



**DR.REDDY'S
INSTITUTE OF LIFE SCIENCES**

DRILS ANNUAL REPORT

2021-2022

CONTENTS

Contents	3
Mission and Vision	5
From the Director's Desk.....	7
Board of Directors	9
Centers.....	11
Center for Innovation in Molecular and Pharmaceutical Sciences.....	11
Center for Advancement of Research Skills	15
Center for Process Research Innovation	17
Special Initiatives.....	19
DRILS Rare Disease Initiative (DRIVE) - the ongoing effort	19
FCT Hub	20
SARS-CoV2 programs	20
Industry Programs	21
Publications and Patents	23
Publications	23
Patents	25
Events	26
Grants and funding	28
Committees	30
Human Resource and Development and Finance	31

MISSION AND VISION

Dr. Reddy's Institute of Life Sciences (DRILS) is a not for profit Research Institute with a mission to be the preferred research partner to the pharma and life sciences industry. DRILS focuses on original research and advancement of relevant skills, with emphasis on solution-oriented interdisciplinary research for solving unmet needs and for process innovation. The Institute has been set up on a public-private partnership model by Dr. Reddy's Laboratories, the Government of Telangana, and the University of Hyderabad, and is governed by a Board of Directors comprising eminent scientists and visionaries.



The vision of our Founder Chairman, Padmabhushan Dr. Kallam Anji Reddy, can be eloquently summarized in his own words:

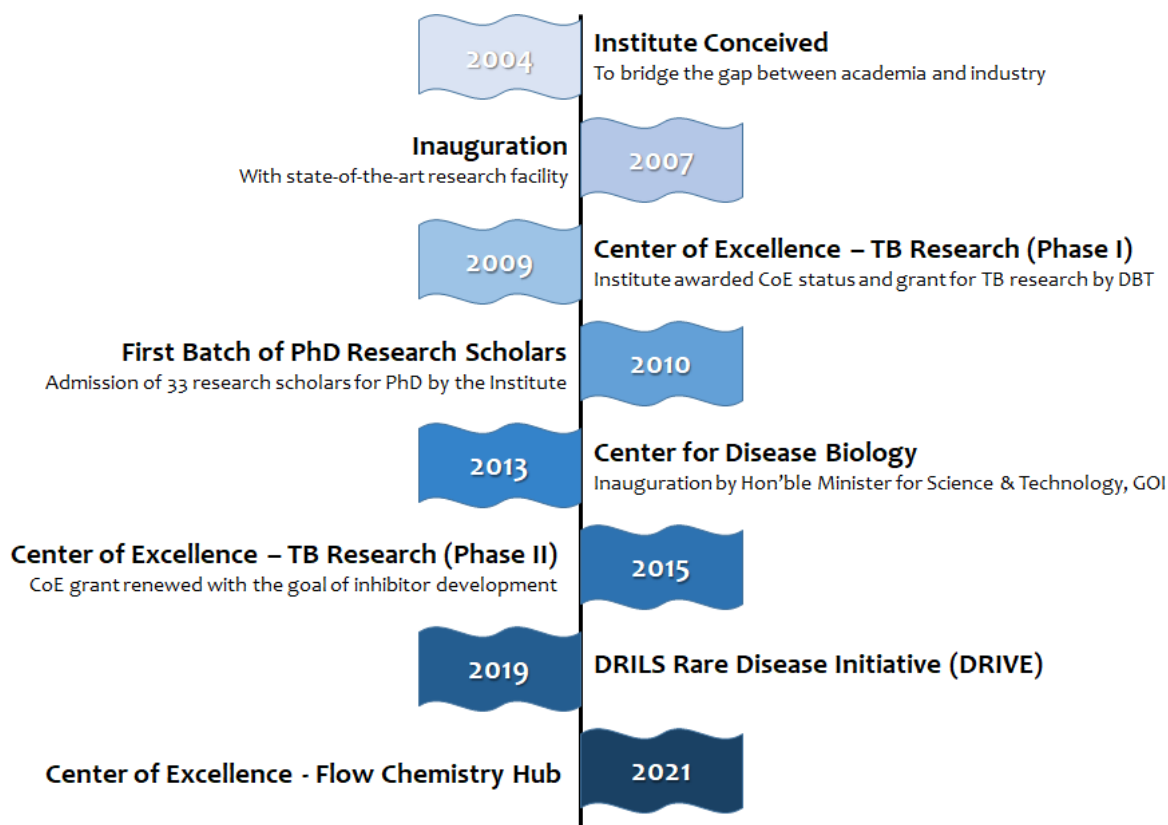
"If the world's burden of disease is to be diminished, it needs science that is both good and cost-effective. India has the potential to deliver on science that is both. I have great confidence in our army of chemists and biologists. And I firmly believe that walking on the trail of innovation will lead to creating a great company - a company that doctors, patients, investor and the public will admire."

DRILS as a research center became operational in 2007. Since then, it has provided a vibrant platform to several scientists from industry and academic backgrounds in their pursuit of advanced knowledge and relevant skills. Dr. Reddy's Institute of Life Sciences has emerged as a unique non-governmental research institute, with a passion for science and learning and a purpose to catalyze innovative and sustainable research with societal benefit and indigenous innovation. Research at DRILS is supported by external funds such as government grants or industry-sponsored grants, or internal funds for high priority areas. DRILS is organized into three centers, the Center for Innovation in Molecular and Pharmaceutical Sciences (CIMPS), the Center for Process Research Innovation (CPRI) and the Center for Advancement of Research Skills (CARS).

CIMPS represents the Institute's core research activity, and comprises scientists with diverse technical backgrounds spanning advanced molecular biology, cell biology, pharmacology, organic and medicinal chemistry and nanochemistry. CPRI is the Institute's chemistry vertical engaged in addressing the industry's chemical research and innovation needs, with the main thrust areas being process R&D and medicinal chemistry. CARS focuses on training programs to advance the skills and aptitude in basic science and industry-relevant areas, among students, teachers and industry recruits. Scientists at DRILS are also actively engaged

in mentoring Masters and Ph.D students and post-doctoral fellows supported by government fellowships and research grants.

HISTORICAL MILESTONES



FROM THE DIRECTOR'S DESK



As the world recovers from another year spent in the grips of the COVID-19 pandemic, DRILS is grateful to have emerged from it stronger in terms of both the scientific and societal contributions made by the team. We are grateful for the new opportunities that came our way in a tough year, and I am proud of the progress we have made despite the challenges. Consistent with our mandate, DRILS scientists pivoted to rapidly contribute to COVID-19 research in multiple ways, including vaccine development and testing, clinical studies and medicinal chemistry and process chemistry efforts to support drug discovery and development.

In the last year, DRILS has successfully accomplished several challenging and novel projects, with the common underlying theme of benefiting society via problem-solving for partners and collaborators. A Flow Chemistry Technology (FCT) hub was established with funding and patronage from Dr. Reddy's Laboratories and Laurus Labs and strategic support from the government of Telangana. This initiative is aimed towards ensuring greater incorporation of flow chemistry techniques during pharma research and development and greater adoption of continuous green synthesis for manufacturing of APIs of a drug.

DRILS is part of the team that received a Clinical Research Center grant focussed on Rare Disease research, from DBT/Wellcome Trust India Alliance, in 2021. This is a significant boost to the DRILS Rare Disease Initiative, an ongoing program engaged in the creation of relevant rare disease models, mechanistic studies and therapeutic development.

DRILS scientists were able to set up assays critical for vaccine testing, and thus contribute in a timely manner to the vaccine development efforts in the country. In a COVID-19 clinical research collaboration with Asian Institute of Gastroenterology, we generated data on vaccine efficacy and responses to new variants in real-time, enabling rapid clinical and policy decisions.

These technical and strategic accomplishments have formed an unshakeable foundation for the emergence of Pillars of Innovation in niche and futuristic thematic areas, which are imperative to carry on the Institute's mandate and be responsive to a changing innovation ecosystem.

DRILS is now at a pivotal stage to embark on the next phase of its journey as a strong research and innovation hub to support innovation needs in various aspects of drug development and next-generation therapeutics. DRILS has been pursuing the goal of setting up platforms for leading-edge research in a wide variety of critical disciplines. These comprise flow chemistry and automation for API synthesis, and process research and engineering as part of Process Chemistry Innovation; molecular biology, CRISPR-Cas, cell-based and zebrafish platforms for a clinically-oriented Rare Disease Initiative; and new bio-therapeutic platforms focused on gene therapy as part of Biology Process Innovation. These strategic areas will be critical to indigenous innovation, product and technology development, and DRILS will engage diverse collaborators in academia, industry and government via dynamic partnerships in these specific domains. Through these

interdisciplinary research collaboration and external partnerships, DRILS will continue to maximize its societal impact in these fields.

We recognize and value the continued support and guidance received from Dr. Reddy's Laboratories, the University of Hyderabad and the Govt. of Telangana, all of whom have been an integral part of our journey. We are grateful to all our well-wishers and look forward to cultivating valuable and long-lasting relationships with our future collaborators and partners.

