2020), Hyderabad, 03rd-07th February, 2020

- Studies on Autophagy Associated Apoptosis in Colorectal Cancer Cell Lines by Selective Estrogen Receptor Modulator Ormeloxifene. *Nishakumari Singh, Rohit Sahai, Swetapadma Majhi, Mayank Maheshwari, Jayanta Sarkar and Kalyan Mitra.*
- Anti-Proliferative Effects and Ultrastructural Changes of a Second Generation Napthoquinone Derivative in *Leishmania donovani*. *Swetapadma Majhi, Bhanu Priya Awasthi, Rohit Sahai and Kalyan Mitra.*

India-EMBO symposia-Mycobacterial Heterogeneity and Host Tissue Tropism, New Delhi, 11th–15th February, 2020

- Functional Insights into an Uncharacterized Cupin Protein of *Mycobacterium Tuberculosis*. *Suman Bharti, Rahul Kumar Maurya, Umamageswaran Venugopal, Manju Yasoda Krishnan*
- Insights on the Enzymatic Property and Functional Roles of Rv3371, A Putative Triacylglycerol Synthase of *Mycobacterium tuberculosis*. *Rahul Kumar Maurya, Suman Bharti, Umamageswaran Venugopal and Manju Krishnan.*

International Conference on Emerging Trends in Chemical Sciences (ETCS-2020), Guwahati University, Guwahati, Assam, 13th-15th February, 2020

- Mechanochemical Synthesis of New Solid Forms of Zaltoprofen, their Physicochemical Evaluation and the Rationalization Of Cocrystal Formation Based on MESP and Free Energy Computations. *Sibananda G. Dash and Tejender S. Thakur.*

8th International Translational Cancer Research Conference, Varanasi, 13th-16th February, 2020

- Cancer Germline Antigen can be explored for the Early Diagnosis of Cervical Cancer. *Vyas A, Agnihotri SK, Jain A, Hakim BA, Firdausi N, Singh D, Tyagi V, Singh R, Srivastava N, Bhatt MLB, Srivastava K, Sachan R and Sachdev M.*

30th Annual Meeting of the ISSRF along with the World Congress on Reproductive Health with Emphasis on Reproductive Cancers, Infertility and Assisted Reproduction (ISSRF-2020) Jammu and Kashmir, 14th-16th February, 2020

- Novel Pathogenic Mutation in SRD5A2 and SRD5A3 Genes in 46, XY Atypical Genitalia Cases. *Poonam Mehta, Sandeep Singh and Singh Rajender.*
- Ablation of BMP Type-I Receptor Impairs Male Germ Cell Proliferation and Differentiation. *Meghali Joshi, Vertika Singh and Singh Rajender.*

Indian Society for the Study of Reproduction & Fertility (ISSRF 2020), Jammu, 14th-16th February, 2020

- Investigation of Oocyte Maturation Markers Through Chemo-ablated Mouse Model. *Tyagi V, Hakim BA, Singh D, Firdausi N, Singh R, Agnihotri SK, Vyas A and Sachdev M.*

Young Investigators Meeting-2020, Chennai, 14th-18th February, 2020

- Role of Mitochondrial Dynamics in Immune Activation. *Shaziya Khan and Amit Lahiri*

Global Cancer Summit 2020 Online (Virtual Platform), 19th February, 2020

- Evaluation of Novel CGA for the Early Detection of Cervical Cancer. *Vyas A, Agnihotri SK, Jain A, Tyagi V, Srivastava N, Kumar N, Srivastava K, Gupta R, Sachan R, Bhatt MLB and Sachdev M.*

National Conference on Drug Repurposing: Reinvent, Recycle & Reuse, Lucknow, 03rd-05th March, 2020

- Leprosy Drug Clofazimine Activates Peroxisome Proliferator-Activated Receptor-γ and Synergizes with Imatinib to Inhibit Chronic Myeloid Leukemia Cells. *Harish Kumar and Sabyasachi Sanyal*

International Conference on Organometallics and Catalysis (ICOC-2020), Goa, 07th-10th March, 2020

- Hantzsch Ester as Photo-Organocatalyst under Visible Light Irradiation. *Namrata Rastogi*

Monsoon Brain Meeting Online presentation, 24th-26th June, 2020

- Stress Induced Glial Activation in Brain Leads to Impaired Hippocampal Neurogenesis and Anxious Depression like Behavior. *Parul, Akanksha Mishra, Sonu Singh, Seema Singh, Virendra Tiwari, Swati Chaturvedi, Muhammad Wahajuddin and Shubha Shukla.*

Emerging Innovation and Advancement in Biological Science, Human Welfare and Agriculture Research in Current Era, Mathura, 25th- 27thJuly, 2020

- DNA Relaxation by Human DNA Ligase I: A Cause of Drug Resistance. *Pooja Maurya, Sampa Gupta, Shagun Krishna, M.I. Siddiqui, K.V. Shashidhara, D. Banerjee.*

Quantum Crystallography Online Meeting 2020 (QCrOM2020), organized by Commission on Quantum Crystallography of IUCr Online international conference, 22th-19th August, 2020

- Theoretical Charge Density Analysis of Cation··· Cation Hydrogen Bonds in Synephrine Salts. *Sibananda. G. Dash and Tejender S. Thakur.*

21st International Vascular Biology Meeting, Seoul, 09th-12th September, 2020

- Lymphatic Regulation in Heart. *Kumaravelu J*

Molecular Parasitology Meeting XXXI, Woods Hole in Falmouth, Massachusetts, 21st-24th September, 2020

- The Malarial Stearoyl-CoA Desaturase is Essential Only for Parasite Late Liver Stage Development. *Narwal S, Choudhary H and Mishra S*

e-Colloquium on "Emerging Trends in Health and Disease Research" ETHDR-2020, Haryana, India, 20th October, 2020

- A Study of Underline Health Factors that Influence the Outcome of Covid-19 Patients in Different Indian States. *D. Banerjee and B. Rakhecha*

Annual meeting of Indian Society of Bone Mineral Research, 2020 Virtual- online platform, 29th October - 1st November, 2020

- Kappa Opioid Receptor Agonist Protects Rat Articular Chondrocytes Against IL-1β Induced Osteoarthritis. *Shradha Sinha and Ritu Trivedi*
- Identification of a New Class of BMP-2 Targeted Bone Anabolic Agent. *Anirban Sardar, Alisha Ansari, K V Sashidhara and Ritu Trivedi*

International Conference on Molecular Structure and Instrumental Approaches (ICMSI-2020), Department of Chemistry, School of Science, RK. University, Rajkot, Gujarat, India, 26th-27th November, 2020

- Amino Acid-Catalyzed Direct Synthesis of β-Ketosulfones via Aerobic Difunctionalization of Terminal Alkynes in an Aqueous Medium. *Deepak Bhadoria, Navaneet Kumar and Atul Kumar*

57th Annual Convention of Chemists (ACC) & Recent Trends in Chemical Sciences – Organic Bio-Chemistry (RTCS-OBC-2020), Indian Chemical Society (ICS), Department of Chemical Sciences, IISER Kolkata, 26th-29th December, 2020

- Tuning the Chemoselectivity of Dehydroacetic Acid Derived Enones by Isoniazid and Phenylhydrazines: An Efficient Access to 3-Styryl Pyrano[2,3-c]pyrazolones. *Sumedha Swarnkar, Mohd Yeshab Ansari and Atul Kumar*
- Amino Acid-Catalyzed Direct Synthesis of β-KetoSulfones via Aerobic Difunctionalization of Terminal Alkynes in an Aqueous Medium. *Deepak Bhadoria, Navaneet Kumar and Atul Kumar*

4. Invited Lectures Delivered by Institute Scientists

Prof. Tapas K. Kundu

- Epigenetics, Life Beyond Gene Sequence: Implications in Health and Disease, 107th Indian Science Congress -2020, University of Agricultural Sciences in Bengaluru, 06th January, 2020
- Natural Product Based Small Molecule Modulators of Epigenetic Enzymes: Implications in Therapeutics. Plenary Lecture in Conference on "Chemistry and Biology of Natural Products", CSIR-NEIST, Jorhat, 25th July, 2020
- Epigenetics, Life beyond your Genes, Key Note Address in the International Symposium (Online), Bidhan Chandra Krishi Viswavidyala, Mohanpur, Nadia, 20th September, 2020
- Fight Against COVID 19-We Shall Overcome, Key Note Address in the National Webinar, SBS Government College, Hili, Dakshin Dinajpur, 19th October, 2020
- Epigenetics, Life Beyond Your Genes, University of Mysore, 15th December, 2020
- Epigenetics: Targets of Drug Discovery, National Level Webinar, Advanced Research Centre, Department of Microbiology, Lady Brabourne College, Kolkata, in Collaboration with Royal Society of Chemistry (Eastern India Section) 20th December, 2020

Dr. S.K. Rath

- Research Methodology for Biologists, Webinar, Research Cell, Lucknow University, 5th July, 2020
- COVID 19: The Pandemic; Yesterday, Today & Tomorrow, Webinar Netaji Shubhash Bose Memorial College Cuttack, Odisha, 9th August, 2020
- Challenges in Human Health care in Covid -19 situation, International E. Seminar, Lucknow Christian College, Lucknow, 7th-8th September, 2020
- Antimicrobial Resistance, International Webinar, RDS College, Keonjhar, Odisha, 18th December, 2020

Dr. Sanjay Batra

- Drug Discovery and Development: Holistic Approach and Strategic Advances, Online Faculty Development Program on Impact of Biotechnology and Molecular Biology on Drug Discovery, 17th-22th December 2020, 19th December, 2020
- Metal-free Oxidative Coupling Reactions, TEQIP-III Sponsored Online Webinar, National Institute of Technology Manipur, 6th-10th December, 2020
- Drug Repurposing in the Era of Covid-19 (nSARS-CoV-2), Chemical Sciences for Drug Discovery & Therapy (CSDDT 2020) VNIT, Nagpur, 22th-26th June, 2020
- Metal-free Amidation of Aryl á-Ketocarboxylic acids with Nitroarenes and Nitrosoarenes. National Conference on Organic Synthesis, 2th-3th Mar, 2020, Behrampur University
- Antileishmanial Assessement of Isoxazole Derivatives, International Symposium on Current Trends in Pharmaceutical and Medical Sciences (CTPMS-2020), GIPER, Kashipur, Uttarakhand, 26th-29th Feb, 2020

Dr. Gautam Panda

- Amino Acids and Trisubstituted Methanes (TRSMs) as Versatile Synthon: Rays of Hope for Autophagic Cell death and Tuberculosis respectively? Nara University, Japan (Webinar) 28th May, 2020
- Amino Acids Derived Compounds Towards Autophagic Cell death, Sharda University, New Delhi through (Webinar), 27th May, 2020
- Corannulene Derived Antimicrobial Peptides: Synthesis and Properties, Osaka University, Japan, 11th May, 2020
- Trisubstituted Methanes (TRSMs) as Versatile Synthon: Synthesis and Antimycobacterial Activities, Hiroshima University, Japan, 01st May, 2020
- Amino Acids Towards Anticancer Alkaloids and Steroidomimetics: Rays of Hope for Autophagic Cell death? Keio University, Japan, 15th May, 2020

Dr. T. Narender

- Chemical and Biological Exploration of Indian Medicinal Plants for Human Health Care, Nirma University, Ahmadabad, 26th ISCB International Conference (ISCBC-2019), 24th, January 2020
- Chemical and Biological Exploration of Indian Medicinal Plants for Human Health Care, Mahatma Gandhi Central University, Motihari (East Champaran) Bihar, International Conference on Frontier Areas of Chemistry (ICFAC), 28th February, 2020
- Natural Products in Drug Discovery and Development, AICTE sponsored Online QIP Short Term Course on "Natural Products in Holistic Healthcare – Recent Trends & Future Prospects (NPH2)" Organized by IIT, Banaras, 24th December, 2020

Dr. Bhupendra N Singh

- Genome and Biology of Infection, Lucknow University, 4th July, 2020

Dr. D.P. Mishra

- Proteomic Biomarkers in Cancer Diagnosis, CME Session on "Current Trends in Cancer Proteomics", 7th September, 2019
- Targeting Metabolic Reprogramming for Anti-angiogenic Therapy in Glioblastoma. ILS, Bhubaneswar, India, 3rd December, 2019

Dr. Ravi Sankar Ampapathi

- Key note lecture "Challenges in the Analysis of Drugs of Abused in the Field of Forensic Science-Role of LC-NMR to Meet the Challenges in the Identification of Mixture of Drugs" Ist Course on Analysis of Drugs and Explosives by LC-NMR & FT-IR from 12th to 16th Oct, 2020 through Online-Mode,12th October, 2020

Dr. Rajender Singh

- Sperm: Not just a DNA Vehicle, International Conference on Advances in Biosciences and Biotechnology - ICABB-2020, 31st January, 2020

Dr. Prem Prakash Yadav

- Recent Advances in Drug Repurposing for Combating SARS Cov-2-International E-Conference organized by: S. S. Khanna Girls' Degree College, Prayagraj on "Sustainability Challenges & Transforming Opportunities Amidst Covid-19" from 26th-30th July, 2020
- Phytochemicals and Plant Based Drug Discovery" SRISTI in Collaboration with BIRAC, BIIS-7 Webinar (Biotech Innovation Ignition School), 1-21st December, 2020

Dr. Kalyan Mitra

- The Role of Electron Microscopy in Biomedical Sciences and Drug Discovery, Dr. APJ Abdul Kalam Technical University Sponsored Online Faculty Development Program (FDP) on "Impact of Bioinformatics, Biotechnology and Molecular Biology on Drug Discovery" during 17th-22th Dec, 2020 by Department of Biotechnology, Bansal Institute of Engineering & Technology, Lucknow, 18th December, 2020

Dr. Aamir Nazir

- Targeted Downregulation of Estradiol Binding Na+/H+ exchanger nhx-2, Mimics Calorie Restriction, Extends Reproductive Longevity and Ameliorates Effects Associated with Alpha Synuclein Aggregation in *C. elegans*, International Symposium on Present and Future Challenges of Xenobiotic Mediated Mutagenesis: Impact on Human Health & Environmental Safety" (EMSI-2020) CSIR-IITR, Lucknow, 19th February, 2020
- Functional Characterization of Protein Quality Control Machinery in Context of Age Associated Neurodegenerative Diseases: Studies Employing Transgenic *Caenorhabditis elegans*, Webinar on Alternate Animal Models in Biological Research (AAMBR-2020) CSIR-IITR, Lucknow, 27th May, 2020
- Novel MicroRNA-4813-3p, Acts as a Common Trigger for Regulating Multiple Checkpoints of Protein Clearance Machinery in Alpha Synuclein Expressing *C. elegans* Model, Annual Conference of Society for Alternatives to Animal Experiments-India. Tiruchirapalli, Tamil Nadu, India (Webinar), 28th December, 2020

Dr. Rabi Sankar Bhatta

- Computational Approaches Applied to Drug Discovery and Dosage Form Designing, Webinar, 12th December, 2020

Dr. Sanjeev Kanojiya

- Digital Library of Indian Medicinal Plants and Their Metabolites [A Mass Spectrometry-Based Bioinformatics Tool] National Webinar at Kalinga University Naya Raipur, Chhattisgarh, 23rd November, 2020

Dr. Jayanta Sarkar

- Targeted Cancer Therapy, Amity University, Lucknow (via MS Team),13th April, 2020

Dr. Kumaravelu Jagavelu

- Experimental Animal Studies using Laboratory Small animals, Sri Venkateswara College of Engineering, Sriperumbudur, 29th May, 2020

Dr. Kishor Mohanan

- Three-Component Synthesis of Trifluoromethy-lated Heterocycles Employing Trifluorodiazoe-thane International Conference on Organo-metallics and Catalysis, Goa, 8th March, 2020

Dr. Mukesh Pasupuleti

- Next Generation Anti-microbial Biotherapeutic Agents: Therapy to Development Raghavendra Institute of Pharmaceutical Education and Research (RIPER) – Autonomous, Anantapur, A.P India, 31st October to 2 November, 2019

Dr. Madhav Nilakanth Mugale

- Data & record Management as per GLP guidelines and Animal Handling in *in vivo* Studies, CSIR-HRDC Ghaziabad, 25th February, 2020

Dr. Mrigank Srivastava

- Multicolor Immunophenotyping using Flow Cytometry, Flow Cytometry Workshop "Basics of Flow Cytometry and its Applications in Biomedical Sciences" BBAU, Lucknow, 5th-7th March, 2020

- The Tussle for survival: An Immunological Perspective of Lymphatic Filariasis, 12th Annual Conference and Workshop of the Cytometry Society of India, 9th–12th October, 2019, SGPGI, Lucknow, 09th October, 2019

Dr. Susanta Kar

- Rheostatic Control of Host Immunity: Decoding the Immunological Playmakers that Drive the Host-Pathogen Arms Race of Visceral Leishmaniasis, 89th Annual Meeting of SBC(I) in Conjunction with the 8th Annual Symposium of Coastal Karnataka Chapter, 18th November, 2020

