

ANNUAL REPORT

2022
2023



ट्रांसलेशनल स्वास्थ्य विज्ञान
एवं प्रौद्योगिकी संस्थान

TRANSLATIONAL HEALTH SCIENCE
AND TECHNOLOGY INSTITUTE





thsti

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Mission

By integrating the fields of medicine, science, engineering, and technology into translational knowledge and making the resulting biomedical innovations accessible to public health, to improve the health of the most disadvantaged people in India and throughout the world.

Vision

As a networked organization linking many centers of excellence, THSTI is envisioned as a collective of scientists, engineers, and physicians that will effectively enhance the quality of human life through integrating a culture of shared excellence in research, education and translational knowledge with the entrepreneurial spirit to take technologies into the public sphere. In fulfilment of its vision, the THSTI will work with other constituents of the technology cluster at Faridabad through long term partnerships.



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THSTI SOCIETY

S. No	Member	Position
1.	Honourable Minister Dr. Jitendra Singh Ji Minister for Science & Technology, Minister of Earth Sciences, Minister of State in the PMO, MoPPP, DAE and DoS, Govt. of India	President
2.	Shri Anil Vij Minister-in-charge of the Department handling Science and Technology matters in the State of Haryana	Member, Ex-officio
3.	Dr. Rajesh S. Gokhale Secretary to the Government of India, Department of Biotechnology, New Delhi	Member, Ex-officio
4.	Dr. Srivari Chandrasekhar Secretary to the Government of India Department of Science and Technology, New Delhi	Member, Ex-officio
5.	Dr. Rajiv Bahl, Director General, Indian Council of Medical Research, and Secretary, Department of Health Research, New Delhi	Member, Ex-officio
6.	Shri Ashok Khemka, Principal Secretary for Science and Technology, Government of Haryana	Member, Ex-officio
7.	Shri Chaitanya Murti, Joint Secretary (Administration), Department of Biotechnology Government of India	Member, Ex-officio
8.	Shri Vishvajit Sahay Additional Secretary & Financial Adviser, Department of Biotechnology, New Delhi	Member, Ex-officio
9.	Professor U.S.N. Murty Director, National Institute of Pharmaceutical Education & Research (NIPER), Guwahati	Nominated Member
10.	Dr. Jagat Ram, Former Director, Post Graduate Institute of Medical Research (PGIMER), Chandigarh	Nominated Member
11.	Dr. Mammen Chandy, Director, Tata Medical Centre, Kolkata	Nominated Member
12.	Lieutenant General (Dr.) Madhuri Kanitkar (Retd.), Vice Chancellor, Maharashtra University of Health Sciences (MUHS), Nashik, Maharashtra	Nominated Member
13.	Dr. Vijay Chauthaiwale, Member, Atal Innovation Mission, Government of India	Nominated Member
14.	Shri Vivek Sharma, Executive in Residence, Frazier Healthcare Partners, Seattle	Nominated Member
15.	Dr. Pramod Kumar Garg Executive Director, Translational Health Science and Technology Institute (THSTI) Faridabad	Member Secretary, Ex-Officio

THSTI GOVERNING BODY

S.No	Member	Position
1.	Dr. Rajesh S. Gokhale Secretary to the Government of India, Department of Biotechnology, Ministry of Science & Technology, New Delhi	Chairperson, Ex-Officio
2.	Shri Chaitanya Murti, Joint Secretary (Administration), Department of Biotechnology, Government of India	Ex-officio member
3.	Shri Vishvajit Sahay Additional Secretary & Financial Adviser, Department of Biotechnology, New Delhi	Ex-officio member
4.	Dr. Alka Sharma Advisor / Scientist-H, Department of Biotechnology & Scientific Coordinator, Translational Health Science and Technology Institute (THSTI)	Ex-officio member
5.	Dr. Jyoti M. Logani Scientist F, Department of Biotechnology and Nodal Officer, Translational Health Science and Technology Institute (THSTI)	Ex-officio member
6.	Dr. Pramod Kumar Garg Executive Director, Translational Health Science and Technology Institute (THSTI), Faridabad	Ex-officio member
7.	Senior most faculty Translational Health Science and Technology Institute (THSTI), Faridabad	Ex-officio member
8.	Shri M. V. Santo Head-Administration, Translational Health Science and Technology Institute (THSTI), Faridabad	Ex-officio member
9.	Dr. Tanuja Nesari, Director, All India Institute of Ayurveda (AIIA), New Delhi	Nominated member
10.	Dr. Pankaj Chaturvedi, Professor and Surgeon, Tata Memorial Hospital (TMH), Mumbai	Nominated member
11.	Dr. V. K. Tiwari, Former Medical Superintendent (MS), Dr. Ram Manohar Lohia Hospital, New Delhi	Nominated member
12.	Dr. Minu Bajpai, Professor and Head, Department of Paediatric Surgery, AIIMS, New Delhi	Nominated member

THSTI SCIENTIFIC ADVISORY COMMITTEE

S.No	Member	Position
1.	Dr. Nikhil Tandon Professor & Head, Department of Endocrinology and Metabolism and Diabetes, All India Institute of Medical Sciences (AIIMS), New Delhi	Chairperson
2.	Dr. Alka Sharma Advisor / Scientist-H, Department of Biotechnology & Scientific Coordinator, Translational Health Science and Technology Institute (THSTI)	Member
3.	Dr. Tanuja Nesari, Director, All India Institute of Ayurveda (AIIA), New Delhi	Member
4.	Dr. Pankaj Chaturvedi, Professor and Surgeon, Tata Memorial Hospital (TMH), Mumbai	Member
5.	Dr. V. K. Tiwari, Former Medical Superintendent (MS), Dr. Ram Manohar Lohia Hospital, New Delhi	Member
6.	Dr. Pramod Kumar Garg Executive Director, Translational Health Science and Technology Institute (THSTI), Faridabad	Member Secretary, Ex-officio
7.	Dr. Minu Bajpai, Professor and Head, Department of Paediatric Surgery, AIIMS, New Delhi	Member
8.	Dr. Rakesh Aggarwal, Director, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry	Member
9.	Dr. Rama Jayasundar, Professor and Head, Department of NMR, AIIMS, New Delhi	
10.	Dr. Sanjay Mehendale, Director Research, P.D. Hinduja Hospital and Medical Research Centre, Mumbai	Member
11.	Dr. Arun Kumar Ghosh, Ian P. Rothwell Distinguished Professor Of Organic Chemistry and Medicinal Chemistry, Department of Chemistry, Purdue University, Indiana, USA	Member



FROM THE EXECUTIVE DIRECTOR

It is time to reflect on yet another year gone by which was full of hope, some trepidation, a sense of achievement and overall hugely satisfying. Institutions are known for what they do and how people perceive them. Substance and not spectacle is what should define an institution. THSTI has excelled in its mission of translational medicine over the years. The technical prowess, quality of research and academic finesse of THSTI have been widely recognized owing to the innovative approach and dedicated efforts of our researchers.