Srinivas Oruganti

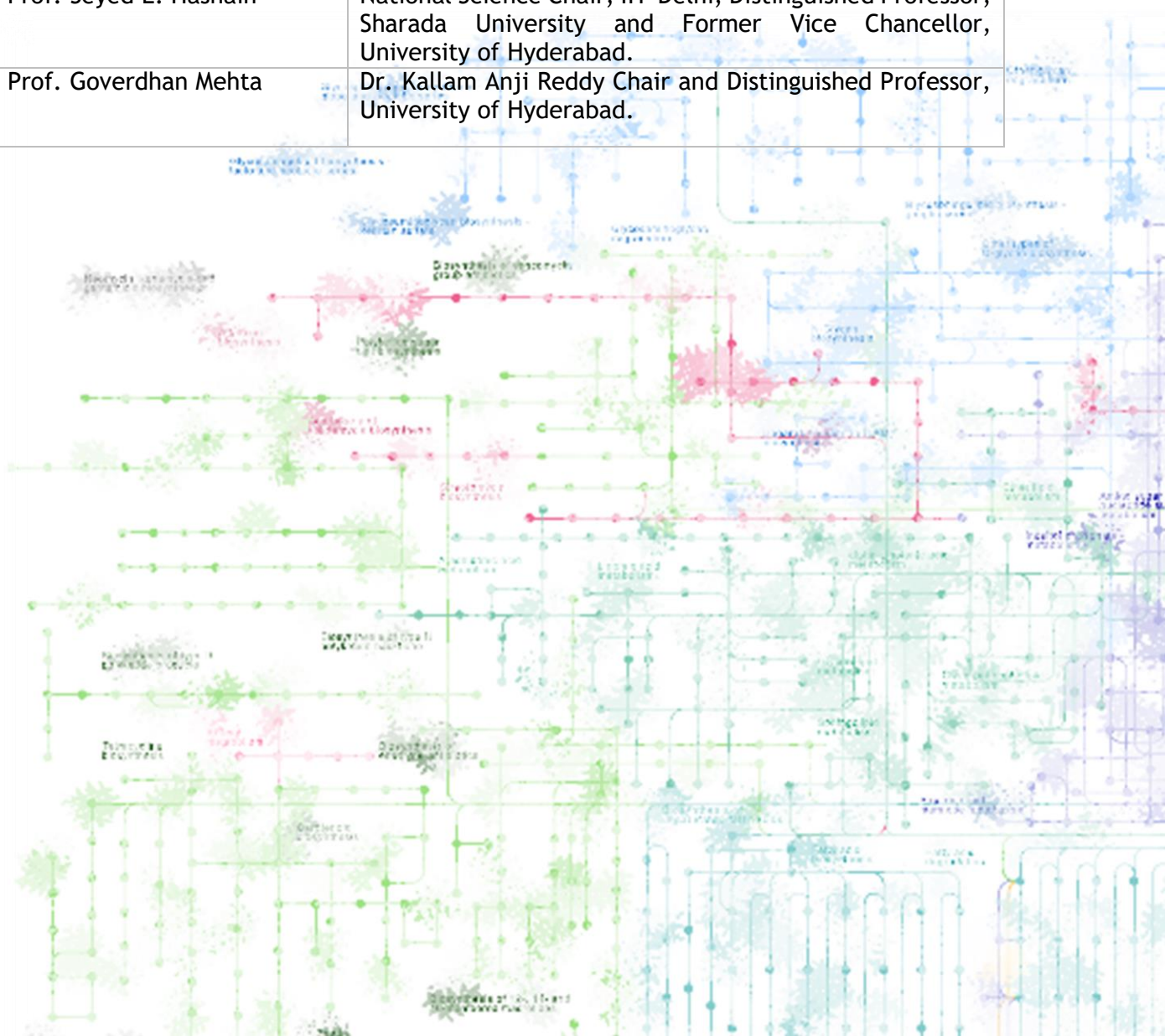
Director, DRILS, Hyderabad

April 2022



BOARD OF DIRECTORS

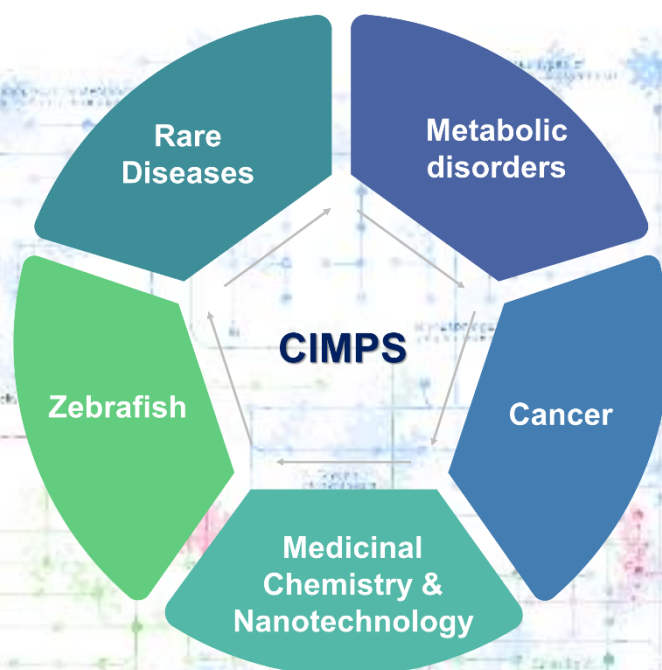
NAME	DESIGNATION
Mr. G.V. Prasad, Chairman of the Board	Co-Chairman & Managing Director, Dr. Reddy's Laboratories Ltd.
Mr. Satish Kallam Reddy	Chairman, Dr. Reddy's Laboratories Ltd.
Ms. Mahima Datla	Managing Director, Biological E Ltd.
Prof. Basuthkar Jagadeeshwar Rao <i>Ex-officio</i>	Vice Chancellor, University of Hyderabad.
Shakthi Nagappan <i>Ex-officio</i>	Nominee of Principal Secretary, Dept. of Industries and Commerce, Govt. of Telangana.
Dr. Srinivas Oruganti	Whole time Director, DRILS
Dr. A. Venkateswarlu	Former Director, DRILS
Prof. D. Balasubramanian	Distinguished Scientist and Director Emeritus, Prof. Brien Holden Eye Research Centre, L.V. Prasad Eye Institute.
Prof. Seyed E. Hasnain	National Science Chair, IIT-Delhi, Distinguished Professor, Sharada University and Former Vice Chancellor, University of Hyderabad.
Prof. Goverdhan Mehta	Dr. Kallam Anji Reddy Chair and Distinguished Professor, University of Hyderabad.



CENTERS

CENTER FOR INNOVATION IN MOLECULAR AND PHARMACEUTICAL SCIENCES

The Center for Innovation in Molecular and Pharmaceutical Science (CIMPS) represents the institute's core research activity. Scientists at CIMPS have diverse technical backgrounds, spanning advanced molecular biology, cell biology, pharmacology, organic and medicinal chemistry, and nanochemistry. Research at CIMPS is supported by external funds such as government grants or industry-sponsored grants, or via internal funds for high priority areas. Ph.D. Students and post-doctoral fellows with government fellowships work on government-funded research projects.



INVESTIGATORS:

PARIMAL MISRA
Chief Scientist

MANOJIT PAL
Chief Scientist

KIRANAM CHATTI
Senior Principal Research Scientist, HOD (CARS)

KISHORE PARSA
Senior Principal Research Scientist, HOD (CIMPS)

AARTI SEVILIMEDU
Principal Research Scientist

MARINA RAJADURAI
Senior Research Scientist



PARIMAL MISRA
Chief Scientist

Our group works on metabolic disorders. Transcriptional coactivators play a crucial role in regulating gene expression. PRIP Interacting protein with Methyl Transferase domain (PIMT)/ Trimethyl guanosine synthase 1 (TGS1) is a co-activator interacting protein with an RNA methyl transferase domain. PIMT serves as a bridge between HAT and non-HAT coactivators and differentially modulates gene expression. Disruption of PIMT is embryonic lethal. PIMT regulates hepatic gluconeogenesis and TNF- α induced insulin resistance in the skeletal muscle. As a methyl transferase, PIMT controls HIV-1 post transcriptional regulation and is essential for human telomerase RNA biogenesis. To provide a comprehensive understanding of the dual role of PIMT, which promises to be a potential target in the treatment of several metabolic disorders, our group is working to understand its function in other important metabolic tissues like pancreas, adipose and macrophages using different knock down animal models and normal and diseased human tissues.

Rebecca Kristina Edwin, Challa Nagalakshmi, Rahul Sharma, K Satyamoorthy, Kishore Parsa* and Parimal Misra*. PIMT/TGS1: an evolving metabolic molecular switch with conserved methyl transferase activity. *Drug Discovery Today* (2022), in press. <https://doi.org/10.1016/j.drudis.2022.04.018> * Corresponding authors



MANOJIT PAL
Chief Scientist

My group mainly focuses on the development of new chemical entities under the drug discovery programme in therapeutic areas namely tuberculosis, inflammation, obesity, psoriasis and cancer. The group contributed in identification of a small molecule as inhibitor of chorismate mutase that showed POC in animals and could be effective against tuberculosis (WO 2020/240272 A1). The molecule was found to be effective against MDR-Mtb ATCC 35825 as well as *Staphylococcus aureus*. This group also identified a selective 5HT_{2C} agonist (PAAM) towards the potential management of obesity (WO/2021/028935). In another project the group identified a lead molecule as a selective inhibitor of 12R-LOX with anti-psoriatic effects in animal (WO 2020/255156 A1) for which the patent is granted in India. The group is also involved in the identification of selective and potent inhibitors of PDE4 for the potential treatment of inflammatory diseases.

The other major areas of focus include transition metal / non-metal catalysed reactions, sonochemical approaches, green chemistry, heterocycle synthesis etc (see: [Research.com: https://research.com/u/manojit-pal](https://research.com/u/manojit-pal)).