Dr. Vineeta Tripathi

- Transgenic: An approach for Crop Improvement (webinar), Department of Botany, Ramnagar College, Depal-721 453, West Bengal, India, 29th September, 2020

Dr. Ajay Kumar Srivastava

- Development of Post-IMCR Modifications En Route to Natural Products and Mimetics, International Conference 'Natural Products – Quality, Safety and Efficacy' SIES_College of Arts, Science & Commerce, Mumbai, 07th March, 2020
- Exploring Molecular Diversity towards Drug Development, Webinar, ANS College, Barth, Patna, 02nd July, 2020
- Basics of Drug Development, Workshop on "Skill Development Programme-Good Laboratory Practices" at Veer Kunwar Singh University, Ara, Bhojpur, Bihar, India, 24th July, 2020

Dr. Amit Lahiri

- Inflammatory Bowel Disease-looking at genetic susceptibility, Department of Gastroenterology, SGPGI, Lucknow, 11th January, 2020

Dr. Tejender S. Thakur

- Crystal Structure Prediction and Quantum Crystallography Applications (Webinar): Faculty Refresher Course in Chemistry being Organised by HRDC and Department of Chemistry, Guru Jambheshwar University of Science & Technology, Hisar, 30th September, 2020
- Application of X-ray Crystallography in Drug Discovery and Development Refresher Course in Physics and Astrophysics, Department of Physics, University of Lucknow, 21st February, 2020
- Interaction Between Two Cationic Species: Electrostatic Repulsion and the Importance of Hydrogen, Bonding International Conference on Emerging Trends in Chemical Sciences (ETCS-2020), Guwahati University, Guwahati, Assam, 14th February, 2020
- Hydrogen Bonds between Same Charge Species: Insights form Computational Studies. Workshop on One 100 Years of Hydrogen bonding, Indian Institute of Science, Bengaluru, 10th January, 2020

Dr. Ravindra Kumar

- Catalytic and Enantioselective Synthesis of Benzoxasiloles: Direct Application to (R)-Orphenadrine and (S)-Neobenodine, Nirma University, Ahmedabad, 22nd-24th January, 2020
- Oxidative Cyclization: An Expedient Strategy to Diverse Chiral Carbocyles, University of Delhi, 10th-11th January, 2020

Dr. Damodara Reddy N

- Bench to Bedside: The Drug Development Pipeline, Commissionerate of Collegiate Education, Andhra Pradesh, India, 04th July, 2020

5. Networks & Inter Agency Linkages

(Projects completed/ongoing/initiated during 2020)

1. CSIR Mission/Thematic/In-house Projects

Nature	Project Title	PI
Duration upto 31 March 2020		
CSIR Mission	CSIR Phytopharmaceuticals Mission	Dr. Naibedya Chattopadhyay
CSIR Mission	Mission Nutraceuticals and Nutritionals	Dr. Naibedya Chattopadhyay
CSIR - FTT	Validation of potential biomolecules against Parkinson's disease: A Preclinical study	Dr. Aamir Nazir
CSIR - FTT	Development of male infertility diagnostic kits (DeMID)'	Dr. Rajender Singh
CSIR - FTT	Development of a small molecule inhibitor of PCSK9	Dr. Manoj Kumar Barthwal
CSIR - FTT	Clinical development of antiplatelet compound S007-867 for treatment of cardiovascular diseases	Dr. Vivek Vidyadhar Bhosale
CSIR - NCP	Non- alcoholic steatohepatitis (NASH)	Dr. Durga Prasad Mishra
CSIR - NCP	Chronic respiratory disease innovation and solution program (CRISP)"	Dr. Kashif Hanif
CSIR - NCP	Development of therapeutics against skeletal targets to improve bone health: Therapeutic repurposing of Pentoxyfylline	Dr. Naibedya Chattopadhyay
CSIR - NCP	Regulatory development of CSIR-CDRI prioritized lead compounds	Dr. Sharad Sharma
CSIR - NCP	Therapeutics for lifestyle disorders [TheraLSD]	Dr. Prem Narayan Yadav
CSIR - NCP	Cell penetrating peptide, IMT-P8 as a drug delivery vehicle in management of MRSA infections (PEPTIDOCURE)	Dr. Mukesh Pashupulati
CSIR - FBR	Investigating chemical therapeutic space and determinates of survival and virulence in malaria [ParaDlgM]	Dr. Saman Habib
CSIR - FBR	Development of identified lead molecule as novel anti-leishmanial therapeutic agent	Dr. Neena Goyal
CSIR - FBR	Development of therapeutic against skeletal targets to improve bone health	Dr. Naibedya Chattopadhyay
CSIR - FBR	Dissecting the architecture and molecular mechanism of multi protein complexes (BERosomes) involved in DNA Base Excision Repair (BER) and Transcription coupled DNA repair (TCR) pathways from *M. tuberculosis*	Dr. Ravishankar Ramachandran
Facility Creation	Up-gradation of existing non-human primate experimentation facility	Dr. D.S. Upadhyay
Facility Creation	Clinical Pharmacology and Pharmacokinetics Facility at CSIR-CDRI	Dr. Amit Misra
Major Lab Project	Addressing biological processes for designing new strategies of intervention in parasitic diseases and anti-parasitic drug discovery	Dr. Saman Habib
Major Lab Project	AMR: Drug resistant-mycobacterial infections & ESKAPE pathogens	Dr. R. Ravishankar
Major Lab Project	Research on anabolic skeletal targets in health and illness: Bone health and metabolic bone diseases	Dr. Naibedya Chattopadhyay
Major Lab Project	Pre-clinical studies in drug development and translation: Development of new drug entities, phytopharmaceuticals and standardized extracts in AYUSH mode	Dr. Srikanta Kumar Rath
Other Lab Project	Advancing knowledge frontiers in the area of Life style diseases and reproductive health	Dr. Prem Narayan Yadav
Network	CSIR Integrated Skill Initiative programme	Mr. Vinay Tripathi
Network	Jigyasa: Scientist-Student connect" programme	Mr. Vinay Tripathi
Duration upto 31 March 2021		
COVID	Evaluation of Candidate FDA-approved drugs, Candidates from library of Non-toxic compounds that have been pre-clinically cleared and specific Phytopharmaceuticals for reurposing against COVID-19 infection	Dr. Ravishankar R
COVID	Genome sequencing of SARS-CoV-2 samples from Lucknow/Uttar Pradesh	Dr. Rajender Singh
COVID	Development of Fluorescent probes, quenchers and their oligonucleotide conjugates for RT-PCR and Lateral Flow assay based COVID-19 diagnosis.	Dr. Atul Goel

COVID	Testing of COVID-19 samples	Dr. R.Ravishankar
COVID	Production of Indigenous qRT-PCR (INDI-FluorAMP) kit for testing of Covid-19 with all MAKE-IN INDIA ingredients	Dr. Atul Goel
COVID	Development of Drug-target based Assay platforms and screening against COVID-19	Dr. R.Ravishankar
COVID	Clinical Trials: Phase 3, Randomized, Double-blind, comparative trial of Efficacy, Safety and Tolerability of Umifenovir and hydroxychloroquine combination therapy vs hydroxychloroquine therapy in non-severe COVID-19 patients	Dr. R.Ravishankar
Duration upto 31 March 2022		
FTT	IND enabling studies and development of CDRI-4655 as anti-hyper-triglyceridemic formulation	Dr. Anil N. Gaikwad
FTT	Development of new Smac Mimetic against chemotherapy resistant colon cancer	Dr. Dipak Datta
MLP	Creation of BSL-III / ABSL- III facility t CSIR-CDRI campus, Lucknow: A turn Key Projects	Dr. Bhupendra Narain singh
NCP	Development of a biodegradable nano ceramics-bioactive glass-polymer composite material with antimicrobial properties for use in female sanitary hygiene products	Dr. Siddhartha Chopra
Duration upto 31 March 2023		
FBR	Metabolic engineering of bacopa monnieri by redirecting the flux towards triterpenoid biosynthesis for enhanced bacosides production	Dr. Vineeta Tripathi
FBR	Identification of diagnostic targets and therapeutic methods for infertility	Dr. Rajender Singh
FBR	Mechanisms of Autophagy-mediated cell survival in TNBC: Implications in Therapeutics and Diagnostics	Dr. Jayanta Sarkar
FBR	Research in ASTHI: Pre-clinical Development of CDRI optimized lead molecules as dual osteogenic and muscle anabolic agents	Dr. Naibedya Chattopadhyay
FBR	Structural and functional characterization of potential drug target proteins from ESKAPE pathogens	Dr. Ashish Arora
FBR	Unravelling Cognitive Impairments due to Ageing & Neurodegeneration	Dr. Prem Narayan Yadav
FBR	SREBP inhibitors as novel therapeutics for non-alcoholic fatty liver disease: Insights on CRISPR-Cas9 inhibition of SREBPs targeting activated hepatic stellate cells	Dr. Kumarvelu Jagavelu
Duration upto 31 March 2025		
NCP	Discovery of selective KOR ligands for the Treatment Resistant Depression and Neuropathic pain	Dr. Prem Prakash Yadav
NCP	Chemical biology approaches towards dissecting non-canonical protein functions and novel targets in Malaria, Leishmania and Filaria parasites	Dr. Saman Habib
NCP	Multipronged studies on persistence and drug resistance in mycobacteria.	Dr. B.N. Singh
NCP	Novel and Integrative Approaches towards Discovery of Small Molecule Therapeutics for Healthy Ageing (NISTHA)	Dr. Atul Kumar
NCP	Understanding the mechanism of osteopenia and aberrant bone formation, and discovery of new targets for skeletal medicine (Osteo Target)	Dr. Naibedya Chattopadhyay
NCP	Modern innovative solutions for Environmental/ Occupational Lung Health challenges	Dr. Kashif Hanif
NWP	CSIR Integrated Skill Initiative programme - Phase-II	Mr. Vinay Tripathi

2. Grant in Aid Projects

Title of the Project	PI	Project Start Date	Completion Date
CSIR - New Millennium Indian Technology Leadership Initiative Project			
Development of Novel anti stroke phytopharmaceutical formulation from the roots of a Ashwagandha variety, NMITLI-118	Dr. Srikanta Kumar Rath	02-11-2020	31-03-2023
Department of Scientific & Industrial Research and Council of Scientific & Industrial Research			
Creation of DSIR – Common Research and Technology Development Hub (CRTDH) in the area of Affordable Health under DSIR-CRTDH Programme	Dr. Amit Misra	28-12-2018	13-12-2023
Department of Biotechnology, Ministry of Science & Technology, India			
Biotechnology Information System Network Distributed Information sub-centre (BTIS-DIC)	Dr. Anand P Kulkarni	01-01-1989	31-06-2020
Deciphering the roles of secreted proteases in host-*Mycobacterium tuberculosis* interaction: Implications for novel drug discovery and vaccine development	Dr. Arunava Dasgupta	13-07-2016	12-07-2020
Understanding the role of RBR-E3 Ubiquitin ligase in *P. falciparum* and exploring its potential for pharmacological intervention	Dr. Niti Kumar	08-11-2016	09-02-2020
Evaluation of TGF-β mediated signaling mechanism in the endometriosis using mouse model	Dr. Rajesh Kumar Jha	08-11-2016	26-01-2020
Synthesis and anti-parasitic activities of quinoline-tetrahydropyrimidine hybrids with special reference to anti-malarial, anti-leishmanial and anti-filarial activities	Dr. Renu Tripathi	13-10-2016	12-04-2020
Characterization of *L. donovani* S-Adenosyl methionine decarboxylase: Spermidine synthase interactions	Dr. J. Venkatesh Pratap	25-06-2017	14-12-2020
Small molecule inducers of Redox stress targeting antibiotic resistance	Dr. Sidharth Chopra	05-07-2017	29-12-2020
Functional characterization and validation of drug target potential of a unique triacyl glycerol synthase of *Mycobacterium tuberculosis*	Dr. Manju Y Krishnan	17-07-2017	16-07-2020
Exploring the role of Nucleotide binding Oligomerization Domain proteins (NODs)-mediated inflammation in diet-induced insulin resistance	Dr. Akhilesh Kumar Tamrakar	25-07-2017	24-07-2020
Deciphering organellar genome maintenance in the Malaria parasite	Dr. Saman Habib	25-09-2017	24-09-2020
Regulation of pancreastatin to control the energy homeostasis in diabetes	Dr. Jiaur Rahaman Gayen	30-12-2017	29-12-2020
Identification of the role of Serine 7 phosphorylation of RNA polymerase II CTD in the mRNA transcription	Dr. Sohail Akhtar	26-03-2018	25-03-2021
Design and synthesis of hybrid molecules for multi-drug resistant Tuberculosis	Dr. Arunava Das Gupta	02-08-2018	01-08-2021
Novel rationally designed DNA gyrase inhibitors as antibacterials	Dr. Sidharth Chopra	31-07-2018	30-07-2021
Determination and structural elucidation of bioactive compounds from the selected traditional medicinal plants of Mizoram with a focus on anticancer compounds	Dr. Brijesh Kumar	29-09-2018	28-09-2021
In silico design, synthesis, bioassay and elucidation of novel analogues of Vasicine and other quinazolinone compounds as potent antimycobacterial agents	Dr. Vinita Chaturvedi	13-09-2018	12-09-2021
Repurposing Oxconazole: Alone and in combination with PUFA's as a broad spectrum antibacterial	Dr. Sidharth Chopra	02-01-2019	01-01-2022

Screening of phytochemical and bioactive compounds against human pathogenic bacteria from some selected indigenous medicinal plants of Arunachal pradesh, India	Dr. Sidharth Chopra	11-01-2019	10-01-2022
Antileishmanial properties of some selected medicinal plants of North East India: Screening Isolation and identification of active phytoconstituents India: Screening, Isolation and identification of active phytoconstituents	Dr. Narender Tadigoppula	23-01-2019	22-01-2022
Exploration of role of ACE -2/Ang-(1-7) Mas receptor (ACE2/Ang-(1-7)/MasR) axis in neuroinflammation activation in hypertension and neurodegeneration	Dr. Kashif Hanif	04-02-2019	03-02-2022
Repurposing of anticancer drugs for the treatment of malaria	Dr. Renu Tripathi	12-06-2019	11-06-2022
Structure-activity validation of inhibitors of bacterial peptidyl-tRNA hydrolase for tackling AMR	Dr. Ashish Arora	22-07-2019	21-07-2022
To investigate the 4-hydroxyisolucine signaling mechanism in the ovarian follicular development for the management of polycystic ovarian syndrome	Dr. Rajesh Kumar Jha	02-09-2019	01-09-2022
Development of candidate RL348 for methicillin- and vancomycin-resistant *Staphylococcus aureus*	Dr. Sidharth Chopra	21-09-2019	20-09-2020
A cocktail of phages effective against urinary tract infections caused by biofilm forming MDR uropathogenic *E.coli*	Dr. Sidharth Chopra	27-09-2019	26-09-2021
Bio prospecting of medicinal plants of Sikkim Himalaya against breast cancer angiogenesis	Dr. Durga Prasad Mishra	30-09-2019	29-09-2022
To investigate the role of HOXB1 in spermatogenesis and male infertility	Dr. Rajender Singh	02-09-2019	01-09-2022
Studies on clinical efficacy of identified herbal leads on wound healing and veterinary dermatological complication	Dr. Manish Kumar Chourasia	14-01-2020	13-01-2023
Deciphering mechanisms of epigenetic reprogramming involved in macrophage polarization during host-pathogen interaction in experimental visceral *Leishmaniasis*	Dr. Susanta Kar	19-02-2020	18-02-2023
Development of small molecular antivirus against Chikungunya and Japanese Encephalitis Virus	Dr. Sanjay Batra	28-02-2020	27-02-2023
SELECTOR: Selection for antimicrobial resistance by antimicrobial proction waste	Dr. Sidharth Chopra	16-12-2020	15-12-2023
Research Associate, Department of Biotechnology, Ministry of Science & Technology, India			
Screen for identification of small molecule orally active glucagon-like peptide-1 receptor agonist	Dr. Nadanita Das (Mentor Dr. Sabyasachi Sanyal)	02-07-2018	01-07-2019
Ramalingaswami Fellowship, Department of Biotechnology, Ministry of Science & Technology, India			
Discovery of novel cell-autonomous host pathways and the counteracting immune evasion strategies employed by vacuolar pathogens-an approach to identify new antimicrobial host-factors and novel microbial targets	Dr. Arun Kumar Haldar	09-08-2017	08-08-2022
RhoA GTPase in neutrophil chemotaxis and functions during inflammation	Dr. Sachin Kumar	31-05-2016	30-05-2021
Role of the RIPK3-MLKL necrosome in the regulation of TGFβ-signaling mediated renal fibrosis during the development and progression of chronic kidney diseases	Dr. Shrikant Ramesh Mulay	01-02-2019	31-01-2024
Unravelling the role of Musashi2 (Msi2) in cardiac pathophysiology	Dr.Shashi Kumar Gupta	15-05-2020	14-05-2025
Tata Innovation award, Department of Biotechnology, India			
Novel oral combination formulation for the treatment of resistant malaria (*Plasmodium falciparum*) comprising α/β Arteether and Lumifantrine	Dr. Prabhat Ranjan Mishra	01-03-2019	31-03-2022
To elucidate the regulatory role of bioactive molecule from Spinacea oleracea by trancriptome modulation for osteoarthritis	Dr. Ritu Trivedi	01-04-2020	31-03-2023