Annual reports are like a factsheet and a scorecard with human ingenuity and efforts as input costs, and scientific and academic achievements as products. Thus, it assumes significance as a transparent and honest document for others to evaluate the institute on its merits. It is my pleasure to present this year's annual report with facts sans hyperbola and metaphors.

Some outstanding research in the area of Mother and Child Health, Tuberculosis, and COVID-19 vaccines is worth highlighting. Observations from the GARBH-Ini cohort have shown how genetic polymorphisms could play a role in pre-term births and how air pollution can affect birth outcomes. These findings have the potential to guide policy. The discovery of a few novel anti-TB molecules has led to exciting possibilities of taking a couple of them for further clinical development. Anti-dengue molecules, primarily repurposed drugs, have shown a high potential to be taken to clinical trials in the near future perhaps in a multi-country trial. Our in-house Covid vaccine in partnership with industry is in advanced stages of development and is likely to go into phase 1 clinical trials later this year. THSTI studies on the durability of immune responses particularly cell-mediated responses against SARS-CoV-2 have been widely appreciated and have implications for a policy on boosters. Microbiome research has led to new insight into the pathophysiology of diseases, particularly NAFLD and pre-term births. Our researchers have published some outstanding papers in high-impact journals and have filed four patents. This year, THSTI has been granted two national and one international patent.

An important addition to the existing infrastructure has been started with the construction of a medical research centre, translational research laboratories and a hostel for students with a capex outlay of ~Rs.120 crores. The medical research centre will have approximately 140,000 square feet area with facilities for clinical observation studies, clinical trials and at some stage human challenge studies. This facility is being built as per international standards and perhaps would be the first of its kind in the country. Translational



research laboratories being created under the ambit of the IndCEPI program will provide much-needed space for further expansion and take us to the next level of our preparedness against emerging threats in future. It will have integrated facilities for various platform technologies, standardized assays, immunogen designing, and GMP and GLP-like facilities for vaccine development. With an increasing number of students on our campus, the new hostel with modern amenities will surely provide better accommodation to our students. The honourable minister Dr. Jitendra Singh Ji was gracious enough to have laid the foundation stone for these infrastructure facilities and promised all help to the institute to enable it to grow further.

The new facilities that we have established which are functional include a Vaccine Design and Development Centre (VDCC). VDCC is a novel facility that will bridge the gap between an academic research laboratory and the industrial development of a vaccine. We have also established a new library with digital content, the latest books and an inspiring ambience which should inculcate a habit of reading and learning among students in this era of online content. Another important facility that has been added to our armamentarium is an Advanced Nucleotide Sequencing facility. This completes the entire spectrum of high-end sequencing facilities which will benefit all our researchers and students.

We started three important academic courses this year: first being a master's program i.e. M.Sc. in Clinical Research with specialisation in regulatory clinical trials. This course will add significantly to capacity building in the area of clinical research in the country. It is among the few such courses being offered in academic institutions in India. The second program was a School of Innovation and Biodesign with a focus on developing innovative diagnostics. This is in partnership with many other academic institutions, innovators and venture capitalists. I am sure this program will result in the development of novel products that should reach clinics and help patients. The third important program was an Advanced Vaccinology Course, perhaps the first being offered by an academic institution. This course covers almost all aspects of vaccine development starting from antigen designing, concepts on immune responses, animal challenge models, clinical trials, regulatory aspects, funding and commercial licencing of the product.

To further enhance our capabilities in high-end research, we have started the upgradation of our experimental animal facility and hope that it will become one of the best animal facilities in the country within the next one year. It will have facilities for cryopreservation, transgenic and humanized mice, a hemodynamic monitoring lab, mice OTs, and an automated histopathology facility.

With the waning of the Covid pandemic this year, we could organize in-person scientific meetings and symposia on Inflammation, Microbiome, Tuberculosis, and Non-alcoholic fatty liver disease which were attended by a large number of faculty and delegates from around the country. We have also conducted training courses in metabolomics and microbiome research.

In terms of international collaboration and funding, THSTI established further collaboration with WHO, the Gates Foundation, Coalition of Epidemic Preparedness and Innovation (CEPI), and DNDi among others. It is a matter of pride that this year our extramural funding exceeded our core grant. It is a reflection of the trust of funding agencies and experts in the ability of our scientists and their high-quality science to provide innovative solutions.

I am set to bid farewell after finishing my tenure at THSTI this year and return to A.I.I.M.S., New Delhi, my parent organisation. I am overwhelmed by the love, affection and respect showered on me by all my colleagues, students and staff. My journey has been a truly enriching experience at THSTI. It has indeed been a huge privilege to serve this great institution.

I take this opportunity to offer my sincere thanks and gratitude to all those who have provided constant support, guidance and help to me at critical times. The honourable minister for Science & Technology, Dr. Jitendra Singh ji obliged us by visiting our campus many times during my tenure and inspired us with



his wisdom and vision. His leadership is exemplary. Dr. Rajesh Gokhale, Secretary, DBT, has been hugely supportive and generous to THSTI. His personal rapport and friendship have helped me a great deal. I also gratefully acknowledge the guidance of all the esteemed members of our governing body, finance committee, and scientific advisory committee. The support I got from my faculty, scientists and the entire THSTI administration was immense, and I could not have functioned without their constant help.

I wish all my colleagues and students a bright future ahead and I assure them that I'll be happy to be associated with my beloved institution in future as well.