Thirupataiah et al, Fe(III)-catalyzed regioselective and faster synthesis of isocoumarins with 3-oxoalkyl moiety at C-4: Identification of new inhibitors of PDE4, *Bioorganic Chemistry*, 2022, 105667, <https://doi.org/10.1016/j.bioorg.2022.105667>

Reddy et al. Indole derivatives as anti-tubercular agents: An overview on their synthesis and biological activities, *Curr. Med. Chem.* 2021, 28, 4531-4568; DOI: 10.2174/0929867327666200918144709

Kumar et al, Sonochemical synthesis of rosuvastatin based novel 3-methyleneisindolin-1-one derivatives as potential anticancer agents. *Journal of Molecular Structure* 2021, 1240, 130574 <https://doi.org/10.1016/j.molstruc.2021.130574>



KISHORE PARSA

Senior Principal Research Scientist, HOD (CIMPS)

Immune responses/inflammation and metabolism are deeply integrated and tightly regulated processes required for the organismal survival. Coordination between nutrient and pathogen/inflammatory stress sensing mechanisms is required for efficient handling of energy resources. In pursuit of the understanding of the interface between inflammation and metabolism, my laboratory is keenly interested in unravelling the intracellular signaling mechanisms that regulate macrophage inflammatory responses and probe the significance of these signaling networks in metabolic syndrome. Towards this, my group utilizes a combination of cellular, molecular biological and genomics approaches in an attempt to identify signaling hubs that harmonize inflammatory and metabolic processes. In the past year, we along with Dr. Chatti and Dr. Thondamal's laboratories, used cultured cells, PHLPP1-ablated *C. elegans* and PHLPP1 knockout zebrafish as model systems and uncovered the functional significance of Ser/Thr Phosphatase, PHLPP1, in the control of lipid metabolism and the development of foamy macrophages-early lesions of atherosclerosis. In addition, we also collaborated with AIG hospitals, Hyderabad and contributed to the determination of the efficacy of Roche anti-COVID-19 monoclonal antibody therapy against Delta and Kappa variants and identification of a variant of TMPRSS2 protease, which is associated with lesser disease severity.

- Balamurugan K, Medishetti R, Kotha J, Behera P, Chandra K, Mavuduru VA, Joshi MB, Samineni R, Katika MR, Ball WB, Thondamal M, Challa A, Chatti K*, Parsa KVL*. (2022). PHLPP1 promotes neutral lipid accumulation through AMPK/ChREBP-dependent lipid uptake and fatty acid synthesis pathways. *iScience*. Jan 12;25(2):103766. doi: 10.1016/j.isci.2022.103766.
- Effectiveness of REGEN-COV antibody cocktail against the B.1.617.2 (delta) variant of SARS-CoV-2: A cohort study. Kumar V J, Banu S, Sasikala M, Parsa KVL, Sowpati DT, Yadav R, Tallapaka KB, Siva AB, Vishnubhotla R, Rao GV, Reddy DN. *J Intern Med*. 2022 Mar;291(3):380-383. doi: 10.1111/joim.13408. Epub 2021 Nov 1.
- A variant in *TMPPRSS2* is associated with decreased disease severity in COVID-19. Ravikanth V, Sasikala M, Naveen V, Latha SS, Parsa KVL, Vijayasathy K, Amanchy R, Avanthi S, Govardhan B, Rakesh K, Kumari DS, Srikanth B, Rao GV, Reddy DN. *Meta Gene*. 2021 Sep;29:100930. doi: 10.1016/j.mgene.2021.100930. Epub 2021 May 28



KIRANAM CHATTI

Senior Principal Research Scientist

Zebrafish are alternative animal models useful in vertebrate developmental biology, disease biology, toxicology, and pharmacology. We apply CRISPR-based genome engineering in zebrafish to explore tyrosine kinase biology in vivo. Our goal is to generate disease models with tyrosine kinase dysregulation, primarily cancer. We collaborate extensively with other groups in the Institute to contribute to projects where zebrafish is useful, including rare diseases. We have generated c-MET knockout zebrafish and are in the process of reporting this data. In collaboration with Dr. Aarti Sevilimedu, we are generating zebrafish knockouts of selected rare disease genes. In collaboration with Dr. Kishore Parsa's group, we have generated PHLPP1-knockout zebrafish and this work has been published recently. The application of strategies for generating genomic knock-ins and mutations is an ongoing effort.

- Balamurugan K, Medishetti R, Kotha J, Behera P, Chandra K, Mavuduru VA, Joshi MB, Samineni R, Katika MR, Ball WB, Thondamal M, Challa A, Chatti K*, Parsa KVL*. (2022). PHLPP1 promotes neutral lipid accumulation through AMPK/ChREBP-dependent lipid uptake and fatty acid synthesis pathways. *iScience*. Jan 12;25(2):103766. doi: 10.1016/j.isci.2022.103766.



AARTI SEVILIMEDU
Principal Research Scientist

Our group works on two broad thematic areas. As part of the first, we are interested understanding the contribution of RNA to the regulation of gene expression. This includes the role of noncoding RNA molecules as well as RNA motifs and elements in coding RNA that directly or indirectly impact transcription and translation. We study these processes primarily in *S.pombe* and in specific disease contexts in Zebrafish.

The second area of interest of our group is the biology of rare diseases using zebrafish models. We work on adapting new technologies for model creation, studying the disease biology at the level of the whole organism as well as the underlying cellular and molecular pathways and are interested in using multiple data-driven approaches to enable the discovery and development of therapeutics. Currently, the group is working in zebrafish models of Fragile X syndrome (FXS) and Glutaric Aciduria Type I (GA1), and several other knockout and knock-in models are in the pipeline.

In the past year, the group also contributed to COVID-19 research at DRILS by developing a rapid, inexpensive method to synthesize Spike variants to enable vaccine development.

Rani R, Parsa KVL, Kiranam C, Sevilimedu A (2022). An efficient cost-effective method for directed mutagenesis at multiple dispersed sites-a case study with Omicron spike DNA. bioRxiv. DOI: <https://doi.org/10.1101/2022.02.10.480017>



MARINA RAJADURAI
Senior Research Scientist

Current research of our group is focused on development of novel nanoparticles-based drug delivery systems. Transdermal delivery approach using soluble microneedles is one of the predominant areas of interest. We also use other approaches to develop efficient drug delivery machinery. For example, we develop methods for the generation of nano- and sub-micro structures from the existing drugs/ bioactive compounds to manipulate biological activities by controlling their morphology and dimensions.

Additionally, we are interested in contributing to COVID-19 research at DRILS by developing simple and economical methods of synthesis of Solid Lipid Nanoparticles (SLNP) for mRNA delivery, which in future may ease vaccine manufacturing in India.

We are also interested in development of novel methodologies for economical, efficient and eco-friendly nano-catalysts applicable for high-volume synthesis of generic APIs and fine chemicals.

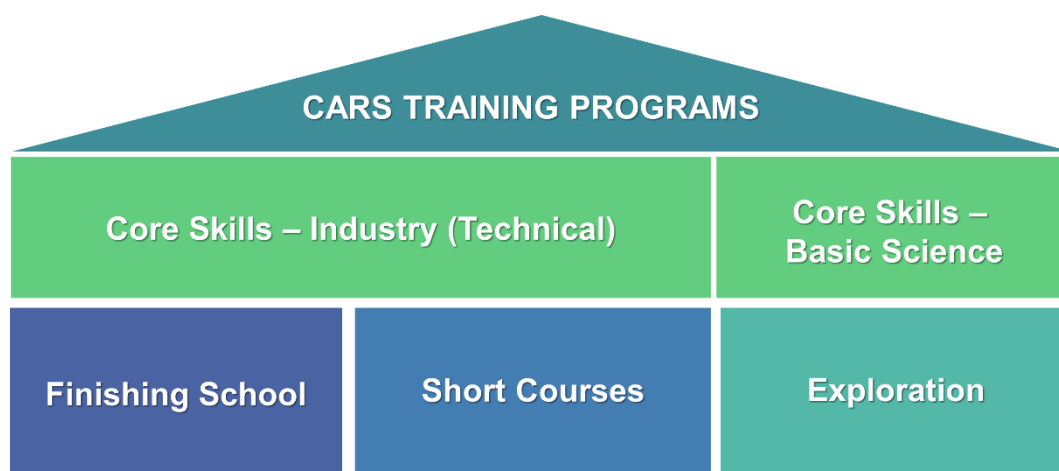
B. Thirupataiah, Gangireddy Sujeevan Reddy, Guntipally Mounika, Jetta Sandeep Kumar, Kazi Amirul Hossain, Jayesh Mudgal, Jessy E. Mathew, Gautham G. Shenoy, Marina Rajadurai, Kishore V. L. Parsa and Manojit Pal. Pd-catalysed general access to 7-membered N/O-heterocyclic compounds as potential agents against inflammation. Chem Commun, 2021, 57, 10091-10094; DOI: 10.1039/d1cc04140a.

Marina Rajadurai* and E. Ramanjaneya Reddy. Tuning the sensitivity towards mercury via cooperative binding to D-fructose: dual fluorescent chemosensor based on 1,8-naphthyridine-boronic acid derivative. RSC Advances, 2021, 11, 14862 - 14870.

[M. Rajadurai, Bhavya Surekha, Sustained Release Compositions. Indian Patent Application No.: E-2/1663/2021/CHE, International PCT Application No. PCT/IN2021/050479, filed on May 18, 2021]

CENTER FOR ADVANCEMENT OF RESEARCH SKILLS

Creation of a research talent pool for the nation's emerging scientific and research needs has been a key area of activity at DRILS. The Center for Advancement of Research Skills (CARS) is engaged in addressing skill development and training needs in industry and academia. Structured into industry-relevant technical skills and academia-relevant basic science skills, CARS conducts training programs for students and industry professionals. In-house scientists and external experts provide the training depending on the requirements of the program.