Welcome DBT India Alliance Department of Biotechnology, India			
Mechanistic insights into epigenetic layers involved in impaired wound healing and cardiovascular diseases in diabetes	Dr. Sadan Chand Das (Mentor: Dr. Manoj Kumar Barthwal)	01-01-2021	31-12-2025
Science & Engineering Research Board, Department of Science and Technology, India			
Sophisticated Analytical Instrument Facility	Dr. Ravishankar Ramachandran	01-04-1975	Long term
Design and synthesis of natural, un-natural analogues of Calothrixins A, B and evaluation of antimalarial and anticancer activity	Dr. Niti Kumar	12-01-2016	31-01-2020
Enantioselective organocatalysis: A novel approach to use acetal as pro-nucleophile and hydroxylactam as pro-electrophile via co-operative catalysis	Dr. Dipankar Koley	27-09-2016	26-03-2020
Decarboxylative cross couplings en route to the synthesis of heterocycles	Dr. Sanjay Batra	04-01-2017	15-08-2020
NMR based metabolic profiling of osteogenic phytoconstituents in *Dalbergia sissoo*	Dr. Sanjeev Kumar Shukla	21-02-2017	20-08-2020
Understanding the role of CTD phosphorylation of RNA polymerase II for the transcription during mitosis	Dr. Sohail Akhtar	22-03-2017	21-03-2020
Novel small molecules as selective and Positive Allosteric Modulators (PAM) of 5 HT2c receptor: Discovery and development of potential anti-obesity agents	Dr. Prem Narayan Yadav	27-06-2017	26-12-2020
Synthesis and therapeutic evaluation of new LpxC inhibitors as potent anti-bacterial agents	Dr. Sidharth Chopra	19-07-2017	18-07-2020
Applications of experimental charge density and crystal structure prediction approaches in multi- component crystal development and for studying intermolecular interactions in protein-ligand complexes	Dr. Tajender Singh Thakur	12-09-2017	31-03-2021
Synthesis of privileged heterocycles via visible light photoredox catalyzed cascade reactions	Dr. Namrata Rastogi	04-09-2017	30-11-2020
In vitro biosynthesis and enrichment of indole alkaloids from *Alstonia scholaris* and elucidation of their metabolic pathway	Dr. Dipak Kumar Mishra	28-09-2017	27-03-2021
Role of autophagy in vascular smooth muscle cell remodelling and phenotype	Dr. Manoj Kumar Barthwal	28-09-2017	27-03-2021
Development of small molecular inhibitor specifically targeting mTORC2 for cancer therapeutics: Development of targeted anti-cancer strategy	Dr. Smrati Bhadauria	17-03-2018	16-03-2021
Plasmodium SCOT1 mutant as experimental malaria vaccine: Implications for inducing pre-erythrocytic and cross-stage immunity	Dr. Satish Mishra	17-03-2018	16-03-2021
Genetic validation of actin as a drug target in Leishmania and development of drug screening assay system	Dr. Amogh Anant Sahasrabuddhe	22-03-2018	21-03-2021
Structural and functional characterization of PadR-like transcriptional regulatory proteins from *Mycobacterium tuberculosis* H37Rv	Dr. Ashish Arora	09-07-2018	08-07-2021
A systematic screen of functional genomics and epigenetic interventions towards identification of novel genetic modulators of Amyloid Beta effects in a transgenic *C. elegans* models of Alzheimer's disease	Dr. Aamir Nazir	10-07-2018	09-07-2021
Modulation of host endocytosis during Plasmodium liver stage development	Dr. Satish Mishra	17-07-2018	16-07-2021
Redox regulation of immune cells, neutrophils in insulin resistance and type 2 diabetes	Dr. Sachin Kumar	27-07-2018	26-07-2021
Targeting Triple Negative Breast Cancer (TNBC) by a plant derived small molecule: An *in vitro* and *in vivo* approach	Dr. Dipak Datta	30-07-2018	29-07-2021

To decipher the role of RHOG in the endometrial receptivity for blastocyst adhesion and invasion process	Dr. Rajesh Kumar Jha	10-06-2018	10-05-2021
Therapeutic evaluation of organometallic compounds as potent antibacterial agents	Dr. Sidharth Chopra	12-10-2018	11-10-2021
Identifying critical hotspots in macromolecular complexes involved in bacterial BER	Dr. Ravishankar Ramachandran	26-10-2018	25-10-2021
Studies to delineate the immunoregulatory role of PD -L 1 /PD-1 pathway and exploring it as a potential tool for vaccination strategies against Visceral Leishmaniasis	Dr. Amogh Anant Sahasrabuddhe	09-05-2018	09-04-2021
Branch chain amino acid biosynthesis in *Mycobacterium tuberculosis* and relevance of ketol– acid reducto-isomerase for antimycobacterial drug discovery	Dr. Sudheer Kumar Singh	02-11-2018	01-11-2021
Trifluorodiazoethane as a precursor for the rapid synthesis of Trifluoromethylated building blocks	Dr. Kishor Mohanan	12-10-2018	11-10-2021
Neuroprotective and neuritogenic effects of a cell-permeable bacterial histone-mimic protein: Therapeutic implications for neurodegenerative pathologies	Dr. Shubha Shukla	15-11-2018	14-11-2021
Targeting DNA repair proteins to overcome topoisomerase drug resistance	Dr. Dibyendu Banarjee	05-11-2018	04-11-2021
Investigating the role of the NLRP3 inflammasome in fractose-included peripheral Insulin resistance	Dr. Akhilesh Kumar Tamrakar	06-11-2018	05-11-2021
To elucidate the role of MAPKAPK2 (MK2) in inflammation mediated lymphangiogenesis during myocardial infarction	Dr. Kumaravelu Jagavelu	06-11-2018	05-11-2021
Identification and characterization of microRNAs controlled by mutations in Phex gene, a regulator of X-linked hypophosphatemic rickets, an intrinsic bone mineralization defect	Dr. Divya Singh	06-11-2018	05-11-2021
Cooperative catalysis through dual activation for stereoselective synthesis of glycosides	Dr. Pintu Kumar Mandal	28-11-2018	27-11-2021
Investigation of the role of small RNAs in genomic imprinting	Dr. Rajender Singh	04-12-2018	03-12-2021
Role of p21Waf1Cip1 in regulation of autophagy: its implication in tumorigenesis and cancer therapy	Dr. Jayanta Sarkar	25-02-2019	24-02-2022
Chalcogenide catalysis for enantioselective olefin functionalization and synthesis of biologically relevant compounds	Dr. Chandra Bhushan Tripathi	04-03-2019	03-03-2022
Synthesis of biologically relevant privileged heterocycles by metal-catalyzed C-H bond functionalization with diazo compounds	Dr. Malleswara Rao Kuram	06-03-2019	05-03-2022
Catalytic asymmetric dearomatization of (Het) Arenes via Decarboxylative cycloaddition: Synthesis of natural product-inspired novel scaffolds for drug discovery	Dr. Nilanjana Majumdar	04-03-2019	03-03-2022
Investigating auxiliary functions of HSP110 in malaria causing parasite *Plasmodium falciparum*	Dr. Niti Kumar	11-03-2019	10-03-2022
Probing sp^3-rich spirocyclic scaffolds in drug discovery: Syntheses of Cyanogramide, FR901483 and their diversified analogues towards leads against Mtb and ESKAPE pathogen	Dr. Ajay Kumar Srivastava	12-03-2019	11-03-2022
Rational design and syntheses of non-natural, silicon and boron based antibiotics: Sila-and boro-b-lactams and beyond	Dr. Ravindra Kumar	12-03-2019	11-03-2022
Cloning and characterisation of PSPG mitif containing glycosyltrasferases genes involved in secondary metabolism from *Calotropis procera*	Dr. Vineeta Tripathi	30-03-2019	29-03-2022
Understanding CTD- Chromatin crosstalk during transcription through nucleosome	Dr. Sohail Akhtar	20-08-2019	19-08-2022
Development of the SPLUNC1 protein loaded composite nanoparticles based targeted therapy for the treatments of lung inflammation	Dr. Sohail Akhtar	28-10-2019	29-10-2022

Endoplasmic Reticulum stress response in orchestrating mucosal immune response: exploring novel therapeutic intervention for Inflammatory Bowel Disease	Dr. Amit Lahiri	19-11-2019	18-11-2021
Unraveling the role of RNA- binding protein Quaking in cardiac remodeling with emphasis on Titin alternative splicing	Dr. Shashi Kumar Gupta	20-11-2019	19-11-2021
Diversification of Azines to Identify Potent Anti-Malarial Agents Via Metal-Catalyzed Site- Selective C-H Functionalization.	Dr. Malleswara Rao Kuram	27-12-2019	26-12-2022
Inhibition of ATP synthase enzyme of drug-resistant mycobacterium tuberculosis through chemical library of Asymmetric tri and Tetrasubstituted methanes (TRSMs) and ethanes (TRSEs)	Dr. Gautam Panda	28-01-2020	27-01-2023
The drugability of a novel antidiabetic pancreastatin inhibitor PSTi8: Preclinical pharmacokinetic and drug-drug interaction studies.	Dr. Jiaur Rahaman Gayen	07-02-2020	06-02-2023
Elucidation of class III CoA- Transferases Rv3272 in virulence of Mycobacterium tuberculosis	Dr. J. Venkatesh Pratap	27-02-2020	26-02-2023
Development of Glycoconjugates based site directed fluorescent sensor for the detection of bacteria	Dr. Ajay Kumar Srivastava	26-02-2020	25-02-2023
A Multi-pronged approach to understand the functional diversity of HSP40s in human malaria parasite and explore small-molecule based pharmacologist targeting	Dr. Niti Kumar	27-03-2020	26-03-2022
Anti-gerogenic Therapy to Augment Lifespan and Health span by Bioactive Peptides from Rasayana Herbs: Generation of PoC for the First-in-class Ayurveda-based Peptide Therapeutics	Dr. Naibedya Chattopadhyay	28-08-2020	27-08-2023
Organo-Photoredox Catalysis for Visible Light-driven Synthesis of Natural/ Synthetic Medicinal Molecules	Dr. Namrata Rastogi	03-12-2020	02-12-2023
Establishing the North India Facility for Cryogenic-Electron Microscopy (cryo-EM) at IIT Kanpur	Dr. R. Ravishankar	18-12-2020	17-12-2025
National Post-Doctoral Fellowship, SERB, DST, India			
Investigation of effect of CDRI08 (keenmind) on Parkinson's disease pathology	Dr. Arun Kumar Yadawa	02-04-2018	30-09-2020
Elucidating the effect of resveratrol on Nrf2 Mediated signalling and unfolded protein responses during Parkinson's disease pathology	Dr. Ashish Singh	02-04-2018	30-09-2020
Investigating the role of high risk human papilloma virus E5 protein in regulation of crosstalk of apoptosis signals between mitochondria and endoplasmic reticulum	Dr. Deepa Gandhi	02-04-2018	01-04-2020
Deciphering the effect of quercetin on the mitochondrial dysfunction endoplasmic reticulum stress and oxidative stress in rotenone induced Parkinsonism	Dr. Pratibha Tripathi	07-05-2019	06-05-2021
Development of mucoadhesive formulation of first-line anti-tuberculosis drugs for the Treatment of gastrointestinal tuberculosis (GI-TB)	Dr. Lubna Azmi	11-02-2020	10-02-2022
JC Bose National Fellowship, SERB, DST, India			
Vaccine development against Visceral leishmaniasis	Dr. Anuradha Dube	09-08-2016	14-07-2021
Woman Scientist Scheme-A, SERB DST, India			
Inflammation,genotoxicity and tumorigenecity in mice Identification of shikimate kinase as a drug target against *Mycobacterium tuberculosis*	Dr. Sapna Pandey	16-01-2017	15-01-2020
Role of estrogen subtype estrone and estriol on hematopoietic stem cells (HSCs) and bone marrow regeneration	Dr. Rupali Saini Kumar	02-04-2018	01-04-2021
Deciphering the roles of *Mycobacterium tuberculosis* proteases in host-pathogen interaction: Implications for novel drug discovery and vaccine development	Ms. Tanu Garg	12-07-2019	11-07-2022

Inspire Fellowship, DST, India			
New approaches to the fluorinated N-heterocycles via A+C109mine radical cation pathway	Dr. Sushobhan Chowdhury	08-09-2017	07-09-2022
TARE, DST, India			
Mechanistic studies of bacteriophage-derived Lysins to combat multidrug resistant bacterial pathogens	Dr. Aditi Singh	05-11-2019	04-11-2022
Indian Council of Medical Research (ICMR), India			
Drug targeting for improved treatment of multi-drug resistant tuberculosis (MDR TB)	Dr. Amit Misra	01-08-2018	31-07-2021
Do Endoplasmic Reticulum stress mediated death signalling pathways involved in Alzheimer's pathology?: Role of transmembrane protein kinase PERK,IRE1 and activation transcription factor 4 and 6 (ATF 4 & 6)	Dr. Sarika Singh	15-10-2018	14-10-2021
Role of Pancreastatin towards amyloid formulation in Diabetes	Dr. Jiaur R Gayen	01-09-2019	31-08-2022
Harnessing therapeutic potential of novel spisulosine derivative as robust autophagy inducer against triple negative breast cancer {TNBC) *in vitro* and *in vivo*	Dr. Dipak Datta	22-08-2019	21-08-2022
Centre for Product Development	Dr. Vivek Vidyadhar Bhosale	11-12-2019	15-12-2024
An investigational study on Mycobacteriophages and their enzymes as new drugs (IND) for treating tuberculosis	Dr. Amit Misra	25-10-2019	24-10-2022
Target identification and hit to lead optimization of SRI 12742 targeting MDR A. *baumannii*	Dr. Sidharth Chopra	25-03-2020	24-03-2023
Synergistic Metal-based Antimicrobial Agents for AMR Bacterial Pathogens: Combinatorial and Multimodal Approach	Dr. Sidharth Chopra	15-10-2020	14-10-2023
Central Council for Research in Unani Medicine, Ministry of AYUSH, New Delhi, Govt. of India			
Reverse Pharmacology of Asrin and Dawa ul Shifa to evaluate their anti-hypertensive efficacy, safety and mechanism of Action	Dr. Kashif Hanif	18-05-2020	17-05-2023
Ministry of Earth Science (MoES)			
Synthesis and bioevaluation of chemical libraries of B- Carboline based mimics of marine natural products	Dr. Sanjay Batra	20-04-2015	31-03-2020
Ligand and structure based screening of designed and synthesized chemical library around Psammaplin A against DNA methyltransferase I (DNMTI) and diversity oriented synthesis of Pachastrissamine as anticancer agents	Dr. Gautam Panda	01-02-2016	31-03-2020
Biological evaluations, discovery of novel bioactive compounds & coordination of the program "Drug From Sea"	Dr. Manoj Kumar Barthwal	06-03-2018	31-03-2020
A high-throughput screening for modulators/inhibitors of quorum sensing, class b-β-Lactamase inhibitor, biofilm and efflux pump	Dr. Mukesh Pasupuleti	21-05-2018	20-05-2021
Third party verification and outsourcing of activities Related to Lead compound GS/IICT5/6 showing anti-angiogenic activity	Director	27-11-2018	31-03-2020
Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (AYUSH)			
Exploration, identification and isolation of bone fracture healing agents from Indian folk traditional plants *Pholidota articulate* and *Coelogyn cristata* (Orchidaceae)	Dr. Narender Tadigoppula	09-01-2018	08-01-2021
Biotechnology Industry Research Assistance Council (BIRAC) New Delhi			
Development of Novel Small Molecule SMAC Mimetics as Cancer Therapeutics	Dr. Dipak Datta	03-05-2019	02-11-2020
Department of Atomic Energy (DAE)			
Design and synthesis of donor-acceptor based new organic fluorescent dyes and their applications	Dr. Atul Goel	06-01-2016	05-01-2021
Amino acids derived steroidal and non-steroidal ligands as inhibitors of steroid 5-α-reductase in cancer	Dr. Gautam Panda	18-06-2018	17-06-2021

Lady Tata Memorial Trust, Mumbai			
Elucidating mechanisms underlying breast cancer invasion and metastasis: Role of E3 ubiquitin ligase Fbw7 in suppressing breast tumorigenesis	Dr. Arun Kumar Trivedi	06-07-2017	05-07-2021
Council of Science & Technology, Uttar Pradesh			
To evaluate anti-metastatic potential of diminished cardiotoxic tumor targeted liposomal formulation of Etoricoxib	Dr. Smrati Bhadauria	01-06-2018	31-05-2021
Global Challenges Research Fund - Network for Neglected Tropical Diseases			
Structural studies of the GTP binding proteins Rab7 from *Leishmania donovani*	Dr. Ashish Arora	01-10-2018	
Structural and functional characterization of early endocytosis related Rab proteins of *Leishmania donovni*	Dr. Ashish Arora	19-08-2019	18-08-2021
Sponsored Projects			
Sub-acute toxicity testing of sample	Dr. Srikanta Kumar Rath	16-09-2019	15-09-2020
Pore size from XRD diffraction using Rietveld refinement	Dr. Tejender Singh Thakur	28-11-2019	27-11-2020
Sponsored project on" Separation and chemical characterization of a major bioactive compounds from microbial origin"	Dr. Sanjeev K. Kanojia	30-12-2019	29-12-2020
In vitro assessment of Sphaera Compounds	Dr. N. Chattopadhyay	28-05-2020	27-05-2022
Micro CT of rat bones from Eurofins Advinus	Dr. N. Chattopadhyay	01-10-2020	30-03-2021