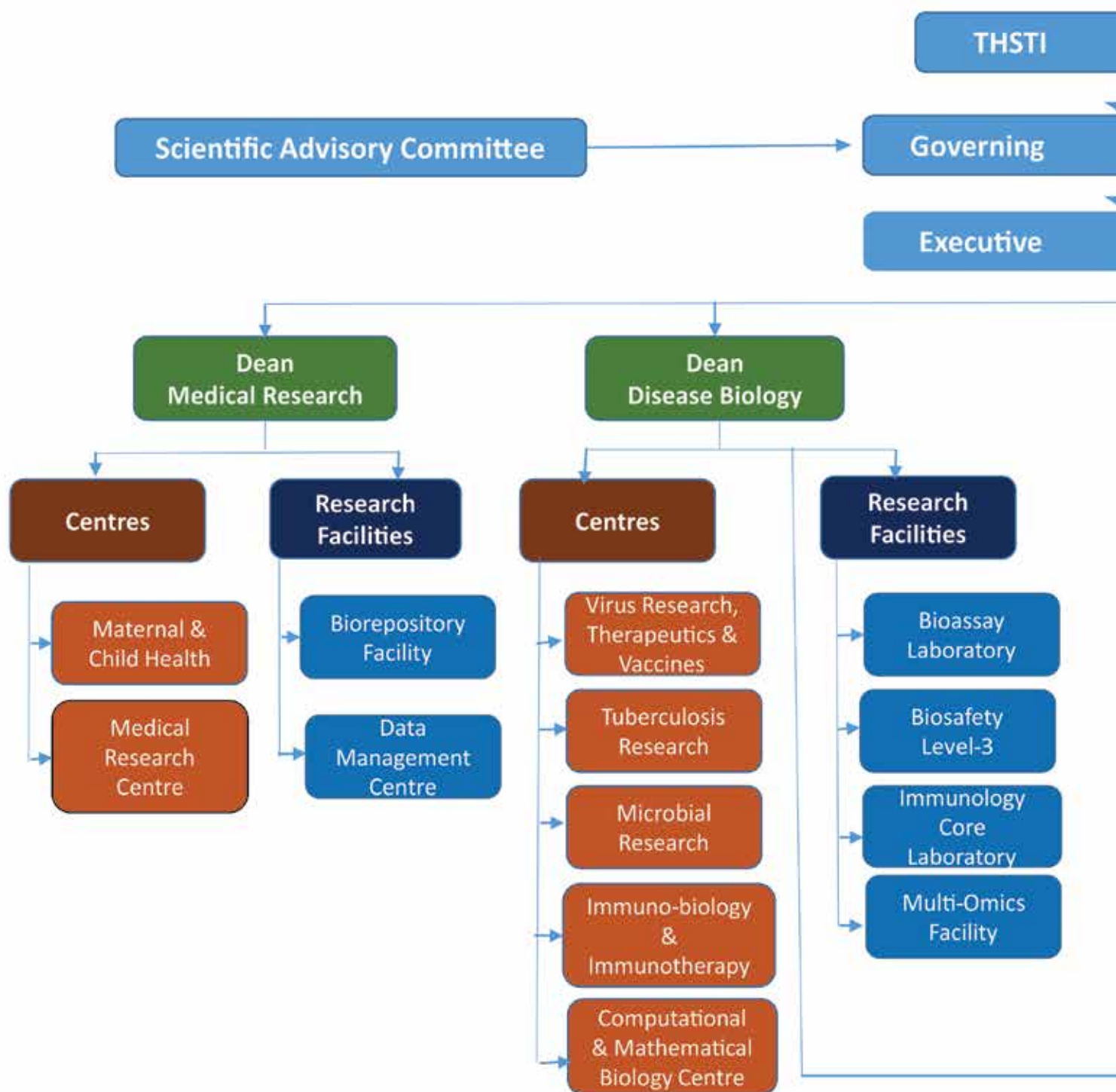
Thanking you,

Jai Hind

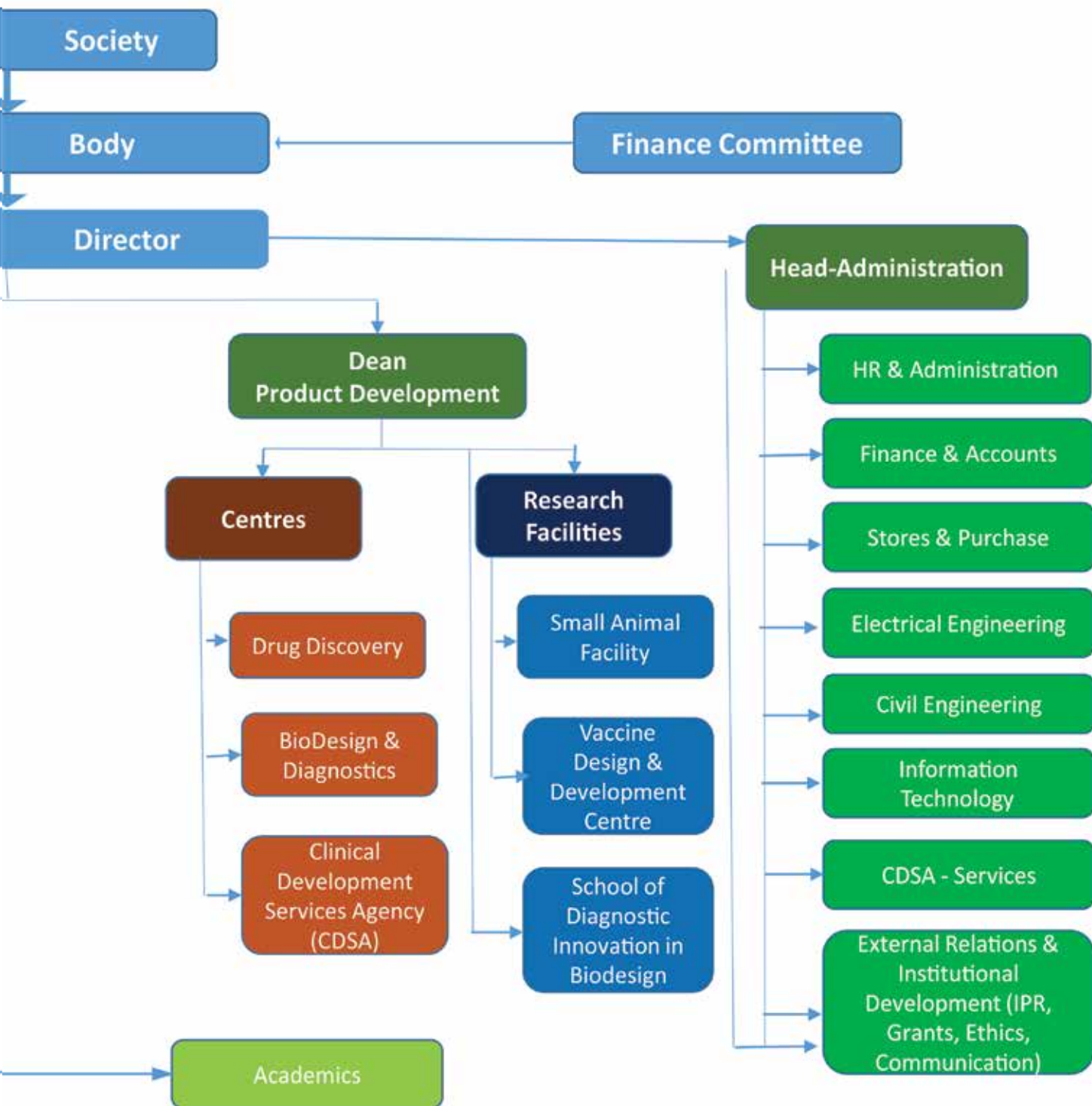
Pramod Garg

ORGANISATION CHART

TRANSLATIONAL HEALTH SCIENCE &



TECHNOLOGY INSTITUTE (THSTI)



Centre of Maternal and Child Health

Faculty and Scientists

Dr. Shinjini Bhatnagar, *Senior Advisor*

Dr. Nitya Wadhwa, *Senior Professor*

Dr. Pallavi Kshetrapal, *Assistant Professor*

Dr. Shailaja Sopory, *Principal Scientist-II*

Dr. Vidushi Gupta, *Senior Research Scientist*

Dr. Suchitra Devi Gopinath, *Research Scientist*

Dr. Antara Sinha, *Research Scientist*

Dr. Manivannan J., *Research Scientist*

Dr. Lovejeet Kaur, *Junior Research Scientist*

Dr. Savita Singh, *Junior Research Scientist*

Dr. Bapu Koundinya Desiraju, *India Alliance Early Career (CPH) Fellow*

Maternal, neonatal and child health (MnCH) is a critical determinant of the health of a society. The overall mandate of the Maternal and Child Health division is to create innovative applications/ interventions for diseases of public health importance that can be successfully implemented in society. The Centre for Maternal and Child Health under the leadership of **Dr. Shinjini Bhatnagar** works towards answering the research questions as a combination of discovery, development and implementation research using fundamental biological methods for understanding disease mechanisms, and analytical observation studies or randomized controlled trials to document associations and causality. Another important objective is to augment platforms for clinical research (biorepository, data management systems and young investigator training programs).



Dr. Shinjini Bhatnagar

GARBH-Ini – Interdisciplinary Group for Advanced Research on Birth outcomes – DBT India Initiative

Primary coordinator: THSTI

Collaborators: National Institute of Biomedical Genomics, Regional Centre of Biotechnology, Gurugram Civil Hospital, Safdarjung Hospital

Principal Investigators: Dr. Shinjini Bhatnagar, Dr. Nitya Wadhwa

The GARBH-Ini cohort, one of the largest pregnancy cohorts established from 2015 onwards at Gurugram Civil Hospital, a secondary care hospital, representing a semi-urban rural population, has completed enrolment of 10,000. A summary of various programs under this program is as follows:



Dr. Nitya Wadhwa

Epidemiological understanding of birth outcomes to inform clinical practice and policy

Maternal and Fetal Nutrition:

i. Region-specific growth trends for Gestational Weight Gain and the association with pregnancy outcomes:

Investigators: *Ramachandran Thiruvengadam, Bapu Koundinya Desiraju, Ayushi, Nitya Wadhwa, Uma Chandra Mouli Natchu, Shinjini Bhatnagar*

Previously, the investigators had described the Gestational weight gain (GWG) trajectories of women enrolled in the GARBH-Ini cohort. They then collaborated with five other cohorts from Southeast Asia and Africa under the Multi-omics for Mothers and Infants (MOMI) Consortium to evaluate the association between gestational weight gain and adverse pregnancy outcomes (N=14,289). The group analysis shows that GWG at its extremes (<-0.15 SD and >2 SD) increases the risk of preterm birth and there is a linear relationship with birth weight. They also found first trimester BMI was a significant effect modifier of the association between GWG and adverse outcomes. Presently, they are evaluating the associations between pre-pregnancy BMI, gestational weight gain and fetal growth.