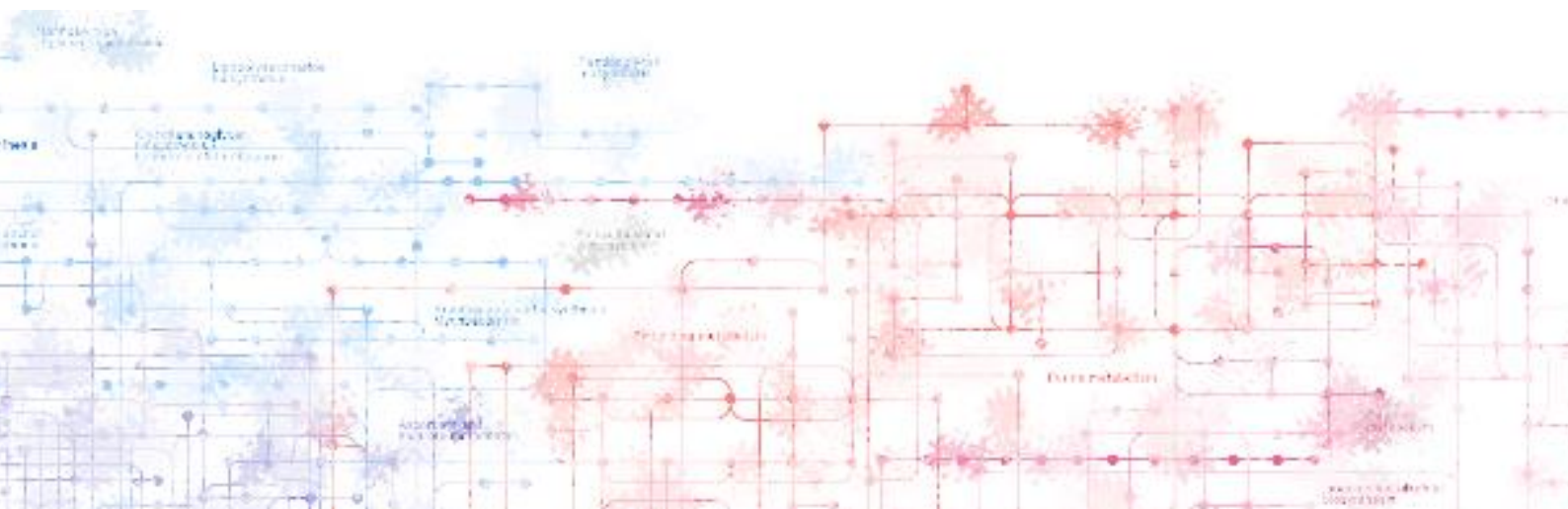


In the past year, a month-long training program for students and jobseekers was conducted, addressing the topic of Quality Control in the Pharmaceutical Industry. An online workshop for Industry R&D staff on the topic of Organic Chemistry for Engineers was conducted. Online workshops for Industry staff on various aspects of Chemical synthesis including methods and processes are ongoing.

A summer internship with online sessions and lab visits for High School students is currently being conducted.

KIRANAM CHATTI
Head, CARS

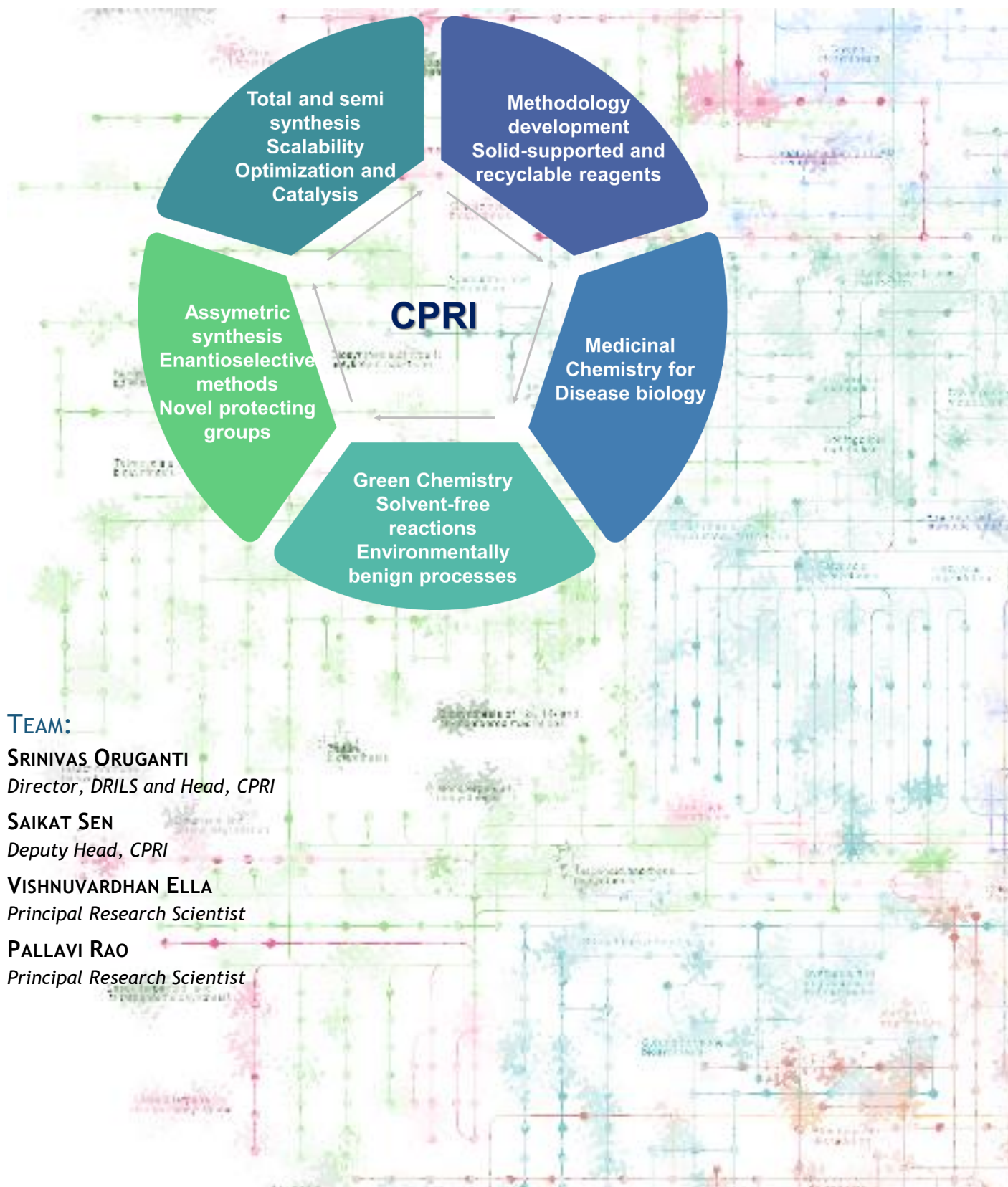
PALLAVI RAO
Deputy Head, CARS





CENTER FOR PROCESS RESEARCH INNOVATION

The Center for Process Research Innovation (CPRI) is engaged in addressing chemical research and innovation needs of the industry. CPRI has two main thrust areas: Process R&D and Medicinal Chemistry. Process research involves the identification and development of novel synthetic routes that targets sustainability through simplicity with potential for IP generation. Chemical industry needs are met not only by de novo approaches, but also through evolution of synthetic routes through a continuous process of incremental improvement and gradual simplification of the existing chemical processes.



TEAM:

SRINIVAS ORUGANTI

Director, DRILS and Head, CPRI

SAIKAT SEN

Deputy Head, CPRI

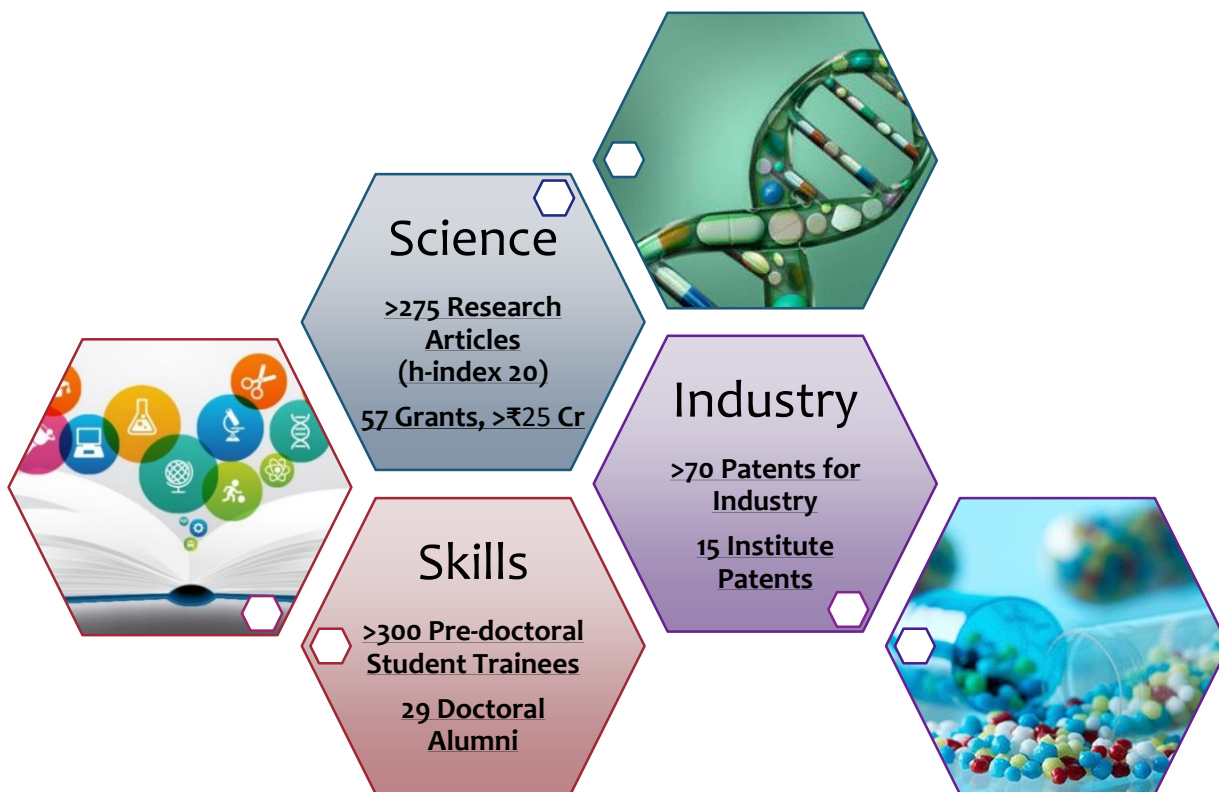
VISHNUVARDHAN ELLA

Principal Research Scientist

PALLAVI RAO

Principal Research Scientist

DOMAINS OUR WORK HAS IMPACTED



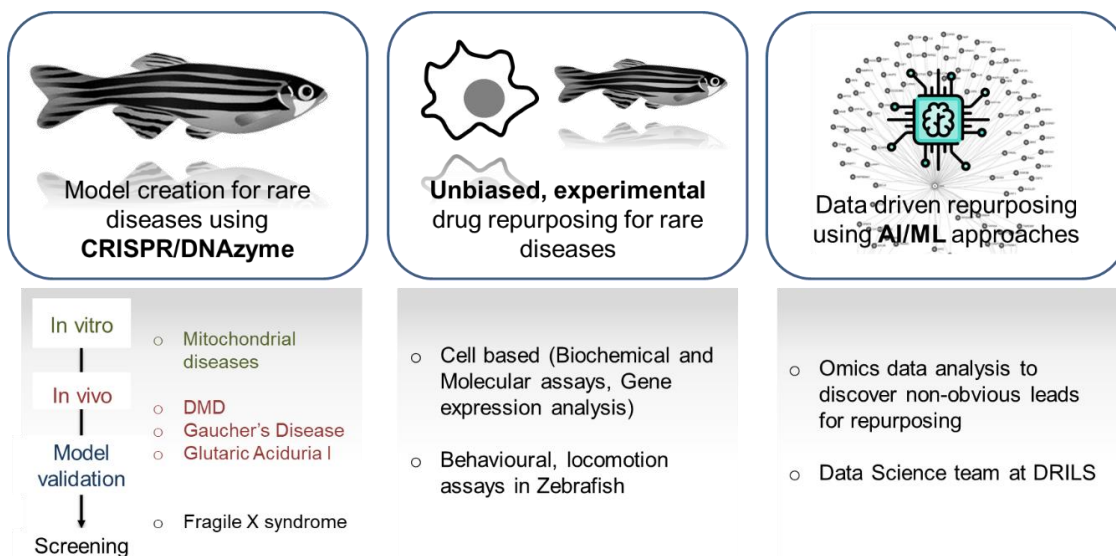
Our Work Over the Last 12+ Years Has Contributed to Fundamental Knowledge in Biology And Chemistry, Significant Value Creation for Industry, And Advancement of Research Skills And Understanding Among Future Scientists.

- Uniquely positioned as an institute driven by a culture of science, and created to support the life sciences and pharma industries, our work is designed to bridge academia and industry.
- The institute has diverse networking and engagement with eminent researchers, start-ups, institutes, universities and reputed companies, and continues to attract the best and the brightest.
- We have contributed to innovation-focused product development across a range of industries including Pharmaceuticals, Nutraceuticals, Agrochemicals and Organic Materials.
- Integrating various disciplines in Chemistry and Biology, we have adopted best industry practices to support product development and innovation in the pharmaceutical industry.

SPECIAL INITIATIVES

DRILS RARE DISEASE INITIATIVE (DRIVE) - THE ONGOING EFFORT

DRILS has engaged in research activities pertaining to rare diseases for the past five years. The availability of an in-house Zebrafish facility has been the single most important enabler for the initial success of this program, along with the strong cell and molecular biology expertise available in the Institute. In the past three years, the Institute has identified Rare disease research as a core focus area, and with the contribution of all the faculty, significant progress has been made in the following three areas. The first, our core strength, involves creation of disease models in cell lines and model organisms like yeast and zebrafish and accompanying assays, which allow us to acquire a mechanistic understanding of the disease pathophysiology. Towards this, we have developed novel tools and adapted cutting edge technologies like CRISPR with great success at the Institute. We currently have models of at least one kind for 4-5 rare diseases. The second direction relies on the chemistry strength of the institute, which provides access to a large and diverse set of small molecule classes (scaffolds), which are routinely tested in throughput assays relevant to rare disease therapy, in an unbiased manner. The third, and most recent direction has been to make use of large-scale datasets containing information pertaining to whole genome sequence, gene expression, proteomics, metabolomics etc and interrogate them with computational tools to uncover new, unexpected pathways and targets that may be of therapeutic relevance.



In addition to government funding to support research in individual disease areas, DRILS is part of a Clinical Research Center award from India Alliance, in a team led by Kasturba Medical College (KMC), MAHE, Manipal, along with the Institute of Bioinformatics (IOB), Bengaluru. The objectives of the this funded five year program include the identification of novel disease causing genes and variants from a large Indian patient cohort as well as functional validation of the identified genes/variants in disease models.



FLOW CHEMISTRY TECHNOLOGY HUB

The setting up of Centre of Excellence on Flow Chemistry Consortium Agreement was signed by Dr. Srinivas Oruganti, Director DRILS with GV Prasad (Co-Chairman and MD, Dr. Reddy's Laboratories), Dr. Satyanarayana Chava (CEO, Laurus Labs), Shakthi Nagappan (Director, Telangana Life Sciences and Pharma; CEO, Hyderabad Pharma City) in the presence of Industries and IT minister KT Rama Rao and Principal Secretary Jayesh Ranjan on 25th November 2021.

The initiative is aimed towards ensuring greater incorporation of flow chemistry techniques during pharma research and development and greater adoption of continuous green synthesis for manufacturing of APIs of a drug development. The hub set up at DRILS will receive funding and patronage from Dr. Reddy's Laboratories and Laurus Labs. The government of Telangana will facilitate strategic support and scale up for the hub and encourage more industries to join the consortium.



Research activities at the CoE will benefit from the scientific mentorship and support from world renowned scientists like Prof. Govardhan Mehta (UoH), international advisors such as Prof. Steven Ley (University of Cambridge, UK), Prof. Oliver Kappe (University of Graz, Austria), Prof. Shu Kobayashi (University of Tokyo, Japan).

SARS-CoV2 PROGRAMS

Collaboration with Vaccine companies

SARS CoV-2 pseudovirus neutralization assays against multiple variants were developed at DRILS and made available as an assay for companies developing vaccines for SARS-CoV2. DRILS continues to be involved in the generation of critical reagents for testing vaccine efficacy.

New programs in the area of vaccines and chemical synthesis are likely to be initiated in 2022.



Collaboration with AIG-AHF:

- Effectiveness of Roche antibody cocktail on Delta variant of SARS-CoV-2 pseudovirus
- Comparison of the pseudovirus neutralization antibody titers of Covishield and Covaxin vaccinated individuals
- Evaluation of neutralization titers of sera of breakthrough infection individuals against Delta variant
- Evaluation of sera of vaccinated individuals against Omicron variant

INDUSTRY PROGRAMS



Collaboration with Prescience InSilico:

The DRILS-Prescience collaboration aims to engage in quality research and development of customized solutions for drug discovery and/or drug repurposing using AI/ML. Projects in the area of inhibitor profiling of zebrafish tyrosine kinases and drug repurposing for rare diseases are ongoing.



Collaboration with Tata Consultancy Services (TCS)

Synthesis and evaluation of 5HT2C agonists. TCS will bring their expertise in molecular modelling to guide structure activity relationship and will support determine the mechanism of action (positive ago allosteric modulator) of DRILS synthesized compounds.

Collaboration with Vaccine companies

SARS CoV-2 pseudovirus neutralization assays against multiple variants were developed at DRILS and made available as an assay for companies developing vaccines for SARS-CoV2. DRILS continues to be involved in the generation of critical reagents for testing vaccine efficacy.

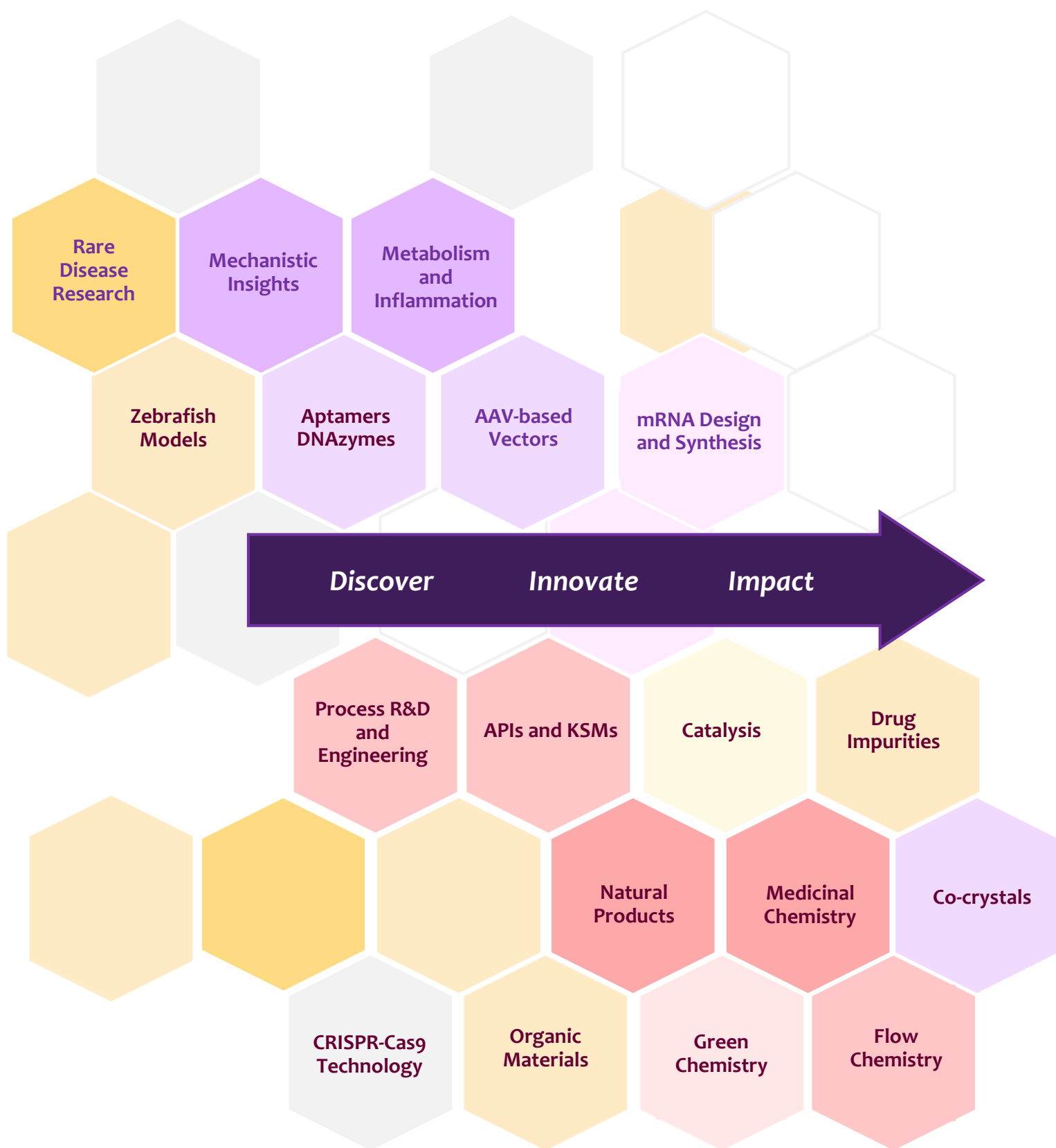
New programs in the area of vaccines and chemical synthesis are likely to be initiated in 2022.