6. Memorandum of Understandings, Agreements & Services

Sl. No.	Title	Client/Collaborator	Signing Date
Demonstration of Technology (Know-how)			
1.	Demonstration of Know-How Process Technology for the Preparation of the Umifenovir during 27-29 April, 2020	Medizest Pharmaceuticals Pvt. Ltd., Goa	29-04-2020
License Agreements			
1.	Process for the Preparation of Umifenovir	Medizest Pharmaceuticals Pvt. Ltd., Goa	24-04-2020
Collaborative Research Agreements			
1.	Identifying and Validating Drug Targets for Malaria Drug Discovery Programs	Medicines for Malaria Venture (MMV), Switzerland	16-12-2020
2.	Developing a Polyherbal Formulation as an Immuno Booster and for the Management of Covid-19 (SARS-2)	Gerah Enterprises Private Ltd., Mumbai (Piramal group)	29-10-2020
3.	Production of Indigenous qRT-PCR (INDI-FluorAMP) kit for Testing Covid-19 with Make-in-India Ingredients	Biotech Desk Pvt. Ltd., Hyderabad	27-10-2020
4.	Synthesis and Assessment of Hydrogen Sulphide Donors for Treating Acute Mountain Sickness	Defence Institute of Physiology and Allied Sciences, DRDO, Delhi	04-03-2020
Sponsored Agreements			
1.	*In vitro* Assessment of Sphaera Compounds	Sphaera Pharma Private Limited, Gurugram	28-05-2020
2.	Separation and Chemical Characterization of a Major Bioactive Compounds from Microbial Origin	AG Bio Systems Pvt. Ltd., Hyderabad	19-12-2019
Consultancy Agreements			
1.	Consultancy Services on Inflammatory Liver Disease	M/s Kinomera Biosciences Pvt. Ltd., Mumbai	16-10-2020
2.	Consultancy Services in the Area of Bone Diseases, Fracture Healing and on Emerging Molecular Pathways for Therapeutic Targeting	M/s Kinomera Biosciences Pvt. Ltd., Mumbai	23-09-2020
Testing Services			
1.	AMES Assay of a Single API/ Extract	CSIR-Indian Institute of Chemical Biology, Kolkata	19-03-2020
2.	LCMS Data Analysis	Lovely Professional University (LPU), Jalandhar,	20-01-2020
3.	LCMS Data Analysis	ICAR-Indian Grassland and Fodder Research Institute, Jhansi	20-01-2020
Memorandum of Understanding signed for joint R&D			
1.	Collaborative Research Activities and Capacity Building of Students and Faculties in the Areas of Mutual Interest.	University of Mysore, Mysuru	23-12-2020
2.	CSIR-CDRI Centre for Science Outreach and Research	Cipla Foundation, Mumbai	18-12-2020
3.	Partnering in Clinical Trials of Niclosamide	Marc Laboratories Ltd., Lucknow	19-08-2020
4.	Collaborative Research Activities and Capacity Building of Students and Faculties in Mutual Areas of Interest.	Foundation for Neglected Disease Research, Bengaluru	15-06-2020
5.	To Provide Collaborative Cooperation between CSIR-CDRI and Reva University, Bengaluru in Specific Fields of Interest	Reva University, Bengaluru	08-06-2020
6.	To Promote Institutional Linkage Between CSIR-CDRI and Madras Diabetes Research Foundation (MDRF), Chennai to Explore for Possible Collaborative Research Programs in Specific Fields of Interest	Madras Diabetes Research Foundation (MDRF), Chennai	03-06-2020
7.	Collaborative Research Work on COVID-19	KGMU, Lucknow	15-04-2020
8.	To Promote Institutional Linkage Between CSIR-CDRI and Integral University, Lucknow to Explore for Possible Collaborative Research Programs in Specific Fields of Interest	Integral University, Lucknow	28-02-2020

9.	*In vivo* Evaluation of Emetine Analogs for Antimalarial Activity in the *P. yoelii* Mouse Model	The University of Salford, Manchester, UK	21-01-2020
10.	To Promote Institutional Linkage Between CSIR-CDRI and Sastra Deemed University, Thanjavur (Tamilnadu) to Explore for Possible Collaborative Research Programs in Specific Fields of Interest	Sastra Deemed University, Thanjavur	03-11-2019
Memorandum of Agreements			
1.	To Investigate the Role of HOXB1 in Spermatogenesis and Male Infertility	DBT, New Delhi	21-10-2020
2.	To Investigate the 4- hydroxyisolucine Signaling Mechanism in the Ovarian Follicular Development for the Management of Polycystic Ovarian Syndrome	DBT, New Delhi	21-10-2020
3.	Structure-Activity Validation of Inhibitors of Bacterial Peptidyl-tRNA Hydrolase for Tackling AMR	DBT, New Delhi	19-08-2020
4.	Repurposing Oxiconazole: Alone and in Combination with PUFA's as a Broad Spectrum Antibacterial	DBT, New Delhi	17-03-2020
5.	Studies on Clinical Efficacy of Identified Herbal Leads on Wound Healing and Veterinary Dematological Complication	DBT, New Delhi	06-02-2020
Secrecy Agreements			
1.	Information Disclosed by CSIR-CDRI to Marc Laboratories for Development of their Hit/Lead/Candidate Drugs/Molecules	Marc Laboratories Pvt. Ltd., Lucknow	01-12-2020
2.	Information Disclosed by CSIR-CDRI and Aizant Drug Research Solutions Pvt. LTd. for Development of their hit/lead/candidate drugs/molecules	Aizant Drug Research Solutions Pvt. LTd., Hyderabad	27-11-2020
3.	Mutual Consideration of the CSIR-CDRI and BMS Working Together On The Following Project or Topic to enable Discussions Regarding Exploratory Projects of Mutual Interest in the Area of Hemato-Oncology	Bristol-Myers Squibb India Pvt. Ltd., Mumbai	16-10-2020
4.	Outsourcing the cGMP Manufacture of Investigational New Drugs (IND-APIs) and their Formulations (tablets/capsules) for the Purpose of Testing & Clinical Trials	Syngene International Ltd., Bengaluru	16-09-2020
5.	Outsourcing the cGMP Manufacture of Investigational New Drugs (IND-APIs) and their Formulations (tablets/capsules) for the Purpose of Testing & Clinical Trials	Laxai Life Sciences, Hyderabad	21-08-2020
6.	Synthetic Compound S007-867 (anti-platelet) for Preventing Platelet Aggregation in the Patients of Coronary Artery Disease/Thrombotic Cerebral Stroke	Medizest Pharmaceuticals Pvt. Ltd., Goa	12-06-2020
7.	Outsourcing the cGMP Manufacture of Investigational New Drugs (IND-APIs) and their Formulations (tablets/capsules) for the Purpose of Testing & Clinical Trials	CIPLA Ltd., Mumbai	16-06-2020
8.	Tablet Formulation Facility at HYGIA for Development of CDRI Compound S007-1500	Hygia Institute of Pharmaceutical Education & Research, Lucknow	09-06-2020
9.	Outsourcing cGMP API as well as Finished Dosage form Manufacturing of a Plant Originated Chemical Entity as per in house Developed Process for Human Clinical Trial	Dr. NS Labs, Hyderabad	30-05-2020
10.	Outsourcing cGMP API as well as Finished Dosage form Manufacturing of a Plant Originated Chemical Entity as per in house Developed Process for Human Clinical Trial	Jubilant Chemsys Limited, Bengaluru	29-05-2020
11.	Outsourcing cGMP API as well as Finished Dosage form Manufacturing of a Plant Originated Chemical Entity as per in house Developed Process for Human Clinical Trial	Sushen Medicamentos Pvt. Ltd., Ahmedabad	29-05-2020
12.	Outsourcing the cGMP Manufacture of Investigational New Drugs (IND-APIs) and their Formulations (tablets/capsules) for the Purpose of Testing & Clinical Trials	Almelo Pvt. Ltd., Hyderabad	19-05-2020
13.	Identification of Potential Lead Compound from FDA Approved Library for Adjunct Therapy for COVID-19 Treatment	Serdia Pharmaceuticals (India) Pvt. Ltd., Mumbai	08-05-2020
14.	Outsourcing the cGMP Manufacture of Investigational New Drugs (IND-APIs) and their Formulations (tablets/capsules) for the Purpose of Testing & Clinical Trials	GVK Biosciences Pvt. Ltd., Hyderabad	06-05-2020

15.	Outsourcing the cGMP Manufacture of Investigational New Drugs (IND-APIs) and their Formulations (tablets/capsules) for the Purpose of Testing & Clinical Trials	Eurofin Advinus, Bangalore	05-05-2020
Material Transfer Agreements			
1.	Plasmid construct of SARS CoV 2 NSP 1, NSP 7, NSP 8, NSP 10 and NSP15 genes	Addgene, USA	08-10-2020
2.	Expression plasmid of mammalian (Ds-Red Rab11 & GFP-WT-Rab9)	Addgene, USA	02-06-2020
3.	DNA of *Plasmodium cynomolgi* B and *P. knowlesi* (malaria parasite)	ICMR-National Institute of Malaria Research, New Delhi	30-05-2020
4.	Plasmid constructs: alpha-pET-28a(+)-alpha, beta--pET-28a(+)-beta and –alpha-pET-28a(+)-beta	Tel Aviv University, Israel	25-03-2020
5.	Recombinant Plasmid cloned, GFP-Ub(#11928), Ub-G76V-GFP, pAD-CMV-STAT5A-CMV-GFP, pAD-CMV-STAT5A-CA-CMV-GFP, pEGFP-RNF138-WT, pEGFP-RNF138-delta18-58 for expression in mammalian cells	Addgene, USA	18-03-2020
6.	Plasmids in agar stab: psPAX2, pMD2, Bnip3L, RNAi pSuper-retro, shERK1a-mlpx-puro, pcDNA GNSTM-3-RVG-10-Lamp2b-HA	Addgene, USA	03-03-2020
7.	Recombinant trypanothione reductase enzyme from *Leishmaina donovani*	University of Kalyani, Kalyani	27-02-2020
8.	Recombinant plasmids clones HRS, paGFP-HRas G12V, pcDNA3-HA-H-Ras-wt	Addgene, USA	27-02-2020
9.	pET28HIS-hAPE1 (#70757) Ecoli based expression plasmid (DNA)	Addgene, USA	05-02-2020
10.	pSAM *E. coli* based expression plasmid cat No.#45174	Addgene, USA	14-01-2020
11.	Recombinant plasmids clones for expression in mammalian cells	Addgene, USA	07-01-2020

7. Human Resource Development

7.1 Ph.D. Thesis Submitted in 2020

S. No.	Name of Student	Title	Name of Supervisor
		CSIR-CDRI-Jawaharlal Nehru University Ph.D. Program	
1	Mr. Arun Kumar Jajoriya	Mechanistic studies on the pathophysiology of liver fibrosis	Dr. D. P. Mishra
2	Mr. Sunil Kumar Narwal	Genetic and molecular approaches towards understanding the role of Stearoyl-CoA desaturase and UBC 13 kinase in *Plasmodium*	Dr. Satish Mishra
3	Mr. Ravi Prakash	Identification and characterization of novel regulator of osteoporosis from endogenous and exogenous sources	Dr. Divya Singh
4	Mr. Amar Jeet	Biosynthesis and enrichment of indole alkaloids from *Alstonia scholaris* through plant tissue culture techniques	Dr. D. K. Mishra
5	Ms. Pooja Maurya	Identification of resistance mechanisms and targeting of DNA repair proteins for cancer therapy	Dr. Dibyendu Banerjee
6	Mr. Sachin Gaurav	Structural and functional studies of Drp1, a Rint1 family protein in fission yeast *Schizosaccharomyces pombe*	Dr. Shakil Ahmed
7	Ms. Ekta Dhamija	Delineation of Tyrosine Phosphatase B in post translational modification of proteins during growth and intracellular survival of Mycobacteria	Dr. Kishore K. Srivastava
8	Mr. Swetarka Das	Development and evaluation of murine models for mycobacterial infection	Dr. Arunava Dasgupta
9	Mr. Vaibhave Ubba	Evaluation of the RHOGTPases role in ovarian pathophysiology	Dr. Rajesh Kumar Jha
10	Mr. Ankit Ghosh	Using reverse genetics to elucidate the role of sporozoite proteins S14 and SCOT1 in *Plasmodium*	Dr. Satish Mishra
11	Ms. Ankita Shukla	Structural and functional characterization of protein(s) involved in mycobacterial DNA repair	Dr. R. Ravishankar
12	Mr. Jitendra Kuldeep	Computer-aided molecular modeling and structural bioinformatics studies for identification and design of anti-tubercular and anti-leishmanial agents	Dr. M. I. Siddiqi
13	Mr. Priyank Chaturvedi	Role of tumour microenvironment in maintaining cancer stem cell properties	Dr. Dipak Datta
14	Mr. Upendra Kumar Soni	Role of Integrin Linked Kinase (ILK) in the chronic inflammation driven pathophysiology of endometriosis and subsequent pregnancy outcome	Dr. Rajesh Kumar Jha
15	Ms. Priya Gupta	Investigation of novel immuno-metabolic mechanisms regulating inflammasome and macrophage activation	Dr. Manoj Kumar Barthwal
16	Mr. Sandeep U	Exploration of self-assembled multifunctional nanocarriers for the delivery of anti-cancer agents	Dr. Prabhat Ranjan Mishra
17	Ms. Anupama Tiwari	Investigation of the DNA repair machinery in organelles of *Plasmodium falciparum*	Dr. Saman Habib
18	Mr. Mohammad Sadik	Analysis of putative nuclear–encoded proteins involved in the biogenesis of Iron–Sulfur clusters in the *Plasmodium falciparum* mitochondrion	Dr. Saman Habib
19	Mr. Mohammad Anas	Understanding the cooperation of PfHSP70 with its co-chaperones in malaria causing parasite *Plasmodium falciparum*	Dr. Niti Kumar
20	Mr. Mohammad Afsar	Structural and functional characterization of protein(s) involved in nucleic acid metabolism in mycobacteria	Dr. R. Ravishankar
21	Mr. Ramanand	Phytochemical investigation of indian medicinal plants in search of bio-active compounds for female fertility and metabolic diseases and synthesis of natural products like molecules	Dr. T. Narender
22	Mr. Saumya Sarkar	Analysis of DNA methylation in male infertility and germ cells development	Dr. Rajender Singh

23	Mr. Pavneet Kaur	Identification and characterization of interacting partner(s) of MAP Kinase1 in *Leishmania donovani*	Dr. Neena Goyal
24	Mr. Vijay Nath Mishra	Synthesis of glycosides, saccharides and glycoconjugates as antidiabetic agents	Dr. Pintu K. Mandal
25	Mr. Narendra Kumar Vaishanv	Novel strategies for the synthesis of functionalized heterocycles using Allenic esters and their applications toward the synthesis of antimalarial agents	Dr. Kishor Mohanan
26	Mr. Chetan Prakash	Understanding extra-ribosomal functions of ribosomal proteins during stress and infection	Dr. Niti Kumar
27	Mr. Mohd Khalid Zaheer	Novel Carbon-Carbon bond-forming reactions employing hypervalent iodine reagents for the synthesis and biological evaluation of Arylfluoroamides as antifilarial agents	Dr. Kishor Mohanan
28	Mr. Pankaj Singh Parihar	Structure and functional characterization of protein(s) of the purine salvage pathways and structural domain protein from kinetoplastids	Dr. J. V. Pratap
29	Mr. Anil Kumar Shakya	Structural and functional Studies on proteins of *Leishmania donovani* polyamine biosynthesis pathways and from other pathogens	Dr. J. V. Pratap
30	Ms. Suman Bharti	A study on the cupin protein Rv1717, over-expressed by *Mycobacterium tuberculosis* persisting in the host during anti-tubercular therapy	Dr. Y. K. Manju
31	Mr. Amrendra Kumar	Diversity oriented synthesis of natural products like molecules of biological importance	Dr. T. Narender
32	Mr. Ravi Prakash Shukla	Investigating synergism between anticancer agents and their nano-carrier system against breast cancer	Dr. Prabhat Ranjan Mishra
33	Mr. Ashok Kumar	Phytochemical investigation of Indian medicinal plants in search of anti-obesity and anticancer and synthesis of bioactive molecules	Dr. T. Narender
CSIR-CDRI-Academy of Scientific and Innovative Research (AcSIR) PhD Program			
34	Ms. Pragya Yadav	Isolation, chemical transformation of natural products and synthesis of natural product analogues of biological importance	Dr. T. Narender
35	Ms. Sapna Pandey	Studies on the essentiality of Shikimate Kinase in Mycobacteria and the characterization of its functional domains with respect to enzyme activity and inhibitor binding	Dr. Kishore K Srivastava
36	Mr. Amit Manhas	Analysis of High-Mobility Group Box isoform 3 in myocardial infarction and investigating the cardioprotective potential of natural products in various rodent cardiac stress models	Dr. Kumaravelu J
37	Mr. Ratnakar Dutt Shukla	Design and synthesis of novel N-heterocyclic scaffolds as anti-tubercular agents	Dr. Atul Kumar
38	Ms. Priya Pathak	Effect of diet induced dyslipidemia on vasoreactivity, systemic and skeletal muscle insulin sensitivity in C57BL/6 and NOS2KO mice	Dr. Kumaravelu J
39	Ms. Nagode Savita Babasaheb	Visible – Light – Photoredox catalyzed synthesis of privileged heterocycles/carbocycles	Dr. Namrata Rastogi
40	Mr. Sourav Chattopadhyay	Investigating the effect of sexual dimorphism on AdipoR1 expression and adiponectin signalling pathway	Dr. Sabyasachi Sanyal
41	Mr. Sukka Santosh Reddy	Exploration of novel immunometabolic mechanisms regulating cardiometabolic disorders	Dr. Manoj K Barthwal
42	Mr. Rohit Singh	Isolation and chemical transformation of natural products and synthesis of natural products analogues of biological importance	Dr. T. Narender

7.2 Skill Development Program (Healthcare & Life Science)

Skill India is an initiative launched to empower the youth of our country with skill sets which make them more employable and productive in their work environment. Skill shortage remains one of the major constraints to the continued growth of the Indian economy. We wish to address this knowledge-gap by professionally trained youth of India. The courses have been designed to meet the aspirations of students, young researchers and industry-sponsored personnel looking for training. We offer six certificate courses under the CSIR-CDRI, Skill Development Program. These courses provide an opportunity for skill development and hands-on experience in the area of healthcare and life science.