ii. Comprehensive longitudinal dietary (patterns, macro & micronutrient) analysis across pregnancy:

Several nutrients are crucial for normal pregnancy, neonatal and early infant growth. The investigators focus on the nutritional biomarkers of adverse pregnancy outcomes, primarily preterm birth, and neonatal health. The overarching aim is to understand associations between maternal nutrition and pregnancy and neonatal outcomes and identify critical window periods during pregnancy or in infancy when interventions can be applied to ensure healthy pregnancy and/or infant growth and development. This is being done by analyzing the population and gestation-specific dietary intake and nutritional profiles in the GARBH-Ini cohort, measuring associations between coexisting multiple nutritional deficiencies, their absorption and transport across the maternal-fetal dyad.

Assessment of dietary patterns and nutrient intake across pregnancy

Investigators: *Neera Parmar, Ramachandran Thiruvengadam, Bapu Koundinya Desiraju, Uma Chandra Mouli Natchu, Ayushi, Babita Upadhyaya, Shilpa Chopra, Shailaja Sopory, Nitya Wadhwa, Shinjini Bhatnagar*

A validated tool for assessing long dietary patterns in pregnancy was developed. Four dietary patterns have been identified through principal component analysis (PCA)

in the preliminary analysis that shows a cumulative variance (sum of the individual variance of all four dietary patterns) of 53.3 %, 50.8% and 50% respectively at visits <14 weeks POG, 18-20 weeks POG and 26-32 weeks POG reflecting each trimester across pregnancy. The trimester-specific macro and micronutrient intake has also been calculated. Almost 90% of women across trimesters were seen to have inadequate iron consumption.

The analysis will continue in up to 10,000 women with a focus on protein quality estimation, micronutrient assessment and longitudinal changes in dietary patterns and nutrient intake across pregnancy.



Dr. Bapu Koundinya Desiraju

Maternal micronutrient deficiency and genetic association with pregnancy outcomes in North India

Investigators: *Shailaja Sopory, Lovejeet Kaur, Ramachandran Thiruvengadam, Nitya Wadhwa, Shinjini Bhatnagar*

Collaborators: *Uma Chandra Mouli Natchu (SJRI), Dr. Arindam Maitra (NIBMG), Dr. Partha Majumder (NIBMG), International Selenium Consortium*

The MCH team has successfully analyzed early pregnancy sera samples from 2,000 GARBH-Ini cohort participants for multiple elements like Selenium, Copper, Zinc (ICP-MS), Vitamin D and Ferritin, Vitamin B12, Folate, Iron, Iron binding Capacity, Calcium, Magnesium, Transferrin. More than >45% of participants were deficient in Zinc, Iron, B12 and vitamin D at < 20 weeks of gestation. Over 90% of women have anaemia (defined by haemoglobin < 11g/dl) during their pregnancy.