Collaboration with Pharmaceutical companies for screening in Zebrafish

Nephrotoxicity evaluation of small molecules using zebrafish larvae.

NIH OLAW (Office of Laboratory Animal Welfare) approval to the DRILS Zebrafish facility (2021-2026; due to NIH funding being involved in studies being performed at DRILS).

MAJOR THEMATIC AREAS OF OUR WORK



PUBLICATIONS AND PATENTS

PUBLICATIONS

Ramesh Samineni, Vishnuvardhan Eda, Pallavi Rao, Saikat Sen, Srinivas Oruganti (2022). Grinard reagents as niche bases in the synthesis of pharmaceutically relevant molecules. *ChemistrySelect*, 7 (5), DOI: 10.1002/slct.202102853

Ramesh B Kumar, Rahul K Varma, Saikat Sen, Srinivas Oruganti (2022). Head-space miniaturization techniques. In book: *Emerging Freshwater Pollutants*, 95-116. DOI:10.1016/B978-0-12-822850-0.00018-1

Rani R, Parsa KVL, Kiranam C, Sevilimedu A (2022). An efficient cost-effective method for directed mutagenesis at multiple dispersed sites-a case study with Omicron spike DNA. *bioRxiv*. DOI: <https://doi.org/10.1101/2022.02.10.480017>

B Thirupataiah, Harshavardhan Bhuktar, Guntipally Mounika, Gangireddy Sujeevan Reddy, Jetta Sandeep Kumar, Sharda Shukla, Kazi Amirul Hossain, Raghavender Medishetti, Snigdha Samarpita, Mahaboobkhan Rasool, PC Jagadish, Gautham G Shenoy, Kishore VL Parsa, Manojit Pal (2022). Fe (III)-catalyzed regioselective and faster synthesis of isocoumarins with 3-oxoalkyl moiety at C-4: Identification of new inhibitors of PDE4. *Bioorganic chemistry*, 121: 105667. doi: 10.1016/j.bioorg.2022.105667

B Keerthana, Raghavender Medishetti, Jyothi Kotha, Parameshwar Behera, Kanika Chandra, Vijay Aditya Mavuduru, Manjunath B Joshi, Ramesh Samineni, Madhumohan R Katika, Writoban Basu Bal, Manjunatha Thondamal, Anil Challa, Kiranam Chatti, Kishore VL Parsa (2022). PHLPP1 promotes neutral lipid accumulation through AMPK/ChREBP dependent lipid uptake and fatty acid synthesis pathways. *iScience*, 25 (2), 103766. DOI: <https://doi.org/10.1016/j.isci.2022.103766>

Shukla, C.A., Udaykumar, B., Saisivanarayana, Y. et al. Delineating a green, catalyst free synthesis of a popular nutraceutical methylsulfonylmethane (MSM) in continuous flow (2022). *Journal of Flow Chemistry*, 12, 1-7. DOI: <https://doi.org/10.1007/s41981-021-00186-x>

Sonochemical synthesis of rosuvastatin based novel 3-methyleneisoindolin-1-one derivatives as potential anticancer agents. J. S. Kumar, G. S. Reddy, R. Medishetti, A. Ray, S. D. Bele, K. A. Hossain, B. Thirupataiah, R. K. Edwin, P. Behera, A. Joseph, G. G. Shenoy, C. M. Rao, M. Pal. *Journal of Molecular Structure* 2021, 1240, 130574 <https://doi.org/10.1016/j.molstruc.2021.130574>

PdCl₂-catalyzed synthesis of a new class of isocoumarin derivatives containing aminosulfonyl / aminocarboxamide moiety: First identification of a isocoumarin based PDE4 inhibitor. B. Thirupataiah, G. Mounika, G. S. Reddy, J. S. Kumar, K. A. Hossain, R. Medishetti, S. Samarpita, M. Rasool, J. Mudgal, J. E. Mathew, G. G. Shenoy, C. M. Rao, K. Chatti, K. V. L. Parsa, M. Pal. *European J. Chem* 2021, <https://doi.org/10.1016/j.ejmech.2021.113514>

Tuning the sensitivity towards mercury via cooperative binding to D-fructose: dual fluorescent chemosensor based on 1,8-naphthyridine-boronic acid derivative. Marina Rajadurai* and E. Ramanjaneya Reddy. *RSC Advances*, 2021, 11, 14862 - 14870.

Pal S., Pal M. (2021) Anti-diabetes Research in India: Contributions from Industrial Organizations. In: Dikshit M. (eds) Drug Discovery and Drug Development. Springer, Singapore. https://doi.org/10.1007/978-981-15-8002-4_8

G. S. Reddy, J. S. Kumar, B. Thirupataiah, K. A. Hossain, S. B. Nallapati, V. B. Giliyaru, R. C. Hariharapura, G. G. Shenoy and M. Pal. Propargylamines in Pd/Cu-catalyzed tandem coupling-cyclization-N-deprotection in a single pot: Construction of N-unsubstituted vs N-sulfonyl indole ring. *Tetrahedron Lett.* 2021, 77, 153213 <https://doi.org/10.1016/j.tetlet.2021.153213>

B. Thirupataiah, G. Mounika, G. S. Reddy, J. S. Kumar, R. Kapavarapu, R. Medishetti, J. Mudgal, J. E. Mathew, G. G. Shenoy, C. M. Rao, K. Chatti, K. V. L. Parsa, M. Pal, CuCl₂-catalyzed inexpensive, faster and ligand/additive free synthesis of isoquinolin-1(2H)-one derivatives via the coupling-cyclization strategy: Evaluation of a new class of compounds as potential PDE4 inhibitors. *Bioorganic Chemistry*, 2021, 115, 105265, <https://doi.org/10.1016/j.bioorg.2021.105265>

Gangireddy Sujeevan Reddy, Rajamanikkam Kamaraj, Kazi Amirul Hossain, Jetta Sandeep Kumar, B. Thirupataiah, Raghavender Medishetti, N. Sushma Sri, Parimal Misra, Manojit Pal. Amberlyst-15 catalysed synthesis of novel indole derivatives under ultrasound irradiation: Their evaluation as serotonin 5-HT_{2C} receptor agonists. *Bioorganic Chemistry* 2021, 116, 105380; <https://doi.org/10.1016/j.bioorg.2021.105380>.

B. Thirupataiah, Gangireddy Sujeevan Reddy, Guntipally Mounika, Jetta Sandeep Kumar, Kazi Amirul Hossain, Jayesh Mudgal, Jessy E. Mathew, Gautham G. Shenoy, Marina Rajadurai, Kishore V. L. Parsa and Manojit Pal. Pd-catalysed general access to 7-membered N/O-heterocyclic compounds as potential agents against inflammation. *Chem Commun* 2021, 57, 10091-10094; DOI: 10.1039/d1cc04140a

Prashanth Panta, Kiranam Chatti, Archana A. Do saline water gargling and nasal irritation confer protection against COVID-19?. *Explore*, 2021, 17 (2), 127-129.

Pal S., Pal M. (2021) Anti-diabetes Research in India: Contributions from Industrial Organizations. In: Dikshit M. (eds) Drug Discovery and Drug Development. Springer, Singapore. https://doi.org/10.1007/978-981-15-8002-4_8.

Effectiveness of REGEN-COV antibody cocktail against the B.1.617.2 (delta) variant of SARS-CoV-2: A cohort study. Jagadeesh Kumar V, Sofia Banu, Mitnala Sasikala, Kishore V. L. Parsa, Divya Tej Sowpati, Rupali Yadav, Karthik Bharadwaj Tallapaka, Archana Bharadwaj Siva, Ravikanth Vishnubhotla, G. V. Rao, and Duvvur Nageshwar Reddy. *Journal of Internal Medicine*, 2021, doi: 10.1111/joim.13408

A variant in TMPRSS2 is associated with decreased disease severity in COVID-19. Vishnubhotla, Ravikantha, Mitnala Sasikala, Vankadari Naveen, Sabbu Sai Latha, Kishore Venkata Laxmi Parsa, Ketavarapu Vijayarathy, Ramars Amanchy, Steffie Avanthi, Bale Govardhan, Kalapala Rakesh, Daram Sarala Kumari, Bojja Srikanan, Guduru Venkat Rao, Nageshwar Reddy. *Meta Gene*, 2021, 29, 100930.