7.3 Skill Development Program for Postgraduate Students

The course meets the aspirations of students/young researchers looking for training and hands-on experience in the chosen area. Students pursuing their post-graduation course from universities/ colleges in any of the relevant areas can develop skills through these courses. Candidates have taken training for a duration of 4 months to 1 year depending upon the recommendations from their HOD. During the period of report 15 post graduate students received training at CSIR-CDRI.

7.4 Advance Training Courses for the employees of R & D Institutions/ Pharmaceutical Industry/ Government Laboratories etc.

Institute conducts different kinds of training of short duration in various disciplines against payment. These courses comprise both lectures and practicals by our experienced scientists with emphasis on practical R & D aspects in a particular domain. During the period of report 03 aspirants received training at CSIR-CDRI.

7.5 Training for Scholarship Awardees

Under this category candidates getting scholarships/ selected/nominated from some of the prestigious institutions of India are provided training. The training comprises of both lectures and practical by our scientists and technical staff.

A. Indian Academy of Sciences, INSA-IASc-NASI Summer Research Fellowship

B. INSPIRE Fellowship

C. UPCST Fellowship:

D. AcSIR–Dr APJ Abdul Kalam Summer Training Program

8. Honours & Awards

Prof. Tapas K. Kundu

- Shri Om Prakash Bhasin Award 2019 in the field of Health & Medical Sciences

Dr. Wahajuddin

- Shakuntala Amir Chand Prize 2019 by ICMR
- Fellow Royal Society of Chemistry London (UK) 2020

Dr. Saman Habib

- Elected Fellow of the Indian National Science Academy, Delhi

Dr. Satish Mishra

- Dr. Tulsi Das Chugh Award by National Academy of Medical Sciences, India

Dr. Atul Goel

- Elected Fellow of the Indian Academy of Sciences, Bangalore

Dr. Anuradha Dube

- Prof. Bhim Shankar Trivedi Oration Medal - 2020 by Indian National Science Academy (India)

Dr. Ritu Trivedi

- NASI Reliance Industries Platinum Jubilee Award 2020.

Dr. T. Narender

- ISCB Award for Excellence in Drug Research-2020, Indian Society of Chemists and Biologists (ISCB)
- Elected as a Fellow of Telangana Academy of Sciences (FTAS) in 2020
- Dr. Mridula Kamboj Award for Drugs, Diagnostics, Vaccines and Related Basic Research

Dr. Niti Kumar

- SERB Women Excellence Award 2020

Dr. Gautam Panda

- JSPS-Bridge Professor by Japan Society for the Promotion of Science

Dr. Susanta Kar

- Prof. A N Bhaduri Memorial Lecture Award-2020 by Society of Biological Chemists (India)
- Shakuntala Amir Chand Prize 2019 by ICMR

Dr Manoj Barthwal

- Fellow of International Academy of Cardiovascular Sciences (FIACS) by International Academy of Cardiovascular Sciences

Dr. Sarika Singh

- Women Scientist Award-2019 by Society for Bioinformatics and Biological Sciences

Dr. Madhav Nilakanth Mugale

- Diplomat of "Indian Board of Toxicopathology In India" by Society of Toxicopathology India

Ms. Pooja Maurya

(Student of Dr. Dibyendu Banerjee)

- Women Research Excellence Award by Department of Biotechnology and Microbiology'

Ms. Swetapadma Majhi

(Student of Dr. Kalyan Mitra)

- First Prize in Micrography Contest under Transmission Electron Microscopy Category in Life Sciences with a cash prize of Rs. 2000

Mr. Anirban Sardar

(Student of Dr Ritu Trivedi)

- 2nd Prize in Poster Presentation Indian Society for Bone and Mineral Research, 16th Annual National Conference of the Indian Society of Bone and Mineral Research (ISBMR 2020)

Ms. Ekta Gupta

(Student of Dr. Kishor Mohanan)

- Dr. MM Dhar Memorial Distinguished Career Achievement Award-2020 in Chemical Sciences

Ms. Tripti Mishra

(Student of Dr T Narender)

- Dr. MM Dhar Memorial Distinguished Career Achievement Award-2020 in Chemical Sciences

Mr. Anand Prakash Gupta

(Student of Dr Jiaur Rahaman Gayen)

- Dr. MM Dhar Memorial Distinguished Career Achievement Award-2020 in Biological Sciences

Mr. Mohammed Riyazuddin

(Student of Dr Jiaur Rahaman Gayen)

- Dr. JM Khanna Memorial Distinguished Career Achievement Award-2020 in Pre-clinical & Clinical Sciences

Mr. Salil Varshney

(Student of Dr Anil Gaikwad)

- Dr. JM Khanna Memorial Distinguished Career Achievement Award-2020 in Pre-clinical & Clinical Sciences

Mr. Sukka Santosh Reddy

(Student of Dr Manoj Barthwal)

- Dr. JM Khanna Memorial Early Career Achievement Award 2020

Ms. Priyanka Kothari

(Student of Dr Ritu Trivedi)

- Dr. Swarn Nitya Anand Memorial Early Career Achievement Award 2020 for Women Research Scholars

Ms. Pallavi Awasthi

(Student of Dr Atul Goel)

- Dr. Swarn Nitya Anand Memorial Early Career Achievement Award 2020 for Women Research Scholars

Notes

Section IV:
Events and Activities Organized

आइवीएफ तकनीक में पारंगत करेगा चूहे का भ्रूण-अंडाणु

शोध में मददगार

कोरोना काल में 81 फीसद बढ़ी गर्भनिरोधक गोलियों की मांग

विश्व गर्भनिरोधक दिवस

परिवार नियंत्रित करने में भी महिलाएं पुरुषों से आगे

विश्व गर्भ निरोधक दिवस की पूर्व संध्या पर सीडीआरआई व सीएफएआर का वेबिनार

81% बढ़ी गर्भ निरोधक छाया की मांग

माई सिटी रिपोर्टर

सीडीआरआई व सीएफआर के वेबिनार में मौजूद विशेषज्ञ।

इसलिए मनाया जाता है विश्व गर्भनिरोधक दिवस

आईआईटीआर मनाएगा सीएसआईआर का स्थापना दिवस

तीन युवा वैज्ञानिकों को सीडीआरआई का प्रतिष्ठित पुरस्कार

my city

हम लोग

अमर उजाला

प्रोस्टेट कैंसर के चिकित्सकीय समाधान को नई दिशा देने के लिए पुरस्कृत

कैंसर की अनसुलझी गुत्थी सुलझाने में सफल अनुसंधान के लिए दिया गया सम्मान

सीपीपी का कैंसररोधी औषधि के रूप में भूमिका का पता लगाया

कैंसर सहित अनेक रोगों के कारणों पर किया काम

युवा वैज्ञानिकों को सीडीआरआई पुरस्कार

प्रोस्टेट कैंसर पर शोध के लिए मिला सम्मान

सीपीपी की कैंसर रोधी औषधि के रूप में भूमिका का पता लगाया

कैंसर सहित अन्य रोगों के कारक को बताया

स्वास्थ्य सेवा पर तैयार किया जाए राष्ट्रीय कानून

1. Events & Activities

CSIR-CDRI's 69th Annual Day Celebrations

CSIR-CDRI celebrated its 69th Annual Day on 17th February, 2020. Dr. YK Hamied, Chairman, CIPLA graced the occasion as Chief Guest for the celebrations. During the day, the prestigious 45th Sir Edward Mellanby Memorial Oration was delivered by Dr. Hamied. The topic of his talk was ***"Science and Society***". In his oration he said, India is regarded as the Pharmacy Capital of the World. The Indian pharma industry sales was valued at $ 33 billion in 2017 and is due to grow to $ 50 billion this year. Despite all this expansion and growth, healthcare is only guaranteed to 10% of the world's population. One third does not have access to even basic medicines. We are at the threshold of an Indian scientific revolution. This requires us to rethink, redesign and rebuilt our scientific base through appropriate technology i.e. scientifically bound, relevant, adaptable to local needs and using available resources. This should ensure that we dream of an India, where every citizen can share a decent quality of life. We all are accountable to our future generations.

During the event, CSIR-CDRI transferred technology for enriched fraction CDR219C002 from *Cassia occidentalis* for the treatment of "Glucocorticoid-induced osteoporosis" to M/s Pharmanza Herbal Pvt. Ltd., Gujarat. Event was followed by felicitation of staff & students for their distinct achievements in Publications, Patents and Thesis. The day started with the distribution of awards to the winners of the Annual Day sports 2020 and concluded with Cultural program and dinner.

79th CSIR Foundation Day Celebrations at CSIR-CDRI, Lucknow

CSIR-CDRI, Lucknow celebrated the 79th CSIR Foundation Day Celebrations on 28th September 2020. In view of the COVID-19 protocols, the event was held on an online platform. Prof. Shiv Kumar Sarin, Director, Institute of Liver and Biliary Sciences, New Delhi participated online as chief guest and delivered Foundation Day lecture on “Heart of the Liver”. Apart from creating scientific curiosity in the functioning of liver, his talk spread the awareness regarding importance of liver health for happy, healthy and long life. In his oration he emphasized that one should keep his/her liver fat less than 5%.

On the occasion of CSIR Foundation Day celebration the Dr Mridula Kamboj Award for Drugs, Diagnostics, Vaccines and Related Basic research was announced. Dr T. Narender, Senior Principal Scientist, Medicinal & Process Chemistry and his team received the Dr Mridula Kamboj Award for their outstanding contribution for developing a Phytopharmaceutical for management of Benign Prostate Hyperplasia (BPH) which is also called prostate gland enlargement: a common condition as men get older.

On this occasion, Director CSIR-CDRI released 70th Year's Celebration Logo of CSIR-CDRI and briefed about the yearlong celebrations planned for the same. Besides this, Hindi version of Annual Report 2019-20, Institutes Newsletter - BITS & BYTES and an e-booklet, "Living with COVID-19: Experience & Fight Against Pandemic were released.

CDRI colleagues who superannuated in the previous year and those who have completed 25 years of service in CSIR were felicitated. Besides, the meritorious ward of CDRI colleagues who has secured more than 90% in science subject in High School and Intermediate also received the cash prize and certificate for their outstanding academic performances.

CDRI Awards 2020 for Excellence in Drug Research: Award Oration and Felicitation of Awardees

With an aim to promote drug discovery and development research in India, CSIR-Central Drug Research Institute, Lucknow has instituted CDRI Awards in the year 2004. These prestigious awards are given annually to the Indian Nationals below 45 years of age who have carried out outstanding research work in the area having direct bearing on Drug Research and Development. There are two separate individual awards in the area of Chemical Sciences and Life Sciences. On the occasion of CSIR Foundation Day Celebrations, CDRI Awardees for the year 2020 delivered the Award oration and were felicitated. Details of the awardees are as follows:

Recipient of CDRI Award 2020 in Biological Sciences, **Dr. Bushra Ateeq** currently holds a position as an Associate Professor and a Senior Fellow of the Wellcome Trust/DBT India Alliance at the Department of Biological Sciences and Bioengineering, Indian Institute of Technology Kanpur.

She has shared her notable contribution during the award oration, entitled "Mechanistic insights into etiology of aggressive SPINK1-positive prostate cancer: a quest for new therapeutic avenues." She discovered the underlying molecular mechanism involved in SPINK1 (A Pancreatic secretory trypsin inhibitor (PSTI) which is also known as serine protease inhibitor Kazal-type 1: SPINK1) upregulation, wherein miRNA-338-5p and miRNA-421 plays a critical role in posttranscriptional regulation of SPINK1.

Collectively, her findings provide an explanation for the paradoxical clinical-outcomes after Androgen Deprivation Therapy (ADT), possibly due to SPINK1 upregulation, and offers CK1 inhibition as a strategy for Prostate Cancer adjuvant therapies.

Dr Surajit Ghosh received CDRI Award 2020 in Biological Sciences, for the development of efficient cell penetrating peptides (CPPs) which has tremendous implications in medicine. Dr Ghosh is presently working as Professor in the Department of Bioscience and Bioengineering at Indian Institute of Technology Jodhpur.

His extensive research work enlightened us about the importance of two amino acids, arginine and tryptophan in the cell penetration. In his award oration Dr Ghosh has focused on a top-down approach to show how spatial positions of two tryptophans regulate the cellular entry and nuclear localization. This enables us to develop short nontoxic tetra peptides with excellent potential of cell penetration and nuclear localization. Among them Glu-Thr-Trp-Trp (ETWW) tetra peptides emerges as most promising one. It enters into the cancer cell following endocytic pathway and binds at major groove of nuclear DNA, where successive tryptophan plays major role.

His study provides major fundamental insights about the positional importance of tryptophan and opens new avenues towards the development of next generation cell penetrating peptides (CPP) and major groove specific anticancer drugs.

Dr Ravi Manjithaya, received CDRI Award 2020 in Chemical Sciences. He is presently working as Associate Professor at Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore.

In his award oration, he sneaked about Autophagy, a cellular waste recycling process which is critical for maintaining organellar, cellular and organismal homeostasis. Dysfunctional autophagy results in a plethora of diseases including neurodegeneration, intracellular infections, and cancer.

Using sensitive, kinetic and phenotype-based HTS assays, He has identified and characterized several autophagy-modulating small molecules. Elucidating their effect on autophagy has provided mechanistic insights regarding autophagic flux. These include initiation of autophagosome biogenesis, expansion and completion, its eventual fusion with lysosomes, and degradation of cargo.

In addition, these molecules have revealed regulatory aspects of selective forms of autophagy such as aggrephagy (selective autophagic degradation of protein aggregates) and xenophagy (selective autophagic clearance of intracellular pathogens).

In his award oration, he also discussed how, using cellular and a preclinical mouse model of Parkinson's, some of these

molecules can have therapeutic potential. Thus, chemical genetics approach, while shedding light on basic cellular principles, also reveals potential therapeutic avenues towards diseases that currently have no cure.

CDRI @ 70 Lecture Series

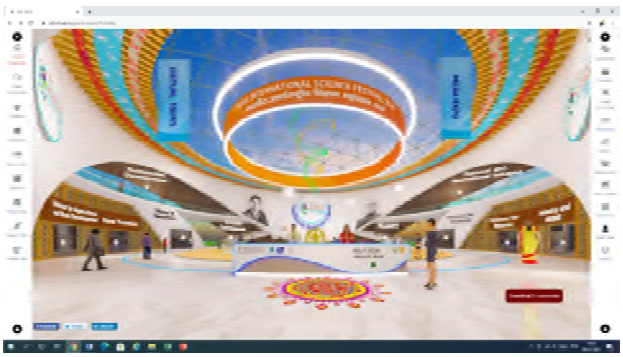
CSIR-CDRI is celebrating 70 glorious years of its existence. During these 70 years, our institute has proudly been at the forefront of drug discovery and development, bringing out blockbuster molecules like Chhaya (Centchroman-the first non-steroidal oral contraceptive) and E-MAL (Arteether-a life-saving drug for cerebral malaria), amongst others. The institute has also spearheaded the efforts within the country towards training quality man power for the academic and pharma sector. The expertise and infrastructure that CSIR-CDRI created along with other CSIR laboratories, has been at the core of growth of pharma sector within the country.