To understand the genetic predictors of these nutrients, a Genome-Wide Association Study (GWAS) is being conducted, in



Dr. Shailaja Sopory



Dr. Lovejeet Kaur

collaboration with NIBMG. Further, it is planned to elucidate the nutrition-induced epigenetic mechanisms of programming/re-programming of the infants during the perinatal and postnatal window period. Multiple micronutrients are being evaluated in the GARBH-Ini participants

Public health implications: Estimation of the burden of nutrient deficiencies will identify women at risk of poor pregnancy outcomes and inform policy decisions to prioritize and address these deficiencies. Further, the focus is to develop hypotheses based on these associations to design clinical trials of nutrient and multiple micronutrient supplementation to improve pregnancy outcomes.

Gestational Diabetes Mellitus

Investigators: Pallavi Kshetrapal, Ramachandran Thiruvengadam, Savita Singh, Deepika Rathna Murugesan, Ayushi, Dharmendra Sharma, Nitya Wadhwa, Shinjini Bhatnagar

Collaborators: Tushar Maiti, Regional Center for Biotechnology (RCB), Yashdeep Gupta (AIIMS, New Delhi), Alpesh Goyal (AIIMS, New Delhi), Nikhil Tandon (AIIMS, New Delhi)

Fourteen per cent of women who underwent screening for gestational diabetes (GDM) were diagnosed with GDM in the



Dr. Pallavi Kshetrapal

GARBH-Ini cohort; this rate is higher for a secondary-level care hospital. The effect of glycemic status at various time points in pregnancy on fetal growth and uteroplacental blood flow is being analyzed to establish the importance of glycemic control for fetal well-being. Alternative diagnostic strategies combining fasting blood glucose, random blood glucose, glycated haemoglobin and clinical risk profiling at various time points have been analysed as alternatives. Other proteins with dysregulated N-linked glycosylation are being evaluated as novel marker/s for the prediction and/or diagnosis of GDM. Samples of cases & controls have been identified and the platform technology for the assay is being developed for the identification of markers. A patient-friendly diagnostic test will improve compliance and aid in capturing more GDM cases.

Air Pollution and its association with pregnancy outcomes

Investigators: Ramachandran Thiruvengadam, Nikhil Sharma, Nitya Wadhwa, Shinjini Bhatnagar

Collaborators: Sagnik Dey, Indian Institute of Technology Delhi and Raghunathan Rengaswamy, Indian Institute of Technology Madras,

In the context of high air pollution in North India, understanding the link between air pollution and pregnancy outcomes is incomplete. The specific exposure periods and limits that elevate risks like fetal growth restriction and preterm birth are uncertain. Key questions remain: What's a safe exposure level? Is there a critical threshold for complications? Are certain pregnancy phases more sensitive? Can interventions mitigate exposure effects?

Exposure to ambient air pollution was estimated using satellite AOD-derived PM_{2.5} concentrations in 3868 Garbhini participants (enrolment <14 weeks gestation) at their household address. The primary outcomes measured were preterm birth and fetal growth restriction. PM_{2.5} exposure data (1-km resolution) was generated by integrating satellite-retrieved AOD with scaling factors from MERRA-2 reanalysis data and extensively validated against the ground-based reference-grade monitors maintained by the Central Pollution Control Board, India.

Previously, they found that higher exposure to PM_{2.5} was linked to shorter pregnancies and increased

preterm birth risk. Above the threshold of $110\mu\text{g}/\text{mL}$ of $\text{PM}_{2.5}$ concentration, the team reported a one-week gestation reduction per $50\mu\text{g}/\text{mm}^3$ increase in $\text{PM}_{2.5}$ during the first trimester. Additionally, cervical length at 30-32 weeks was reduced by 0.5 cm for every $50\mu\text{g}/\text{mm}^3$ increase in $\text{PM}_{2.5}$ exposure. $\text{PM}_{2.5}$ rise also reduces birth weight and increases the umbilical artery pulsatility index, suggesting placental blood flow reduction possibly impacting birth weight.

Currently, the team is performing household measures in 100 women using low-cost sensors developed by IIT-Madras and modelling composite exposure of ambient and household $\text{PM}_{2.5}$. Considering the correlation between ambient air pollution and climate change, a large study has been initiated to evaluate the interactions between air pollution and environmental heat on their effects on pregnancy outcomes.

Estimated drivers of preterm birth that can help in risk stratification of mothers early in pregnancy for effective triaging and early referral for appropriate care

Investigators: *Ramachandran Thiruvengadam, Bapu Koundinya Desiraju, Deepika Murugesan, Ayushi, Dharmendra Sharma, Nitya Wadhwa, Shinjini Bhatnagar*

The relationship between multiple baseline and trimester-specific factors and the risk of preterm birth among women who delivered singleton, live babies, after adjusting for potential confounders identified using DAG was evaluated.

Results of significant findings are listed below:

Participants with working or educated (collegiate) heads of family were at lower risk of PTB. Furthermore, participants from nuclear families had a lower risk compared to those from non-nuclear families.

The findings confirm certain known risk factors of PTB like history of preterm birth, cesarean section, multiparty, and short interpregnancy interval. Other well-known risk factors like smoking, alcohol use and chewing tobacco use could not be evaluated due to the small number of women indulging in them. However, biomass fuel use for cooking increased the risk of PTB by 30% and exposure to second-hand smoke by 20%. Both being underweight and overweight have a higher risk of PTB.

Throughout pregnancy, vaginal bleeding and shortening of cervical length increased the risk of preterm birth twofold. Short cervical length was associated with a higher than two-fold increased risk of preterm birth in the second trimester. Vaginal bleeding had an increased risk of preterm birth in the second trimester while the presence of vaginal discharge was associated with an increased risk of preterm birth in the second and the third trimester.

Non-reproductive tract infection was associated with an increased risk of preterm birth across the last two trimesters respectively.

Similar results were seen with the occurrence of jaundice with fever. There was a 30% increased risk for women with symptoms suggestive of preeclampsia.