Corrigendum to: Double PEGylation Significantly Improves Pharmacokinetic Properties of Irinotecan Containing Nanoparticles in a Zebrafish Model. Saxena, Uday; Rajadurai, Marina;

Basaveni, Surendar; Yellanki, Swapna; Medishetti, Raghavender; Sevilimedu, Aarti; Kulkarni, Pushkar. *Current Nanomedicine*, 2021, 11 (2), 139

Tuning the sensitivity towards mercury via cooperative building to D-fructose: dual fluorescent chemosensor based on 1,8-naphthyridine-boronic acid derivative. Marina, Rajadurai, E. Ramanjanya Reddy. *RSC Advances*, 2021, 11, 14862.

Misra P., Chakrabarti R. (2021) Type 2 Diabetes Mellitus: Marketed Drugs and Mechanisms. In: Dikshit M. (eds) *Drug Discovery and Drug Development*. Springer, Singapore. https://doi.org/10.1007/978-981-15-8002-4_7

Misra P., Chakrabarti R. (2021) Introduction to Diabetes and Prevalence in India. In: Dikshit M. (eds) *Drug Discovery and Drug Development*. Springer, Singapore. https://doi.org/10.1007/978-981-15-8002-4_6

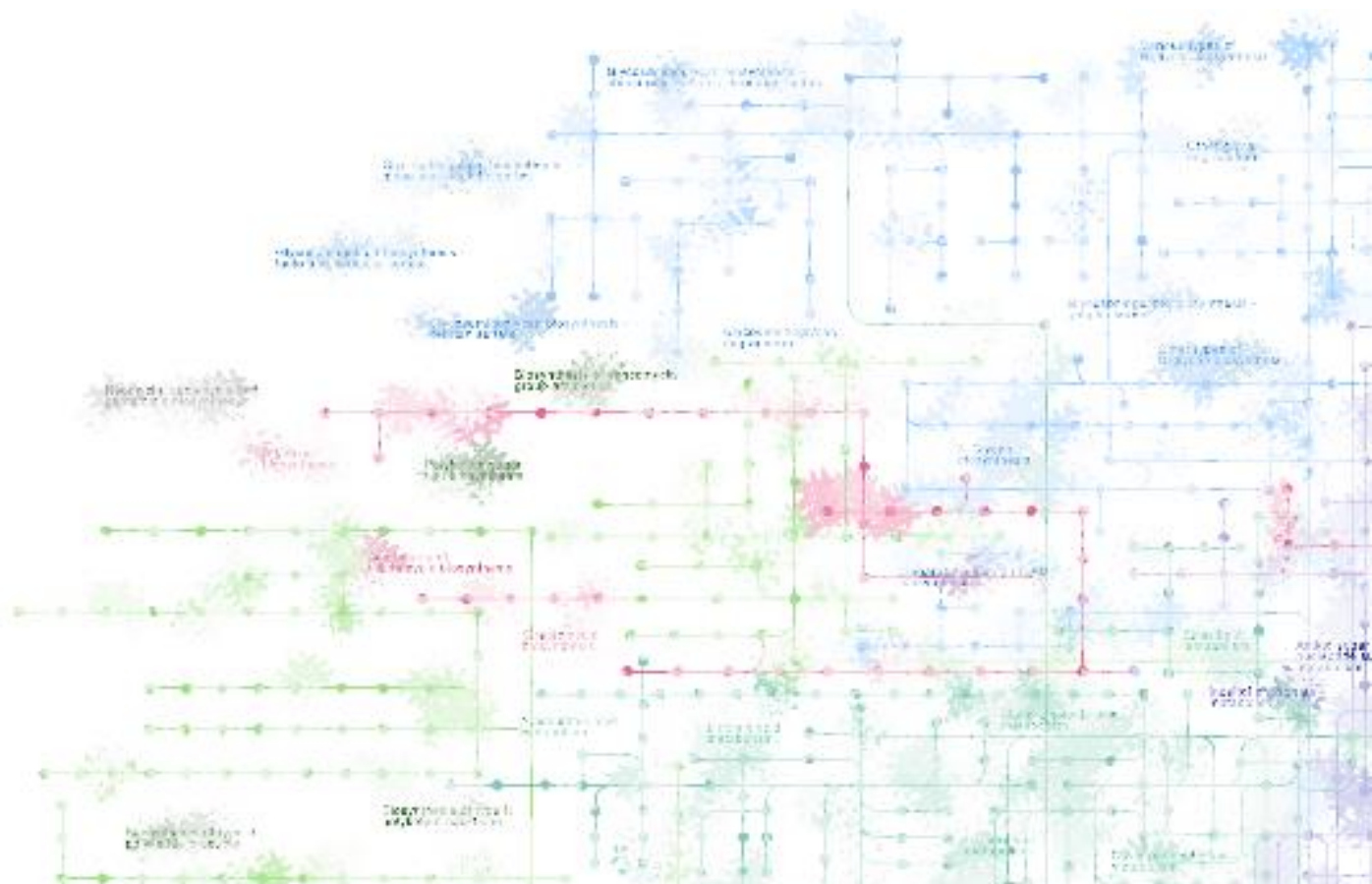
PATENTS

P. Reddanna, K. K. Reddy, N. Khan, H. D. Bhuktar, S. Shukla, M. Pal, Heterocyclic compounds as lipoxygenase inhibitors. Provisional Indian Patent Application no. 201941024295 filed on June 19, 2019; PCT/IN2020/050455 filed on May 20, 2020. World Patent Application WO 2020/255156 A1, 24 Dec 2020; Indian patent granted with number 377565 on 22/9/2021. National phase application has been filed in US on Dec 19, 2021.

G. S. Reddy, R. K. Edwin, P. Misra, M. Pal, Bicyclic heterocyclic compounds for treatment of tuberculosis. Indian Patent Application No.: 202041050115 filed on November 18, 2020. PCT/IN2021/051081 filed on Nov 18, 2021.

M. Rajadurai, Bhavya Surekha, Sustained Release Compositions. Indian Patent Application No.: E-2/1663/2021/CHE, filed on May 18, 2021.

M. Rajadurai, Bhavya Surekha, Sustained Release Compositions. PCT, No.: E-5/1816/2021/CHE, filed on May 18, 2021.



EVENTS

SUSTAINABILITY & DIGITALIZATION ROADMAP FOR CHEMICAL INDUSTRY

1st February 2022 & 2nd February 2022
0930 hrs Onwards

Register Now for Virtual Event - rsc.li/SandRoadmap21

CHIEF GUEST
Shri. Jayesh Ranjan, IAS
Principal Secretary, Industries & Commerce (I&C) and Information Technology (IT), Government of Telangana State

PATRONS
Dr. Ajit Rangnekar, Research and Innovation Circle of Hyderabad
Shri. G. V. Prasad, Dr. Reddy's Laboratories
Prof. Goverdhan Mehta, University of Hyderabad

CONVENER
Dr. Srinivas Oruganti, Dr. Reddy's Institute of Life Sciences

SPEAKERS
Prof. Stephen Hilton, UoL, UK
Dr. S. Venkata Mohan, CSIR-ICR, Hyderabad
Dr. Rajgopal Srinivasan, ICS
Prof. Jayant Kumar Singh, IIT Kanpur
Mr. Saurabh Biswas, Dr. Reddy's Laboratories
Mr. Sauri Gudlavalleti, SA I, Hyderabad

A virtual event on “Sustainability & Digitalization Roadmap for Chemical Industry” was hosted by DRILS in association with the Royal Society of Chemistry (RSC) & the Research and Innovation Circle of Hyderabad (RICH) in the month of February, 2022. The event focused on recent advancements that would serve as enablers for the chemical industry in its journey towards meeting UN’s Sustainable Development Goals.

DRILS initiative to celebrate scientists and their work addressing unmet medical needs.
Lecture 1: Prof. Amitabha Chattopadhyay, Oct 21, 2021.
Lecture 2: Prof. K.M.Girisha, February 28, 2022

A-I-C
(ACADEMIA - INDUSTRY - CLINIC)
DISTINGUISHED LECTURES
... Celebrating Science

DRILS A-I-C Distinguished Lecture Series celebrates the path-breaking contributions by Eminent Individuals whose pioneering work has a strong impact on addressing unmet medical needs, scientific solutions that impact society at large.

Dr. Reddy's Institute of Life Sciences (DRILS) & RxCella organize

Bootcamp on Pharma & Biopharma - How it works in Industry

- The journey from “Molecule to Medicine”
- 200+ Essential Pharma Know-hows & How do they relate
- “Cross-Functional” Awareness

WHO SHOULD ATTEND:

- Existing employees of Pharma & Biopharma industries engaged in HR, Engineering, Safety, Clinical, Sales, IT, Project Management, Business Development, SCM & relevant functions
- Teachers from Pharmacy/Biotech/Microbiology/Management or relevant streams
- Research Scholars in Science/Tech/Engineering who wish to work in Pharma Industries
- Start-up Professionals, who want to venture in Pharma & Biopharma

WHO SHOULD NOT ATTEND:

- Existing employees of Product R&D, Production, Quality & QA of Pharma Industries

Program Overview

Global Pharma Market, Regulatory Affairs, Quality, Business Development, SCM & relevant functions, Research Scholars in Science/Tech/Engineering, Start-up Professionals.