As part of the celebrations of our 70th Annual Day, Institute planned for CDRI@70 Lecture Series. In this series, lectures are being delivered by renowned scientists in multidisciplinary areas.

Lecture by	Title of the Lecture	Date
 Dr. Tavpritesh Sethi Assistant Professor IIIT, Delhi	Solving grand challenges in drug discovery by Artificial Intelligence	14-12-2020
 Dr. Suneel Kumar BVS Director, Computational Chemistry Sai Life Sciences Limited, Hyderabad	Artificial Intelligence/ Machine Learning practices in Drug Discovery	22-12-2020
 Prof. Dipshikha Chakravortty ASTRA Chair Professor DAE SRC Fellow, Humboldt Fellow Indian Institute of Science Bangalore	Revolving around Vacuole- Why Salmonella loves to live in Vacuole	15-01-2021
 Dr. Sajikumar Sreedharan Assistant Professor National University of Singapore	Age-related changes in hippocampal-dependent synaptic plasticity and memory mediated by p75 neurotrophic receptor	10 February 2021

India International Science Festival (IISF-2020)

India International Science Festival (IISF), launched in 2015, is a celebration to promote Science and Technology and demonstrate how science could lead India towards a developed nation within a short span of time. The aim is to engage the public with science and celebrate the joy of science and show the ways how science, technology, engineering and mathematics (STEM) provide us with the solutions to improve our lives.



The 6th India International Science Festival was held in virtual format from 22nd to 25th December, 2020 It was a reflection on Indian Science & Technology Innovations for Atmanirbhar Bharat and Global welfare. CSIR spearheaded the IISF 2020 with support of all other concerned ministries and departments.

In the IISF-2020 Curtain Raiser Ceremony organized at CSIR-CDRI, Dr V.P. Kamboj, Former Director, CSIR-CDRI, Lucknow delivered a lecture on “Atmanirbhar Bharat for Covid-19” on 27 November 2020. He gave a detailed account of efforts being made by research organizations across India to prevent and treat the COVID-19.

As a part of the IISF-2020, an outreach program about the Women Health was organized on 26 November 2020 as a pre-event activity of IISF-2020 in Hanuman Prasad Rastogi Girls Inter College, Lucknow. The program was coordinated by Dr. Namrata Rastogi, Sr Scientist. There were two lectures, one by Dr. Ritu Trivedi Principal Scientist on “Menstrual Health & Hygiene” and another by Dr. Monika Sachdeva Principal Scientist on “Women Reproductive Health” followed by a poster session by students on women health which was managed and judged by Dr. Namrata and Dr. Vineeta Tripathi. The program was followed by an interactive session in which with about 50 students, around 15teachers and all the four scientists participated.

Four of the winners were felicitated for the poster competition among students. Several of students and teachers showed interest and willingness to visit CDRI in future

Outreach program about the Women Health organized on 26 November 2020 as a pre-event activity of IISF-2020 in Hanuman Prasad Rastogi Girls Inter College, Lucknow.

74th Independence Day Celebrations

As a part of 74th Independence Day celebrations, on 15 August 2020, Prof. Tapas K. Kundu, Director, CSIR-CDRI hoisted the tricolour flag followed by national anthem by CSIR-CDRI staff and their family. During the occasion, Director addressed all the staff and students. An yearlong celebration of 70 Glorious years of CDRI was launched with lighting of 70 lamps in the evening of Independence Day.

72nd Republic Day Celebrations

Institute celebrated 72nd Republic Day on 26 January 2021, to commemorate the date on which the Constitution of India came into effect replacing the Government of India Act (1935). Prof. Tapas K Kundu, Director, CSIR-CDRI hoisted the National Flag and addressed all the staff members and students of the Institute. In his address, he recalled the efforts and sacrifice of our freedom fighters in establishing a sovereign democratic country. He also recounted the struggle faced by our nation as well as the world due to COVID-19. He informed that the drug being positioned by CSIR-CDRI to treat COVID-19 is at its final stage of clinical trial. It may reach the market very soon.

CSIR–CDRI Scientific Lecture Series

In January 2019, CSIR-CDRI Scientific Lecture Series were initiated with an aim to create an interacting platform among the scientists of the Institute and eminent contributors in the field of drug discovery and development/ disease biology/other related field. In this series monthly series of lectures, researchers from India and abroad, who have made pioneer contribution in the field of biomedical research towards unmet medical needs, will be delivering a scientific lecture covering their contribution in advancing the knowledge frontiers.

During the year 2020, 7th lecture of the series was delivered by Prof. Uday Kumar Ranga, JNCASR on "Sleep Like HIV to Win The World" on 23rd November 2020.

Popular Health Talk

In order to enlighten the scientists by the real field clinical practices, Institute designed the popular health talk series, where the renowned physicians from all over the country will bring the realistic view of up-to-date therapeutic practices and future need of the nation. Fourth lecture in this series, was delivered by Prof. Rakesh Shukla, DM Neurology, KGMU, Lucknow on 1 January 2021. He spoke on "Therapeutic modalities and challenges of Parkinson's disease: A Clinician's perspective". Dr. Nitya Anand, former Director, CSIR-CDRI graced the occasion as Guest of honour. He was felicitated by the Director, CSIR-CDRI for his immense contributions in the growth of CSIR-CDRI in the national and international arena.

CSIR-CDRI Nobel Symposium 2020

Research Scholars of CSIR-CDRI organized the 3rd CSIR-CDRI Nobel Symposium on January 13th, 2021 in honour of the Nobel Laureates in the fields of Chemistry and Physiology/Medicine 2020. This student-led symposium series, initiated in 2018, is aimed at inspiring young scientific minds and encourage coming up with innovative ideas that will benefit the society. The symposium featured a series of lectures by Research Scholars on topics illustrating the discoveries in the fields of Chemistry and Physiology/Medicine, which received Nobel Prize in 2020.

In the session I, CSIR-CDRI research scholars, Ms. Surbhi Mundra and Ms. Divya Singh delivered lectures on discovery and development of method for genome editing by the Nobel laureates and also latest developments in the field. In the session II, Ms. Khushboo Sinha, Ms. Vaishali Tyagi and Ms. Akanksha Vyas delivered lectures on the theme “Discovering and decoding Hepatitis C Virus”.

Entire event was moderated by Mr. Muhammad Fahad Jamali and Mr. Mushtaq Ahmad. Dr. Niti Kumar and Dr. Kumaravelu mentored the Research Scholars. This symposium received wide accolades from all the Scientists and Students of Institute.

Awareness Programs / Thematic Celebrations

Anti-Terrorism day

As per the practice in the past, May 21, 2020 was observed as Anti-Terrorism day to wean away the youth from terrorism and showing as to how it is prejudicial to the national interest. Both English and Hindi version of Pledge were duly solemnized. The staff and students participated in Pledge taking ceremony.

5th International Yoga Day

As per the practice in the past, Institute celebrated International Yoga Day on 21 June 2020. Staff and students enthusiastically participated in celebration of Yoga Day with befitting participation.

Qaumi Ekta Week

With a view to foster and reinforce the spirit of Communal Harmony, National Integration and pride in vibrant, composite culture and nationhood, the "Qaumi Ekta Week" (National Integration Week) was observed at CSIR-CDRI from the 19 to 25 November, 2017. Staff and students of the Institute took National Integration Pledge on 25 November 2020.

Constitution Day Celebration

To celebrate our Constitution day on 26th November 2020 On this auspicious occasion CSIR-CDRI Director Prof. Tapas k Kundu and the staff members of CDRI read the preamble with the President of India Shri Ram Nath Kovind Telecasted through DD channel from New Delhi.

Vigilance Awareness Week 2020

The central Vigilance Commission is the apex organization, which look after the country against Corruption. It promotes country for the integrity, transparency and accountability in public life. In the year 2020 the Vigilance Awareness week was observed from 27th October 2020 to 2nd November 2020.The theme of the week was "Vigilant India Prosperous India". Corruption has been regarded as one of the foremost hindrance to national development and progress. We must strive to promote integrity and to combat corruption in all walks of life. It is our duty to be a vigilant citizen and prevent corruption of any form in the world around us.

In this occasion various activities were held at CSIR-CDRI to make the staff vigilant. The week started with great enthusiasm and zeal. The inaugural function was on 27-10-2020 by conducting an Integrity Pledge.

On 28-10-2020, Lecture on RTI was delivered by Shri. Vimal Kumar Varun, Scientist F DSIR New Delhi through MS Teams. A quiz competition was held on 29-10-2020 in which staff members of the organization taken part actively.

On 2-11-2020 there was a lecture on Employee Conduct Rule by Shri Mukund Sahai CoA (Retd), CSIR for the staff of CSIR-CDRI, which was telecasted online through MS Team. In the eve of 02-11-2020, the closing ceremony was held. Major V.S. Rana, IRTS (99), Chief Vigilance Office, CSIR addressed all the staff. The prizes for participating in various conducted events were given away to the participants who all participated in the events with great enthusiasm in the vigilance awareness week.

Hindi Saptah

Hindi Saptah is an annual celebration starting on 14 September in our Institution. On this day in 1949, Hindi written in Devanagari script became the official language of India under the article 343.Institute observed Hindi Saptah from 14-24 September 2020. Due to covid-19 pandemic, Hindi Saptah was celebrated through online MS-Team. During entire week Hindi competitions including Hindi translation, writing, quiz, essay, debate, etc were organized. Staffs and students actively participated in the programs. Cash prize was transferred to the winners bank account. During Hindi Saptah, Rajbhasha timahi meeting was also organized.

Sports & Recreational Activities: 70th CSIR-CDRI Annual Day Sports Events

As a part of the 70th CSIR-CDRI Annual Day, Staff Club of the Institute organized various Indoor and Outdoor sports activities, including Badminton, Bridge, Campus Run, Carom, Chess, Cricket, Football, Kabaddi, Table Tennis, Volleyball for the staff and students of the Institute. Activities like field events and painting competition was organized for the children of CSIR-CDRI staff and scholars.

2. Visits and Deputations Abroad

Dr. Gautam Panda, Senior Principal Scientist, was granted JSPS Bridge Invitation Fellowship for a period of one month (1-30 March 2020) to write a joint research proposal on possible biomedical application of BuckyBowl with Japanese Professor Hidehiro Sakurai, Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Suita 565-0871. Dr. Panda was on deputation to Japan from 29.02.2020 and joined the institute on 16.06.2020.

3. Distinguished Visitors and Lectures

Distinguished Visitor	Title of Lecture	Date
Prof. Patrick G. Steel Department of Chemistry and Biophysical Sciences Institute, Durham University, Durham	Identifying and validating new drug targets in leishmania	15-01-2020
Dr. RK Shandil Founder Director and Vice President, Foundation for Neglected Disease Research, Bengaluru	Challenges in TB drug discovery and development vs. the current pipeline of antitubercular drugs	30-01-2020
Dr. Sai Prasad Pydi National Institute of Diabetes, Digestive and Kidney Diseases, NIH, USA	Targeting GPCR signalling in Adipose Tissue and AgRP Neurons for the treatment of Obesity and Type 2 Diabetes	06-02-2020
Dr. Uday C Ghoshal Professor, Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow	Pathophysiological basis of irritable bowel syndrome	11-02-2020
Dr. Anjan Kumar Pradhan Virginia Commonwealth University, USA	MDA-9/Syntenin: A potent gene target for breast cancer progression and metastasis	11-02-2020
Dr. Benu Brata Das Associate Professor, Indian Association for Cultivation of Science, Kolkata	New regulators of DNA topoisomerases 1 induced DNA damage, repair and human diseases	19-02-2020
Dr. Jeremy Burros Vice President and Head of Discovery & **Dr. Kirandeep Samby** MMV Open Operational Lead, Chemistry Consultant Medicines for Malaria Venture, Geneva	Current status of antimalarial drug discovery and MMV-Open for chemistry	25-02-2020
Prof. Vishal Rai Associate Professor Indian Institute of Science Education and Research, Bhopal	Precision chemistry of native proteins enabling biology and medicine	31-07-2020
Dr. Vinod Tiwari Assistant Professor, Indian Institute of Technology (BHU) Varanasi	Targeting PAIN before it reaches the brain	23-10-2020
Dr. Anil Kumar Goel Former Chief Scientist & Head, Botanic Garden & Floriculture, CSIR- National Botanical Research Institute, Lucknow	Ethnomedicine: A potential source for bioprospection	11-11-2020
Dr. Mandar Bodas Solution Sales Manager Elsevier, South Asia Region	Application of data analytics for progression of compounds in pre-clinical drug discovery	4-12-2020

Staff List

DIRECTOR

Prof. Tapas Kumar Kundu, PhD, DSc, FNASc, FASc, FNA, Sir J. C. Bose National Fellow

R & D DIVISIONS

DIVISION OF BIOCHEMISTRY

Chief Scientist
Neena Goyal, M.Sc., Ph.D. *Chairperson*
Neeloo Singh, M.Sc., Ph.D. *(Superannuated on 31.01.2021)*

Senior Principal Scientist
Vinita Chaturvedi, M.Sc., Ph.D.
Sabyasachi Sanyal, M.Sc., Ph.D. FNASc

Principal Scientist
Akhilesh Kumar Tamrakar, M.Sc., Ph.D.

Principal Technical Officer
Ramesh Sharma, M.Sc., Ph.D.
B. Maity, M.Sc., Ph.D.

Sr. Technical Officer (1)
Ajay Singh Verma, M.Sc.
Ishbal Ahmad, M.Sc.

Technical Officer
Priyanka Trivedi, M.Sc.
Karthik R., M.Sc., Dip. in DCLM

DIVISION OF BOTANY

Principal Scientist
D. K. Mishra, M.Sc., Ph.D., *Chairperson & Supervising Scientist*
In-charge, Horticulture activity

Senior Scientist
Vineeta Tripathi, M.Sc., Ph.D.

Sr. Technician (3)
J. K. Joshi, B.Sc.
Lab. Assistant
Satya Narayan
R. C. Maurya
Satya Narayan
Makkhan Lal *(Superannuated on 30.11.2020)*
Lakhana Devi

Lab Attendant (2)
N. K. Khanduri
Ashok Kumar (Experimental Garden Work)

DIVISION OF CANCER BIOLOGY

Principal Scientist
Arun Kumar Trivedi, M.Sc., Ph.D.
Dipak Datta, M.Sc., Ph.D., *Chairperson*
Jayanta Sarkar, M.V.Sc., Ph.D.

Senior Scientist
Dibyendu Banerjee, M.Sc., Ph.D.

Sr. Technical Officer (1)
Shyam Singh, M.Sc.

Technical Officer
Sanjeev Meena, M.Sc.

Technical Assistant
Varsha Singh, M.Sc.

DIVISION OF ENDOCRINOLOGY

Chief Scientist
Naibedya Chattopadhyay, M.Sc., Ph.D.

Senior Principal Scientist
Gopal Gupta, M.Sc., Ph.D., *Chairperson*
F. W. Bansode, M.Sc., Ph.D. *(Expired on 04.03.2020)*
Durga Prasad Mishra, M.Sc., Ph.D.

Principal Scientist
Divya Singh, M.Sc., Ph.D.
Ritu Trivedi, M.Sc., Ph.D., FNASc, *In-charge Academic Affairs (w.e.f 01.12.2020)*
Rajender Singh, M.Sc., Ph.D.
Monika Sachdev, M.Sc., Ph.D.
Rajesh Kumar Jha, M.Sc., Ph.D.

Sr. Technical Officer (3)
Mohini Chhabra, M.Sc., CLSc *(Superannuated on 31.08.2020)*
Balvir Singh, M.Sc.

Technical Officer
Konica Porwal, M.Sc.
Jaspreet Kaur, M.Sc.
Amar Deep Lakra, M.Sc.

Sr. Technician (3)
Geet Kumar Nagar, B.Sc.

Jr. Stenographer
Harish Kumar Checker

Lab. Assistant
Mahesh Chandra Tewari, B.Sc.

Lab Attendant (2)
Ram Karan, Intermediate

DIVISION OF MEDICINAL AND PROCESS CHEMISTRY

Chief Scientist
Arun K. Sinha, M.Sc., Ph.D., FNASc *(Voluntary Retirement on 10.07.2020)*
Atul Kumar, M.Sc., Ph.D., *Chairperson & Supervising Scientist In-charge Centralized Utility Services*

Senior Principal Scientist
Sanjay Batra, M.Sc., Ph.D., FNASc, FRSC
Atul Goel, M.Sc., Ph.D.
Gautam Panda, M.Sc., Ph.D., FAScT
T. Narender, M.Sc., Ph.D.

Principal Scientist
K. V. Sashidhara, M.Sc., Ph.D.
Prem Prakash Yadav, M.Sc., Ph.D.
Dipankar Koley, M.Sc., Ph.D.
Kishor Mohanan, M.Sc., Ph.D.
Pintu Kumar Mandal, M.Sc., Ph.D.
Ranvir Singh, M.Tech., *Unit In-charge, Centralized Utility Services*

Senior Scientist
Namrata Rastogi, M.Sc., Ph.D.
Ajay Kumar Srivastava, M.Sc., Ph.D.
Ravindra Kumar, M.Sc., Ph.D.
Richa Pandey, M.Sc., Ph.D.
Nilanjana Majumdar, M.Sc., Ph.D.