Ultrasound and AI-driven tools for personalized prediction of birth outcomes

Investigators: *Bapu Koundinya Desiraju, Ramachandran Thiruvengadam, Nitya Wadhwa, Uma Chandra Mouli Natchu, Shinjini Bhatnagar*

i. Dating models

- a. The investigators have developed India-specific pregnancy dating tools using fetal anthropometry measured in the serial ultrasounds done in GARBH-Ini participants across pregnancy. This GARBH-Ini-GA2 model has been validated in a hospital cohort at Christian Medical College and the results from this validation have been incorporated to improve the model. Garbhini-GA2 reduced the GA estimation median error by more than three times compared to the Hadlock formula. Further, the PTB rate estimated using Garbhini-GA2 was more accurate when compared to the INTERGROWTH-21st and Hadlock formulae that overestimated the rate by 1.2-1.8 times, respectively. This model will now be validated on other external cohorts across different regions of the country. This tool becomes very relevant for India as more than 60% of women visit the antenatal clinic for the first time in their second or third trimester. Once the external validation has been completed the process of clinical deployment will be initiated.
- b. The ultrasound image-based pregnancy dating tool (GAUGE) developed performs nearly 40% more accurately than the currently used biometry-based models in external validation studies. These models are now being validated in external cohorts.
- c. Three separate CNN regression models were developed using the US images of the head, femur, and abdomen, respectively to identify which anatomy is best to use in a model. The model trained using images of the head was most accurate with an MAE of 3.5 days, compared to the models trained using images of the femur (MAE:6.3 days) and abdomen (MAE:7.1 days) on the internal test dataset. Therefore, using the images of the head, a novel multi-task model (GARbh-Ini Ultrasound image-based Gestational age Estimator (GAUGE)) was designed that segments the head along with GA estimation. The MAE varied by less than a day during bootstrapping (30 runs) demonstrating the good convergence of the model. The CP framework identified images from 7.7% of participants from the internal test and 62% from the external test set as out-of-distribution samples and rejected them before the prediction. The GAUGE model had an overall MAE of 2.8 days on the internal test dataset and was chosen as the final model for GA estimation. In the 18-20 (329 images), 20-30 (30 images) and 30+ week (475 images) windows, the MAE of the GAUGE model was 2.3, 5.6, and 3.0 days respectively. When compared with existing biometry-based models, the GAUGE model was 44% (MAE 0.73 vs 0.41) and 35% (MAE 0.63 vs 0.41) more accurate than the widely used Hadlock16 and Intergrowth-21st2 GA models respectively on the internal test dataset. On the external test dataset, the GAUGE model achieved an overall MAE of 5.9 days and had an MAE of 4.1, 8.4, and 4.9 days in 18-20, 20-30 and 30+ week windows respectively.

ii. Predicting Preterm Birth using Convolutional Neural Networks and Ultrasonographic Images

Investigators: *Bapu Koundinya Desiraju, Ramachandran Thiruvengadam, GARBH-Ini study team*

The investigators extracted an updated dataset of 25,016 images of the cervix taken during 18-20 weeks of pregnancy from 5394 participants who delivered term (4726) and preterm (668). Image pre-processing techniques like normalization and contrast enhancement were performed on these images. It was observed that there was a lot of variation in the cervix images. Therefore, the team extracted the cervix region first using image segmentation techniques and then built the classification models. The team manually curated the dataset of 500 cervical images to build image segmentation models. The cervix

region and the cervical canal using which the cervical length was measured and annotated separately. The team used segmentation models to extract the cervix and built the models to predict preterm birth. These models have shown better performance than the models built with the original images. The best model for segmentation has SegFormer architecture which uses the latest transformer-based architectures. The model has an IOU of 0.66 for recognising the cervix and 0.6 for recognising the cervical canal line. When this model was used with images having extracted regions of interest, the AUROC for predicting preterm birth had increased to 0.64. The team is currently working on improving these models and validating them externally.

iii. Real-time AI models to automate antenatal ultrasonography

The MCH team at THSTI posits that a suite of AI algorithms for automated detection of standard USG planes and automated measurement of the fetal biometry in antenatal ultrasonography, will aid in removing inter-operator bias in USG, reduce the time and effort of radiologists and accelerate training of more high-quality sonologists, thereby bringing the invaluable diagnostic tool to the masses. Using the USG images in the GARBH-Ini cohort, the team has built models to detect fetal body parts, measure biometry and estimate gestational age. These models are being validated in external cohorts. They are working on other aspects of automation such as right plane detection and prediction of adverse outcomes using images. Automating the analysis of ultrasound images of the growing fetus and placenta to facilitate referral to the appropriate level of pregnancy care in rural settings is an important unmet need in many LMICs. This data was collected from 1,500 GARBH-Ini participants.

iv. Computer Assisted LOw Point of care UltraSound

Investigators: *Bapu Koundinya Desiraju, Ramachandran Thiruvengadam, Nitya Wadhwa*

Collaborators: *Alison Noble, Aris Papageorgiou, University of Oxford; Ashok Khurana, The Ultrasound Lab, New Delhi*

Computer Assisted LOw Point of care UltraSound is a project in collaboration with the University of Oxford to develop a suite of AI algorithms to detect fetal abnormalities in ultrasonographic videos. The researchers collect videos using a previously validated six-step protocol and build algorithms to extract useful clinical information about heart rate, number of fetuses, position of the placenta and fetal presentation.

The team has performed 5323 scans at < 18 weeks, 18-20 weeks, 30-32 weeks, and 35-37 weeks till now. Nearly 30,599 ultrasound sweep videos have been collected of which 545 have been annotated by expert radiologists from India and the United Kingdom. They have built object detection models to detect fetal anatomies from these videos using YOLOv5 architecture. The preliminary models to identify maternal and fetal organs in these videos have an accuracy of 86% on unseen test videos. These models are being used for the development of clinical applications such as detecting breech presentation and identifying the placental location.

The placenta location algorithm has been evaluated qualitatively in Haryana and Puducherry to seek input from various healthcare professionals. Participants were asked to complete 4 video assessments and questionnaires followed by an interview (with audio + screen recordings on iPad). A total of 37 participants were enrolled, of whom, 31 completed the study. They included Researchers, nurses, radiologists, obstetric consultants, and fetal medicine consultants. These inputs are being used to improve the performance of the models.