DRILS - Dr. Reddy's Institute of Life Sciences, Hyderabad (https://drils.org/)

FEES:

- Rs. 12,000 (includes GST) per participant - Industry
- Rs. 20,000 (includes GST) per participant - Academia
- For full details (20% for web) <https://www.drils.org/industry-academia>

REGISTER HERE

A boot camp on Pharma & Biopharma, “The Journey from Molecule to Medicine”, was organized from 6th to 8th January 2022. Existing employees of pharma & biopharma industries engaged in HR, engineering, safety, clinical, sales, IT, project management, business development, SCM & relevant functions; teachers from Pharmacy/Biotech/Microbiology/Management or relevant streams; research scholars in Science/Tech/Engineering who wish to work in pharma industries; start-up professionals, who want to venture in pharma & biopharma



Dignitaries from the Government of Colombia represented by Prof. Sergio Cristancho Marulanda, Vice-Minister of Knowledge, Innovation and Productivity, and Ms. Susan Benavides, Leader of internationalization in the Ministry of Science, Technology and Innovation, visited DRILS on Sep 30, 2021. They took a tour of the facilities and discussed possible areas and ways of collaboration.

A webinar on “Opportunities & Challenges in Drug Discovery and Development” was co-organized By Elsevier & Dr Reddy’s Institute of Life Science’s and held on 16th July, 2021 at 9:30 AM IST.

Opportunities and Challenges in Drug Discovery & Development
A webinar co organised by Elsevier and Dr. Reddy's institute of life sciences

16th July 2020, Thursday | 9:30 AM REGISTER HERE

Speakers:
 Dr. Srinivas Oruganti, Director, DRILS
 Dr. Madhu Dhillon, Emeritus Professor, TIFIT
 Dr. Anamik Shah, Vice-Chancellor, Gujarat Vidyapeeth & President, Indian Society of Chemist & Biologist
 Dr. Parimal Misra, Chief Scientist, DRILS
 Dr. Rakesh Gopalsubrahman, Principal Scientist, Life Sciences R&D, TCI Innovations Lab
 Dr. Anshu Yerrya, Director of Professional Services, Elsevier
 Prof. Javed Iqbal, Ex-Director, DRILS
 Dr. Pravin Iyer, Sr VP Drug Discovery, Glenmark Pharmaceuticals
 Prof. Indrajit Singh Aithan, Professor, IIT Madras
 Dr. D S Reddy, Sr Principal Scientist, R&D, Home
 Dr. Nishik Ranje, Solution Consultant Life Sciences, Elsevier
 Moderator: Shafiq Dubeey, Marketing Development Manager, Elsevier
 Dr. Mandeep Bhatia, Solution Consultant, Life Sciences, Elsevier

SAMARDH
A Unique Industry-Oriented Skill Development Program

Course Title
Quality Control (QC) in the Pharmaceutical Industry

Being Conducted By
Dr. Reddy's
&
Dr. Reddy's Institute of Life Sciences

Duration and Fee
Four Weeks [Sep 13 - Oct 9]
₹12000*

Venue
Dr. Reddy's Institute of Life Sciences, University of Hyderabad Campus, Cachibowli

Course Topics
Pharmaceutical Industry Overview
Quality Control Essentials
Fundamental Chemistry Lab Skills (Hands-on)
Key Pharmaceutical Analysis Methods (Hands-on/Demo)

Course Details
Professionals of Dr. Reddy's will teach and mentor the participants on Pharma-industry, Quality Management Systems, Quality Control Essentials, and Hand-on experiments as per Global standards. Students will get an opportunity to be "Industry-fit" through this thoughtfully designed finishing school curriculum blended with Industry Visit, Career counselling, and a Behavioral Competency workshop.

A month long Skill development program entitled “Quality Control (QC) in the Pharmaceutical Industry” was jointly conducted by DRILS and Dr. Reddy’s from September 13th to October 9th 2021. Professionals of Dr. Reddy’s taught and mentored the participants on Pharma-Industry, Quality Management Systems, Quality Control Essentials, and Hand-on experiments as per Global standards. Students got an opportunity to be “Industry-fit” through this thoughtfully designed finishing school curriculum blended with Industry Visit, Career Counselling, and a Behavioral Competency workshop.

Special Seminars:

Prof. Praveen Kumar Vemula, Associate Professor from the Institute for Stem Cell Science and Regenerative Medicine (inStem) has delivered a lecture entitled “Developing Prophylactic and Therapeutic Biomaterials for Unmet Clinical Needs” on 16-November-2021 at the Hetero Auditorium (DRILS) from 11:00 AM - 12:00 PM.

GRANTS AND FUNDING

ONGOING				
Title	Agency	PI, Co-PI	Duration	Funding
Understanding the regulatory role of co-activator binding protein PIMT in the pancreatic b-cells of diabetic animals and T3C diabetic (Chronic pancreatitis) humans	DST-SERB	Parimal Misra	2021-2024	₹ 45,13, 696
Identification of the mechanistic basis of early striatal damage in glutaric aciduria Type I	DBT	Aarti Sevilimedu, Pushkar Kulkarni, Dr. A. Radha Rama Devi (Rainbow hospitals)	2018-2022	₹ 40,66,800
Identification of optimal therapeutic window for efficacious intervention in a Zebrafish model of fragile X syndrome.	DBT	Aarti Sevilimedu, Pushkar Kulkarni, Kiranam Chatti	2019-2022	₹ 49,57,000
Use of DNazymes to improve CRISPR-mediated knock-in	DBT	Kiranam Chatti Aarti Sevilimedu	2018-2022	₹ 65,84,000
Molecular analysis of the functional role of ser/thr phosphatase PHLPP in lipid induced formation of foam cells, a hallmark of atherosclerosis	DBT	Kishore Parsa Kiranam Chatti	2019-2022	₹ 56,24,998
A microneedle transdermal patch for supplementing critical micronutrients for prevention and control of anemia	DBT	Marina Rajadurai, Parimal Misra Dr. B.R. Shamanna (UoH) Dr. C. T. Anitha (UoH)	2020-2023	₹ 67,90,920
Molecular characterization of the functional role of ser/thr phosphatase PHLPP in pancreatic beta cells to gain mechanistic insights into diabetes	SERB	Kishore Parsa Parimal Misra, Pushkar Kulkarni Prof. Prakash Babu (UoH) Dr. Sasiskala M (AIG-AHF)	2020-2023	₹ 54,94,004
Understanding the functional role of co-activator binding protein PIMT in adipogenesis and obesity	DBT	Parimal Misra, Kishore Parsa Prof. Satyamoorthy (MAHE) Dr. Manjunath Joshi (MAHE)	2020-2023	₹ 64,21,533
Studies on the role of HDAC inhibitors in reprogramming cancer cell metabolism to reverse cisplatin resistance in patient derived xenograft model of ovarian cancer.	ICMR	Prasenjit Mitra (Co-PI) , Dr. Vasudha Devi (Pharmacology MMMC, MAHE PI) Dr. Naveena AN Kumar (MAHE, Co-PI, KMC, Surgical Oncology)	2021 - 2024	₹ 27,00,000
Center for rare disease diagnosis, research and training	India Alliance / Wellcome-DBT	Dr. Girisha KM (MAHE), Dr. Akhilesh Pandey (IOB), Aarti Sevilimedu (DRILS)	2021-2026	₹ 2,25,00,000
Functional Analysis of PHLPP1 in Myogenesis: Implications for skeletal muscle dystrophies	DBT	Kishore Parsa, Kiranam Chatti and Aarti Sevilimedu	2022-2025	₹ 92,86,720

RECOMMENDED			
Title	Agency	PI, Co-PI	Duration
A pre-clinical lead optimization study of adjunct medicaments for reducing duration and increasing efficacy of anti-tuberculosis drug therapy	DBT	Prof. Hasnain (Coordinator), Manojit Pal (PI), Nasreen Ethesham (PI) Parimal Misra (Co-PI) and Kishore Parsa (Co-PI)	2022-2025
Virtual centre for functional genomics of novel sequence variants in genes for rare monogenic disorders in India	ICMR	Dr. Shubha Phadke (SGPGIMS), Dr. Ashwin Dalal (CDFD), Dr. Girisha KM (KMC), Dr. Madhulika Kabra (AIIMS), Dr. Ratna Dua Puri (Sir Ganga Ram Hospital), Dr. Neeraj Gupta (AIIMS) and Kiranam Chatti (DRILS)	2022-2027

COMMITTEES

INSTITUTIONAL BIOSAFETY COMMITTEE (IBSC)

In compliance with the IBSC rules two meetings were conducted in the year 2021. The meetings were conducted virtually, and the participants included the committee member and Chairman Dr. Kishore Parsa (HOD, CIMPS), DBT nominee Dr. Sunil Kumar Manna (Lab of Immunology, CDFD, Hyderabad), Member secretary Dr. Aarti Sevilimedu (Principal Research Scientist, DRILS), Biosafety Officer Dr. Anupama T Row (Chief Medical Officer, Health Center, UoH), External Expert Dr. Sairam (Senior Vice President, Biological E. Ltd.) and internal members Dr. Parimal Misra (Chief Scientist, DRILS), Dr. Kiranam Chatti (Senior Principal Research Scientist, DRILS), Dr. Rita Rani (Scientist, DRILS) and attendee Dr. Marina Rajadurai (Research Scientist, DRILS). Along with the ongoing research projects (26), three new projects were proposed and subsequently approved by IBSC and RCGM.

INSTITUTIONAL ANIMAL ETHICAL COMMITTEE (IAEC)

As per the CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) norms, two meetings of the DRILS Institutional Animal Ethics Committee (IAEC) were held in the year 2021. The thirteen ongoing proposals were renewed without incident and the requisite documents were submitted.

INTERNAL COMPLAINTS COMMITTEE (ICC)

DRILS continues to be committed to a zero-tolerance policy with regard to inappropriate conduct at the workplace. The committee met to satisfy the statutory requirements and noted no major incidents.

HUMAN RESOURCE AND DEVELOPMENT AND FINANCE

DRILS is supported by an efficient administrative team consisting of HR, Finance, Purchase, IT, Engineering and Maintenance departments in addition to the three scientific Centres.

On-roll employees	72
Consultants	5
Industry sponsored fellowship	10
Grant Based Fellowship	11
Ph.D. Scholars	11
Trainees	15

Audited financial reports for the current financial year are attached as an Annexure.