Scientist
Chandra Bhushan Tripathi, M.Sc., Ph.D.
Malleswara Rao Kuram, M.Sc., Ph.D.
Damodara Reddy N., M.Sc., Ph.D.
Nayan Ghosh, M.Sc., Ph.D.
Ramesh Chintakunta, M.Sc., Ph.D.

Principal Technical Officer
Tara Rawat, B.Sc. *(Superannuated on 31.03.2020)*
Deepali Pandey, B.Sc.

Sr. Technical Officer (1)
Atma Prakash Dwivedi, M.Sc.
K. S. Anil Kumar, M.Sc., Ph.D., P.G.D.C.A.,
Ashok Kumar Sharma, B.Sc., D.Ch.E., A.M.I.E.
Tahseen Akhtar, M.Sc., Ph.D.
Suriya Pratap Singh, M.Sc., Ph.D.

Technical Assistant
Jitendra Singh
Bhawana Sharma, Ph.D.

Sr. Technician (3)
Preeti Rastogi, M.Sc.
Ramjeet, B.Sc., PGDC
Raju Arora, B.Sc.
Anoop Kumar Srivastava, M.Sc.
(Superannuated on 30.06.2020)
Mithilesh Sharma, M.Sc.
(Superannuated on 31.05.2020)
Rajesh Kumar *(Superannuated on 30.04.2020)*
A. K. Pandey, B.Sc.
S. C. Tiwari, B.Sc.
Shailendra Mohan, M.Sc. (Maths), PGDCA

Sr. Technician (2)
Manju, B.Sc.
Ram Lakhan, Intermediate
K. M. Shukla, B.Sc. *(Superannuated on 30.06.2020)*

Technician (2)
H. R. Misra, M.Sc.
N. P. Misra, M.Sc.
Krishna Kumar, B.Sc. *(Superannuated on 31.01.2021)*

Technician (1)
Rajesh Kumar Verma, B.Sc
Kul Bahadur Thapa, BCA, ITI Trade Electronics, Diploma (Electronics)

Principal Private Secretary
Avadhesh Kumar, B.A.

Lab. Assistant
J. C. Rajan
Mohd. Islam

DIVISION OF MICROBIOLOGY

Sr. Principal Scientist
B. N. Singh, M.Sc., Ph.D., *Chairperson*

Principal Scientist
Arunava Dasgupta, M.Sc., Ph.D.
Sudheer Kumar Singh, M.Sc., M.Tech., Ph.D.
Y. K. Manju, M.Sc., Ph.D.
Sidharth Chopra, M.Sc., Ph.D.
Mukesh Pasupuleti, M.Sc, Ph.D.

Scientist
Neha Topno, M.Sc.

Principal Technical Officer
Agney Lal, B.Sc.

Sr. Technical Officer (2)
Sandeep Kumar Sharma, M.Sc., Ph.D.

Technical Officer
Atul Krishna, B.Sc., DMLT
Umamageswaran V., M.Sc.

Sr. Technician (3)
D. K. Tripathi, M.Sc., Ph.D.

Lab. Assistant
A. N. Dixit, B.A.

Lab. Attendant (2)
Ravi Shankar Mishra
Ram Prakash, B.A.
Shyam Sunder Yadav, B.A.

DIVISION OF MOLECULAR & STRUCTURAL BIOLOGY

Chief Scientist
Saman Habib, M.Sc., Ph.D., FASc, FNASc, FNA, *In-Charge, Academic Affairs Unit (up to 30.11. 2020)*
Ravishankar Ramachandran, M.Sc., Ph.D., *Chairperson, Molecular & Structural Biology and Sophisticated Analytical Instruments Based Facility & Research, Supervising Scientist In-charge, Instru., Common equipment & facility management*

Senior Principal Scientist
Jimut Kanti Ghosh, M.Sc., Ph.D., FNASc
J. Venkatesh Pratap, M.Sc., Ph.D.
Mohammad Imran Siddiqi, M.Sc., Ph.D

Principal Scientist
Amogh Anant Sahasrabuddhe, M.Sc., Ph.D.
Mohammad Sohail Akhtar, M.Sc., Ph.D.
Shakil Ahmed, M.Sc., Ph.D.

Senior Scientist
Ashish Arora, M.Sc., Ph.D.
Tejender S. Thakur, M.Sc., Ph.D.

Sr. Technical Officer (3)
R. K. Srivastava, B.Sc. *(Superannuated on 30.11.2020)*

Sr. Technical Officer (2)
Ruchir Kant, M.Sc. Ph.D., PGDCA

Sr. Technical Officer (1)
Anupam Jain, M.Sc.
Rima Ray Sarkar, M.Sc.
Sarita Tripathi, M.Sc.

Sr. Technician (2)
Radhey Shyam Ram, Intermediate

DIVISION OF MOLECULAR PARASITOLOGY AND IMMUNOLOGY

Chief Scientist
Renu Tripathi, M.Sc., Ph.D., FNASc, *Chairperson*

Principal Scientist
Satish Mishra, M.Sc., Ph.D.

Senior Scientist
Mrigank Srivastava, M.Sc., Ph.D.
Susanta Kar, M.Sc., Ph.D.
Niti Kumar, M.Sc., Ph.D.

Scientist
Bidyut Pukrait, M.Sc., Ph.D.

Principal Technical Officer
Rishi Narayan Lal, M.Sc.

Technical Officer
Shikha Mishra, M.Sc.
Ashan Manhas, B.Sc., M.L.T.

Technical Assistant
Shabeer Ali H., M.Sc., PhD.

Sr. Technician (3)
K. K. Singh, M.Sc. *(Superannuated on 30.11.2020)*

Lab. Attendant (2)
Ram Das
Om Prakash, Intermediate *(Superannuated on 31.08.2020)*

DIVISION OF NEUROSCIENCE AND AGEING BIOLOGY

Principal Scientist
Prem N. Yadav, M.Sc., Ph.D.
Aamir Nazir, M.Sc., Ph.D.

Senior Scientist
Shubha Shukla, M.Sc., Ph.D.

Sr. Technical Officer (1)
Sachi Bharti, M.Sc.

Technical Officer
Deepmala, M.Sc.

Sr. Technician (2)
Anil Kumar Verma, B.Sc.

DIVISION OF PHARMACEUTICS AND PHARMACOKINETICS

Senior Principal Scientist
Amit Misra, M. Pharm., Ph.D.
Prabhat Ranjan Mishra, M. Pharm., Ph.D., FNASc *Chairperson*

Principal Scientist
Manish Kumar Chourasia, M. Pharm., Ph.D.
Rabi Sankar Bhatta, M. Pharm., Ph.D.
Wahajuddin, M.S. (Pharm.), Ph.D.
Jiaur Rahaman Gayen, M. Pharm., Ph.D.

Technical Officer
Deepak, M.Sc.

Sr. Technician (3)
Narendra Kumar, B.Sc.
Sr. Technician (1)
Akhilesh Kumar, Intermediate

Lab. Attendant (2)
Ram Bhajan Shukla, Intermediate
Ram Kumar
Chandramani

DIVISION OF PHARMACOLOGY

Senior Principal Scientist
Manoj Kumar Barthwal, M.Sc., Ph.D., *Chairperson*

Principal Scientist
Anil N Gaikwad, M.S. (Pharma.), Ph.D.
Kumaravelu Jagavelu, M.Sc., Ph.D.
Kashif Hanif, M.Sc., Ph.D.

Senior Scientist
Sachin Kumar, M.Sc., Ph.D.
Amit Lahiri, M.Sc., Ph.D.

Scientist
Baisakhi Mohrana, M.V.Sc., Ph.D.
Shrikant R. Mulay, M.S., Ph.D.
Shashi Kumar Gupta, M.Sc., Ph.D.

Principal Technical Officer
C. P. Pandey, M.Sc., Ph.D., M.H.R.

Sr. Technical Officer (1)
Sheeba Saji Samuel, M.Sc., Ph.D.

Technical Officer
Smriti, M.Sc.
Pankaj Kumar Shukla, B.Sc., P.G.D.B.T.

Sr. Technician (3)
Bharti Bhushan, B.Sc., N.C.V.T. (Electrical) Ramesh Chandra, M.Sc.

Sr. Technician (2)
Anil Kumar Verma, B.Sc.

Sr. Stenographer
Renuka Mushran, B.A.

Lab. Attendent (2)
Pankaj Sengupta *(Superannuated on 29.02.2020)*

DIVISION OF TOXICOLOGY & EXPERIMENTAL MEDICINE

Chief Scientist
Sharad Sharma, M.B.B.S., M.D., *In-Charge*

Senior Principal Scientist
S. K. Rath, M.Sc., Ph.D.
Raj Kamal Tripathi, M.Sc., Ph.D.

Principal Scientist
Smrati Bhadauria, M.Sc., Ph.D.
Sarika Singh, M.Sc., Ph.D.

Senior Scientist
Madhav Nilakanth Mugale, M.V.Sc., Ph.D.
Vivek Vidyadhar Bhosale, M.B.B.S., M.D.

Principal Technical Officer
Mukesh Srivastava, M.Sc., Ph.D. (Biometry & Statistics) *(Superannuated on 31.05.2020)*
P. K. Agnihotri, M.Sc., Ph.D.
Sadan Kumar, M.Sc.

Sr. Technical Officer (1)
Anurag Kumar Srivastava, M.Sc.
Shail Singh, M.Sc., Ph.D.

Technical Officer
Anil Kumar Meena, M.Sc., B.Ed.
Navodayam Kalleti, M.Sc.
Sudhaker Yadav, M.Sc., M.L.T.

Technical Assistant
Akhilesh Kumar, M.Sc., Ph.D.

Sr. Technician (3)
M.P.S. Negi, B.Sc., PGDC (Biometry & Statistics)
Anupma, B.Sc.

Private Secretary
Nandita Pandey, B.A., Diploma in Secretarial Practice

Lab. Assistant
R. B. Pawar, *Clinical Pharmacology Unit (CDRI), Seth G.S. Medical College, Mumbai*
Umesh Kumar, Intermediate
Savitri Devi *(Superannuated on 31.01.2021)*

Lab. Attendant (2)
Ram Kumar, High School (Science)
Nand Pal Yadav, Intermediate

TECHNICAL INFRASTRUCTURE DIVISIONS/ UNITS

NATIONAL LABORATORY ANIMALS FACILITY

Chief Scientist
D. S. Upadhyay, M.V.Sc., Ph.D., *In-Charge*

Principal Scientist
S. Rajakumar, M.Sc .
Dhananjoy Hansda, M.V.Sc.

Senior Scientist
Rajdeep Guha, M.V.Sc., Ph.D.
H. K. Bora, M.V.Sc. *(Transferred to CSIR-NEIST)*

Scientist
Shishir Kumar Gupta, M.V.Sc., Ph.D.

Principal Technical Officer
Karunesh Rai, M.Sc.

Technical Officer
Chandra Shekhar Yadav, M.Sc., PGDCA

Technical Assistant
Vijay Kumar Verma, M.Sc., Ph.D.

Sr. Technician (3)
Ravindra Singh, M.Sc., Ph.D.
Sanjeev Kumar Saxena, B.Sc.

Sr. Technician (2)
Ravi Kumar Shukla, Intermediate (Sci.)
Narendra Kumar, B.A.
Dinesh Kumar, B.A.
Pradeep Tirkey, Intermediate

Sr. Technician (1)
Arun Sharma, B.Sc.

Lab. Assistant
V. B. L. Srivastava
S. K. Verma
O. P. Verma, B.A. *(Superannuated on 30.09.2020)*

Lab. Attendants (2)
Jameel Beg
Najibullah

SOPHISTICATED ANALYTICAL INSTRUMENT FACILITY AND RESEARCH

Senior Principal Scientist
N. K. Agarwal, M.Sc.
Ravi Sankar Ampapathi, M.Sc., Ph.D., *NMR Facility In-charge*

Principal Scientist
Sanjeev Kumar Shukla, M.Sc., Ph.D.
Sanjeev Kanojiya, M.Sc., Ph.D. *Mass Spectrometry Facility In-charge*
Kalyan Mitra, M.Sc., Ph.D., *Electron Microscopy Facility In-charge*
Manoj Kumar Rawat, M.Tech.

Principal Technical Officer
H. M. Gauniyal, M.Sc., Ph.D.
A. K. Mandwal, M.Sc., Ph.D. *(Superannuated on 31.08.2020)*
Sunil Kumar, B.Sc.
Pramod Kumar, M.Sc. *(Superannuated on 31.12.2020)*

Sr. Technical Officer (2)
Ram Karan Harijan, AMIE
Sanjay Kumar, B.Tech. (Civil Engg.)
Kavita Singh, M.Sc., Ph.D.

Sr. Technical Officer (1)
Binod Kumar Saw, M.Sc.

Technical Officer
Garima Pant, M.Sc.
Pooja Soni, Diploma (Electronics Engg.), Graduate in Engg.
Tofan Kumar Rout, M.Sc., Ph.D.
Amit Kumar, M.Tech.
Dharmesh Kumar, M.Sc.

Technical Assistant
Vipin Kumar, M.Sc. (Organic Chemistry)
Pooja Singh, M.Sc. (Pharmaceutical Chem.)
Mohan Kumar A.S., M.Sc.

Sr. Technician (3)
Ashok Pandey, B.Sc.
Sandeep Sengupta, B.Sc.
Madhu Chaturvedi, Diploma (Electronics)
S. A. Singh, B.Sc., PGDCA

Sr. Technician (2)
V. K. Maurya, ITI *(Superannuated on 31.12.2020)*
Madhuli Srivastava, B.A.
O. P. Gupta, B.Sc.
D. N. Vishwakarma
Kamal Singh, ITI (Instrument Mechanic)

Sr. Stenographer (Hindi)
Anil Kumar, B.Com. *(Afternoon with Biochemistry Division)*

SCIENTIFIC DIRECTORATE

Principal Scientist
Anand P. Kulkarni, M.Sc., Ph.D., *Head, PME, Supervising Scientist In-charge, Auditorium Management*

Principal Technical Officer
Ravindranath S. Londhe, GD Art (Commercial), Art Teachers Dip.

Technical Officer
Farha Khan, M.C.A.
Arbind Kumar, B.C.A., PGDAM, *Unit In-charge, Auditorium Management*
S. Mehazabeen, M.Sc.
Ashok Kumar, Diploma in Mechanical Engineering

Sr. Technician (2)
Suresh S. Bhakuni, Intermediate, ITI Dip.

Technician (1)
Sumit Khichi , Intermediate, ITI Jodhpur

Sr. Stenographer
Himanshu Upadhyay, B.A.

ACADEMIC AFFAIRS UNIT

Senior Scientist
Sanjeev Yadav, M.Sc., Ph.D., PG Diploma in Bioinformatics

Sr. Technician (2)
A. K. Pandey, B.Sc.

BUSINESS DEVELOPMENT & INTELLECTUAL PROPERTY UNIT

Principal Scientist
Sripathi Rao Kulkarni, M.Sc., Ph.D., P.G. Dip. in Patents Law
Naseem Ahmed Siddiqui., B. Pharma (Hons), M.B.A., *Head-BD*

Sr. Technical Officer (3)
A. S. Kushwaha, B.Sc.

Technical Officer
Neelima Srivastava, M.C.A.

Technician (2)
Preeti Agarwal, M.C.A.

COMPUTER CENTRE

Chief Scientist
Kural, B.E., *In-Charge*

Scientist
Santosh Shukla, B.Tech.

Sr. Technical Officer (1)
Ajay Kumar Maurya, M.Tech.

HUMAN RESOURCE DEVELOPMENT & KNOWLEDGE RESOURCE CENTRE

Chief Scientist
Vinay Tripathi, M.Sc., M.B.A., P.G. Dip.,
In-Charge

Sr. Principal Scientist
Prem Prakash, M.Pharm.

Principal Technical Officer
Sanjay Kumar, M.L.I.Sc.
(Superannuated on 31.12.2020)

Sr. Technical Officer (2)
Ramesh Chandra Gupta, M.L.I.Sc.

Sr. Technical Officer (1)
Savita Tripathi, M.Sc., B.Ed.

Technical Officer
Pankaj Upreti, M.L.I.Sc.

Technician (2)
Susheel Kumar, Intermediate

Sr. Stenogrpaher
Surendra Kumar, B.Com.

Lab. Attendant (1)
Pradeep Kumar Srivastava, B.Sc.

LABORATORY ENGINEERING SERVICES

Senior Superintending Engineer
Parvez Mahmood, B.Sc. Engineering (Civil), *In-Charge*
Kamal Jain, B.E., (Electrical)

Executive Engineer
Mohit Kumar Shukla, A.M.I.C.E. (Civil)
Jai Prakash, Diploma in Mech. Engg. (Ref. & AC)
Sidho Hembrom, Diploma in Mech. Engg.

Assistant Executive Engineer
D. K. Vishwakarma, Diploma in Civil Engg.
Brahma Singh, AMIE in Electrical Engg.