Multi-omics bio-makers to provide customized clinical decision-making tools

Investigators: Pallavi Kshetrapal, Bhabatosh Das, Ramachandran Thiruvengadam,

Collaborators: Arindam Maitra, Souvik Mukherjee (NIBMG), Tushar Maitri (RCB)

Genomics

The researchers are the first to report genome-wide identification of maternal SNPs associated with spontaneous preterm birth (sPTB) from South Asia. The team had earlier reported experimental design in the Annual Report 2021-22. They have found 512 maternal SNPs associated with sPTB. These SNPs are known to alter the expression of genes associated with major pathways in sPTB viz. inflammation, apoptosis, cervical ripening, telomere maintenance, selenocysteine biosynthesis, myometrial contraction, and innate immunity. From a public health perspective, the trans-ethnic association of these SNPs identified in this study may help to stratify women at risk of sPTB in most populations. The results have now been published in *Lancet Reg Health Southeast Asia* (2023) 14:100190, doi:10.1016/j.lansea.2023.100190.

Proteomics

The discovery phase of this study was carried out in the previous year, wherein the proteome-wide quantitation method (SWATH-MS) was used to quantify the proteins in plasma samples collected from 27 preterm and 27 term subjects, at POG 18-20 (V2) and 26-28 (V3) weeks. The differential proteome analysis of this data identified 113 differentially expressed proteins (DEPs) at V2 and 90 DEPs at V3 time points. Gene ontology: Biological Pathway enrichment of these DEPs revealed their involvement in response to biotic stimulus, cellular component biogenesis, signalling by receptor tyrosine kinases, membrane trafficking etc. Normalized protein intensities of all the identified proteins were further subjected to downstream analysis using Machine learning-based classification models for the prediction of the disease outcome. 6 different models accompanied by Stratified K-fold cross-validation criteria were employed for prediction, out of which the top 3 were selected based on their AUROC values, mean accuracy score, Jaccard score and Mathew's correlation coefficient. To extract the proteins that were most significantly involved in the classification of sPTB from TB condition, feature selection was performed using two different methods viz. Recursive feature elimination using cross-validation (RFE-CV) and Shapely additive explanation analysis (SHAP). A total of 43 features were extracted at V2 whereas 29 features at V3 time points employing both the feature selection methods. The plan in this study is to validate the abundance of these selected proteins using the Multiple Reaction Monitoring (MRM) based LC-MS method. The validation of molecular signatures is in progress.

Metabolomics

To investigate metabolite signatures as predictors of PTB, metabolomic profiling of maternal serum was collected early in pregnancy (<20 weeks) in term and preterm delivery mothers (n=62 in each arm). Using an untargeted approach (UHPLC-MS/MS), putative metabolites were identified using selected databases such as HMDB (<http://www.hmdb.ca/>), and METLIN (<https://metlin.scripps.edu/>) to confirm the identity of the candidate molecules. From the 8 metabolites identified 4 metabolites have been verified using an MRM-based LC-MS method. These four putative metabolites i.e. DHA, GCA, MCA, and GDCA have been reported to be directly correlated with various metabolic pathways responsible for maternal health and fetal

growth. Validation studies will now be initiated to develop prediction models that could support healthcare for screening high-risk pregnancies.

In the same study, 71 significant pathway-specific metabolites were identified in spontaneous preterm birth. Comprehensive pathway analysis reveals a significant elevation in the metabolic/biosynthetic processes such as primary bile acid synthesis ($p=0.0000004$) and biosynthesis of unsaturated fatty acids ($p=0.00028$), as two of the major pathways dysregulated between TB and PTB pregnant women at <20 weeks GA.

Microbiome

In total, vaginal fluid from 140 term and 60 preterm mothers was sequenced at all three trimesters ($n=60 \times 3 + 140 \times 3 = 600$ samples) on the Novaseq 6000 platform. The FASTQ files obtained from the massively parallel sequencer were analysed by the in-house pipeline integrating QIIME2 and DADA2 using R-based software packages. A total of 25 microbial phyla and 618 genera were obtained. Core taxa were selected from the total number of taxa. At the phylum level, it was found that Firmicutes was the most abundant phylum in both the groups (TB: 78%, PTB: 74%) followed by phylum Actinobacteria (TB: 11 %, PTB: 11%). Fusobacteria (TB:1%, PTB: 3%) was found to be significantly higher in PTB compared to TB in 1st trimester of pregnancy.

Out of 17 core genera, Lactobacillus was the highest abundant taxa in both TB (74.16%) and PTB (68.83%) groups followed by Gardnerella (TB: 5.24%, PTB: 6.85%), Atopobium (TB:2.98%, PTB:4.05%) and Sneathia (TB:1.17%, PTB:2.94%). After species-level analysis, it was found that a total of 26 species belonged to the Lactobacillus group. By Linear Discriminant Analysis (LDA) it was observed that:

- Lactobacillus crispatus* was the most discriminating taxon in TB followed by *Lactobacillus johnsonii* whereas *Lactobacillus iners* was the most discriminant taxon in PTB samples in the 1st trimester.
- L. crispatus* and *L. iners* were negatively correlated with each other throughout the pregnancy.
- Some non-Lactobacillus vaginal flora were found to be significantly discriminating PTB samples compared to TB samples, such as *Atopobium vaginae*, *Sneathia sanguinegens*, *Prevotella corporis* and *Pseudomonas sp.*, in the 1st trimester.
- L. crispatus* was also found to be negatively correlated with non-Lactobacillus taxa.

In the longitudinal analysis, a distinct signature of a high abundance of *L. iners* was found throughout the pregnancy in PTB-delivering women whereas the high abundance of *L. crispatus* was maintained in women who delivered term.

To identify the microbial gene families and pathways that are differentially enriched in the vaginal microbiome of term or preterm mothers, shotgun whole genome sequencing was performed in a subset of samples. The FASTQ files are now being analysed by the shotgun sequencing data analysis pipeline developed in-house by integrating 17110 microbial reference genomes and UniRef and MetaCyc databases for gene family and pathway level reconstruction.

Growth and developmental outcomes till 2 years of age among children born in the cohort

Investigators: Nitya Wadhwa, Ramachandran Thiruvengadam, Vidushi Gupta, Shinjini Bhatnagar,

Collaborators: Dr Beena Singh (GCH, Gurgaon), Dr Monica Juneja (MAMC, New Delhi); Dr Rani Gera (SJH, New Delhi), Dr Pradeep Debata (SJH, New Delhi, Dr Rachna Sehgal (SJH, New Delhi) Dr Radhika Tondon (AIIMS New Delhi), Dr Alok Thakar (AIIMS New Delhi), Dr Arvind Kairo (AIIMS New Delhi)



Dr. Vidushi Gupta

With the hypothesis that the exposures during the antenatal period (such as maternal dietary patterns, environmental exposures and metabolic status), and infancy (such as feeding practices and environmental exposures) would have an effect modifying role on childhood growth and development, further influenced by the birth phenotypes, a birth cohort was established.