Assistant Engineer
Madhukar Saroj, Diploma, B.Tech. (Civil)
Ajay Kumar, B.Sc., Diploma in Electronics Engg.

Sr. Stenographer (Hindi)
Raj Kumar, B.A.

Multi Tasking Staff
Hanuman
Maikulal-II
Hari Prasad

Sr. Technician (2)
M. S. Verma, B.A., ITI *(Superannuated on 30.11.2020)*
Harish Kumar, Intermediate, ITI
Vijay Kumar, High School, ITI
Swapan Karmi
Ramesh Kunwar, Intermediate, ITI
(Superannuated on 31.12.2020)
Arun Kumar Srivastava, ITI

Lab. Assistants
Popinder Singh *(Superannuated on 31.08.2020)*
S. K. Bhattacharya
S. K. Yadav *(Superannuated on 30.06.2020)*
Bishan Singh Negi
A. K. Misra *(Superannuated on 31.07.2020)*

Lab Attendant (2)
Sandeep Roy, High School
Dhirendra Misra, Intermediate
Mohd. Irfan, Intermediate, ITI
Raju Vishwakarma
Ram Autar *(Superannuated on 30.09.2020)*
Hari Om Garg
Ram Samujh, Intermediate *(Superannuated on 30.09.2020)*
Bindeswari Prasad
Suresh Kumar
Gaya Prasad
Ram Asrey

Lab. Attendant (2)
Darshan Lal

MTS (Non-Technical)
Faizi

GENERAL ADMINISTRATION AND FACILITIES

COA OFFICE

Controller of Administration
Pradip Kumar, B.E.

Asstt. Section Officer (G)
Kamla Kandpal, M.A.

Jr. Stenographer
Kshma Bajpai, B.A.

Multi Tasking Staff
Saurav Sarkar, Intermediate

DIRECTOR'S OFFICE

Private Secretary
Sumit Srivastava, B.Com.
V. P. Singh, B.A.
Sunita Chopra, B.A. *(Superannuated on 31.05.2020)*

Sr. Technician (2) (Driver)
Shakeel Ahmad Khan

Lab. Attendant (2)
Nand Kishore, ITI
Multi Tasking Staff
Rajesh, Highschool

ESTABLISHMENT I

Section Officer (G)
Krishna Raj Singh, B.Sc., MSW

Assistant Section Officer (G)
Jagdish Prasad, B.Sc., MPA
Saju P. Nair
Reena Bisaria, B.A. *(Superannuated on 31.01.2021)*
Riti Chaudhary, B.A.

Senior Secretariat Assistant (G)
Anjali Singh, B.A.
Vinay Kumar Singh, B.C.A.

Sr. Stenographer
Deepak Dhawan, B.A.

Lab. Assistant
Vinod Kumar

Group C
Manju Yadav

ESTABLISHMENT II

Section Officer (G)
Ishwar Nath Jha, B.A., M.B.A.

Assistant Section Officer (G)
Rashmi Srivastava, B.A., B.Ed.
Dilip Kumar Sen, B.Com.
Neena Raizada, B.A.
Aparna Bajpai, B.A.
Ajai Shukla, M.Com.

Senior Secretariat Assistant (G)
Anoop Thakur, B.Tech. (ECE)

Sr. Stenographer
Vinod Kumar Yadav, B.A.

Multi Tasking Staff
Ram Kumar, B.Com.

GENERAL SECTION

Section Officer (G)
Anil Kumar, B.Sc.

Assistant Section Officer (G)
Rajendra Prasad, B.A.
Rani, High School
Mohd. Irfan, Madhyama Visharad

Senior Secretariat Assistant (G)
Deepak Kumar Gupta, M.Com.
Rishi Kant, M.Sc., B.Ed., O-Level

Junior Secretariat Assistant (G)
Mohd. Saleem, Prathama (equi. to High School)

Sr. Stenographer
Seema Srivastava, M.A

Sr. Technician (2) (Driver)
K. K. Kashyap, VIIth

Driver
Daya Shankar Singh *(Superannuated on 29.02.2020)*

Multi Tasking Staff
Kalpanath Sharma, Intermediate

Lab Attendent
K. P. Mishra, Highschool

BILL SECTION

Section Officer (G)
Nitu Kumari, B.Sc., M.A.

Assistant Section Officer (G)
Dilip Kumar, B.A, LLB

Senior Secretariat Assistant (G)
Nida Parveen, B.Com.
Indra Prakash Singh, B.A.
Kumar Saurabh, B.Com.

Sr. Stenographer
Vineet Pandey, B.A., P.G. Comp.

Jr. Stenographer
Lalit Kumar, B.A.

Lab Assistant
V. P. Mishra, Intermediate

Lab. Assistant
Vinod Kumar Sharma, B.A.

VIGILANCE

Section Officer (G)
Ajay Kumar, B.A., L.L.B.

Assistant Section Officer (G)
Vibhash Kumar, B.A. (Hons), CIC

Senior Secretariat Assistant (G)
Jaya Singh, B.Sc.

Lab. Attendant
Ramesh Chandra

HINDI SECTION

Jr. Hindi Translator
Diwakar Pandey

SECURITY

Security Officer
Anil Kumar Upadhyay, M.A.

FINANCE & ACCOUNTS

Controller of Finance & Accounts
I. B. Dixit, M.Sc., M.B.A.

Section Officer (F&A)
Mahesh Babu, B.A.
Harish Chandra, B.A.

Assistant Section Officer (F&A)
Ajay Kumar, B.A.
D. K. Khare, B.Com.
Mahender Kumar, B.Com.
Sanjay Kumar, B.A.

Senior Secretariat Assistant (F&A)
Tahseen Tilat, B.A.
S. A. Siddiqui, B.A *(Superannuated on 30.06.2020)*
Chandrashekhar, Intermediate
Abhishek Kumar, Intermediate

Sr. Stenographer (H) (MACP)
Jitendra Patel, M.A.
Mohammad Sufiyan, B.Com.

Senior Secretariat Assistant (F&A)
Mamata Chourasia, M.A.

Lab. Attendant (2)
Vikramaditya, High School

Multi Tasking Staff
Mohd. Firoz, B.A.
Shekhar Singh, B.Com.. M.B.A.

Lab. Assistant
Satish Chandra Yadav, B.Sc.

STORE & PURCHASE

Store & Purchase Officer
M. P. Singh, M.A., PGDBA, MBA
Prasenjeet Mitra, B.Sc.
Krishna Kumar *(Voluntary Retirement 20.07.2020)*
Section Officer
Amit Kumar, M.A.

Assistant Section Officer (S&P)
P. S. Chauhan, B.Sc. *(Transferred to CSIR-CIMAP)*
Arun Wadhera, Intermediate
H. B. Neolia, M.A.
R. C. Dwivedi, B.Com. *(Superannuated on 30.06.2020)*
Md. Rizwan, B.Tech, MPA
Mahesh Kumar, M.A.

Senior Secretariat Assistant (S&P)
M. C. Verma, B.Com.
Kanchan Bala, B.A.
Anil Kumar, B.A.

Junior Secretariat Assistant (S&P)
G. P. Tripathi, Intermediate

Sr. Technician (3)
Ram Pal, B.Sc., LLB

Sr. Technician (2)
Ravi Kumar Mehra, B.A.

Attendant
Hardwari *(Superannuated on 31.12.2020)*

MultiTasking Staff
Sudhir Kumar Yadav, Intermediate

CSIR DISPENSARY

Medical Officer Group III (6)
N. K. Srivastava, M.B.B.S., *In-Charge*

Medical Officer Group III (4)
Kunal Gupta, M.B.B.S.
Shalini Gupta, M.B.B.S., PGDHHM

Technician (2)
Shraddha, M.A., Diploma in Nursing, Post Basic Diploma in Dialysis, Certificate in child care nutrition
Shabana, B.A., Diploma in Pharmacy

Technician (1)
Shahzada Jalal (Pharmacist)
Simpi Gupta (Pharmacist)

Lab. Assistant
S. K. Paswan, Intermediate

Lab. Attendant (2)
Shubhendra Kumar, Intermediate

CANTEEN

Manager Gr. II (ACP)
J. P. Sati, B.A.

Clerk (ACP)
Ram Jiyawan Tewari (Coupon Clerk)
Acharya *(Superannuated on 31.03.2020)*
Y. K. Singh, B.A. (Count Clerk)

Asstt. Halwai
Uma Shanker Tewari

Bearer
Ganga Ram
Rajender
Sukhdev Prasad

S/Man
Raj Kumar

Wash Boys
Ram Murat
Dinesh Pal Singh, Intermediate

Notes

BusinessLine

Science

Scientist from CDRI gets Tata Innovation Fellowship

Jyoti Singh New Delhi | Updated on February 14, 2020 Published on February 14, 2020

Dr Ritu Trivedi

Dr Ritu Trivedi, Principal Scientist from Central Drug Research Institute (CDRI) has been conferred with prestigious Tata Innovation Fellowship for the year 2019-2020.

The fellowship has been given to her in recognition of her contributions in translational research by innovative scientific knowledge and

समाज के लिए खास है इनका 'वै

आज राष्ट्रीय विज्ञान दिवस पर

सलाम राजधानी की महिला वैज्ञानिकों को

सीडीआरआई के रजत प्रभात की स्थापना आज ही के दिन हुई थी

लखनऊ। आज राष्ट्रीय विज्ञान दिवस पर एक ओर जहां प्रख्यात वैज्ञानिक सीवी रमन को उनके रमन प्रभाव के लिए याद किया जाएगा, वहीं महिला वैज्ञानिकों को उनके योगदान के लिए सलाम करेगा देश। विज्ञान के क्षेत्र में महिलाओं के बढ़ते प्रभाव, उनके योगदान को देखते हुए इस बार की थीम रखी गई है 'विज्ञान में महिलाएं'। राजधानी के पास भी गर्व करने के पर्याप्त मौके हैं। प्रमुख संस्थानों में ऐसी महिला वैज्ञानिकों की बड़ी जमात है, जिनके वैज्ञानिक प्रभाव का असर दूर-दूर तक है। आइए हम भी इन्हें सलाम करते हैं, इनकी उपलब्धियों से आपको रूबरू कराते हैं।

सीडीआरआई ने विज्ञान दिवस पर अनूठी पहल करते हुए संस्थान में कार्यरत महिला वैज्ञानिकों की उपलब्धियों को हर किसी के बीच तक पहुंचाने का फैसला किया है। सीडीआरआई की तरफ से बृहस्पतिवार को एक रिपोर्ट जारी करते हुए कहा गया कि इन्होंने संस्थान को गौरवान्वित किया।

डॉ. रितु ने किया हड्डियों की मजबूती के लिए शोध

ऑस्टियोपोरोसिस और ऑस्टियोआर्थराइटिस पर काम करने वाली प्रधान वैज्ञानिक डॉ. रितु त्रिवेदी को उनके उत्कृष्ट शोध के लिए राष्ट्रीय विज्ञान अकादमी द्वारा टाटा इनोवेशन फेलोशिप 2019-20 एवं डॉ. पी सीमन मेमोरियल-एम सीमन अवार्ड 2019 से सम्मानित किया गया है।

हड्डी की टूट-फूट की चिंता

प्रधान वैज्ञानिक डॉ. दिनेश सिंह को डॉ. अतुल गोयल के साथ संयुक्त रूप से ऑस्टियोआर्थराइटिस मैनेजमेंट प्रौद्योगिकी पुरस्कार 2019 से सम्मानित किया गया। उनके द्वारा विकसित हड्डी की टूट-फूट के त्वरित उपचार के लिए बायोडिग्रेडेबल बोन इम्प्लांट बनाने के लिए यह सम्मान दिया गया।

डॉ. नीति ने मलेरिया की रोकथाम पर किया काम

वरिष्ठ वैज्ञानिक डॉ. नीति कुमार को एसईआरबी उत्कृष्ट महिला अवार्ड (सर्ब वीमेन एक्सीलेंस अवार्ड-2020) मिला है। यह पुरस्कार उन्हें मलेरिया की रोकथाम के लिए वैकल्पिक दवा लक्ष्यों की खोज के लिए एवं मानव मलेरिया परजीवी में प्रोटीन गुणवत्ता नियंत्रण मशीनरी को समझने के उनके प्रयासों के लिए दिया गया।

इनका योगदान भी सराहनीय

डॉ. अनुराधा गुप्ते ने प्लाजमोडियम के लिए वैकल्पिक दवा लक्ष्यों की खोज के लिए

डॉ. रेणु त्रिवेदी ने फार्मास्युटिकल विज्ञान के क्षेत्र में बेहतरीन योगदान

डॉ. सोनिया ने विकास इंजीनियरिंग उद्योग महिला के क्षेत्र में प्रौद्योगिकी

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Science and Technology

CSIR-CDRI Scientist Dr Saman Habib elected as fellow of Indian National Science Academy

Dr. Saman Habib at MSB Lab @CSIR_CDRI (2019)

The Milli Gazette Online, 24 Oct 2020

Dr Habib bagged fellowship of all three premier Science Academies of India.

New Delhi: Dr. Saman Habib has brought the laurels to her institute again through her outstanding work for understanding the malaria parasite. She is elected as fellow of Indian National Science Academy, New Delhi.

BusinessLine

Science

CSIR-CDRI Scientist bags SERB Women Excellence Award

New Delhi | Updated on February 24, 2020 Published on February 24, 2020

Dr Niti Kumar, Senior Scientist from Division of Molecular Parasitology and Immunology, CSIR-Central Drug Research Institute (CDRI), Lucknow, has won the SERB Women Excellence Award for the year 2020. Dr Niti Kumar will receive the Award from the President of India during National Science Day Celebrations on February 28, 2020, at Vigyan Bhawan.

This is a huge recognition of her research group's work on understanding the protein quality control machinery in human malaria parasite. The study could well lead to finding an alternative drug for malaria intervention

आइवीएफ तकनीक में पारंगत

स्वस्थ शिरोमणि ● लखनऊ

केंद्रीय औषधि अनुसंधान संस्थान (सीडीआरआइ) के वैज्ञानिकों ने चूहे का ऐसा विशेष भ्रूण व अंडाणु तैयार किया है, जो मानव से काफी मिलता-जुलता है। कृत्रिम गर्भाधान की विभिन्न तकनीकों को आजमाकर विशेषज्ञता हासिल करने की इच्छा रखने वाले चिकित्सकों के लिए यह वरदान साबित होगा। चिकित्सक सहायक प्रजनन प्रौद्योगिकी (एआरटी) जैसे इन विट्रो फर्टिलाइजेशन (आइवीएफ) व इंट्रा साइटोप्लास्मिक स्पर्म इंजेक्शन (आइसीएसआइ) में इसकी मदद से महारत हासिल कर सकेंगे। देश में

केंद्रीय औषधि अनुसंधान संस्थान की वैज्ञानिक डॉ. मोनिका सचदेव ● जागरण

सीडीआरआइ द्वारा दी जाने वाली यह अपने तरीके की पहली सुविधा है।

सीडीआरआइ की एंड्रोलाइनोलॉजी विभाग की डॉ. मोनिका सचदेव ने आइवीएफ और आइसीएसआइ के साथ-साथ अन्य एआरटी सुविधाओं के प्रशिक्षण के लिए चूहे से संशोधित पशु अंडाणु और भ्रूण विकसित किए हैं। ये अंडाणु एवं भ्रूण, आकार,

शोध में मददगार

डॉ. सचदेव बताती हैं कि [illegible] मानव अंडों के समान व [illegible] तापमान पर विशेष रूप [illegible] रूप से यह भ्रूणविज्ञानी प्र[illegible] होगा, जो आइवीएफ क्ली[illegible] से पहले एंब्रोलॉजिस्ट प्र[illegible]

लोच आदि में लगभग [illegible] समान हैं। इसलिए यह भ्रूणविज्ञानि[illegible] को अंडाणु एवं भ्रूण के साथ काम करने की वास्तविक अनुभूति कराएगा और कृत्रिम गर्भाधान तकनीक में पारंगत बनने में मददगार होगा। पशु अंडाणु और भ्रूण विशेष रूप से एआरटी प्रशिक्षण के लिए विकसित किए जाते हैं, ताकि भ्रूणविज्ञानी मानव अंडे का चूने से पहले अच्छी तरह से प्रशिक्षित हो सकें।

बीते कुछ दशकों में दुनिया भर में निःसंतान दंपतियों की संख्या वृद्धि हुई है। एआरटी निःसंतान दंपतियों के बीच दिन-प्रतिदिन लोकप्रिय हो रही है। एआरटी के लिए भ्रूणविज्ञानियों को मानव अंडे और भ्रूण को संभालने के [illegible] महारत हासिल करने हेतु कोई प्रशिक्षण मॉड्यूल या कार्यप्रणाली सामग्री आसानी से उपलब्ध नहीं हैं। इसे देखते हुए सीडीआरआइ ने पहल कर भ्रूणविज्ञानियों के लिए चूहे से अंडाणु व भ्रूण का वैज्ञानिक मॉडल तैयार किया है।

https://epaper.jagran.com/epaper/03-Nov-2020-11-Lucknow-edition-Lucknow-page-8.html

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