Serial longitudinal follow-up of children born to the mothers in the cohort for assessing growth and development till 2 years of their life is being done.

Growth is measured in terms of weight, length and head circumference and developmental assessment is assessed for (i) motor, (ii) language, (iii) cognitive, (iv) social, and (v) adaptive skills domains at different time points.

To date, more than 1,200 babies have been enrolled in the second phase. Children enrolled have a median (IQR) period of gestation of 39.14 weeks (38.14, 40.00) and a preterm rate of 12%.

Overall birth weight seen in the cohort is 2.77 kg (2.50, 3.05) and length is 48.00 cm (46.50, 49.10) and around 38% have been recorded as small for gestation (<10th centile).

Public health implications: Serial assessment of children for their growth and development will help in identifying possible risk factors and various heterogeneities that may contribute to the variations in their childhood growth, development and morbidities.

Maternal infections, inflammation and associations with pregnancy and fetal outcomes

Investigators: Shailaja Sopory, Khushboo, Ayushi, Ramachandran Thiruvengadam, Bapu Koundinya Desiraju, Nitya Wadhwa.

Inflammation or infectious exposure during pregnancy can disrupt the delicate Th1 and Th2 balance and lead to adverse pregnancy outcomes like fetal growth restriction and preterm birth. Though infections can be recognized by clinical symptoms, subclinical infection or inflammation can only be recognized by measuring biomarkers of inflammation in the blood. The objective is to identify biomarkers of maternal infection and inflammation for risk stratification of pregnant women for preterm birth and/or fetal growth restriction.

As the first step, a multiplex assay was conducted to simultaneously look at the expression of 24 analytes longitudinally across pregnancy (<14 weeks, 18-20 weeks, 26-28 weeks and in cord blood) in 23 women with normal-term deliveries and with no documented comorbidities. Linear mixed modelling (LMM) analysis showed a significant increase in sFLT-1, Flt3L, PLGF, IL-4 and IL-18 and a decrease in VCAM-1 concentration across pregnancy. There was a significant difference in cytokine profiles in maternal serum and cord blood. Gestational age-specific combinations of cytokines were seen to be associated with different fetal growth parameters.

A case-control study was performed with 95 FGR pregnancies (including both early and late FGR) and 95 normal pregnancies matched by parity and gender of the baby to study changes in inflammatory status, using the multiplex assay, between the two groups.

LMM analysis showed that PLGF levels were significantly lower in FGR as compared with normal pregnancies across pregnancy. Detailed analysis for inflammatory markers in pregnancies with fetal growth restriction is in progress.

Human Placenta Research Program for studying possible biological mechanisms

Investigator: Pallavi Kshetrapal

Collaborators: Arindam Maitra, Souvik Mukherjee (NIBMG), Tushar Maitri (RCB), Renu Dhingra (AIIMS, New Delhi)

A multi-institutional collaborative human placental program has been initiated to investigate the role of placental factors in pregnancy complications and adverse outcomes, primarily in PTB. Using the robust omics approaches novel data of miRNA and protein cargo has been generated on placental enriched exosomes. Using an in-silico-based approach putative miRNAs and proteins have been identified. Recombinant molecular resources are being generated to test the putative candidates in in-vitro placental cell culture model systems to study their role in placental structure and function. In collaboration with NIBMG, we are investigating the placental cell-type-specific gene signatures to monitor the maternal-fetal interactions during pregnancy using single-cell transcriptomics. Molecular markers of parturition at the level of proteins, lipids and metabolites in the placenta are also being assessed.

Profiling of placental metabolites using an untargeted metabolomics approach was performed on the placental tissue, collected from the women who had a live, singleton, and normal vaginal delivery without any comorbidity and history of preterm birth. Data analysis was performed using in-house established pipelines on R programming-based packages. Comparison between the two groups i.e., term and preterm (n=35, in each group), revealed significant dysregulation in certain pathways such as arachidonic acid, linoleic acid, and pyrimidine metabolism. An inflammatory reaction with the participation of arachidonic and linoleic acid derivatives (HETEs and HODEs) has been reported in uneventful pregnancies. The results suggest that excessive inflammation may result in early parturition or PTB.

Integrated analysis of data acquired on placental proteomics, lipidomics and metabolomics is underway to provide a systems biology approach to understanding the mechanism of parturition and etiology of spontaneous preterm birth.

As a collaborative study with AIIMS, the team is investigating the underlying signalling pathways and molecules that mediate the effect of H₂S, as a vasodilator to protect placental cells against hypoxia-reoxygenation. Targets of H₂S in treated HTR-8/SV neo cells using RNA sequencing have been identified and are being validated in the preeclampsia placenta for understanding the pathogenesis of disease.

International collaborations on the Garbhini platform

Multi Omics for Mother and Infant (MOMI) Consortium

Investigators: Pallavi Kshetrapal, Shailaja Sopory, Ramachandran Thiruvengadam

The GARBH-Ini team was invited to join the Multi-Omics for Mothers and Infants (MOMI) Consortium. As part of phase I, data harmonization, quality assessment of the stored biospecimens, and nested case-control analysis with other cohorts to identify 12 different serum analytes in mid-pregnancy that could act as predictors of preterm birth have been completed. The combined analysis with the other cohorts is in

progress. In the second phase, a cohort-wise 1x Low-pass whole-genome sequencing (WGS) technology is being used to analyze all MOMI maternal and cord blood DNA samples.

ORCHESTRA: Connecting European cohorts to increase common and effective responses to SARS-CoV-2 pandemic

Investigators: Shailaja Sopory, Pallavi Kshetrapal, Ramachandran Thiruvengadam, Nitya Wadhwa

The ongoing GARBH-Ini pregnancy cohort became a member of the Orchestra consortia, to establish a large-scale population-based cohort with defined structure and protocols to assess prospectively long-term consequences of COVID-19. In the current study, the investigators looked at active SARS-CoV-2 infection at the time of delivery and seroprevalence of SARS-CoV2 across all trimesters of pregnancy and the possibility of vertical transmission through the placenta to the baby.

From March 2022 to June 2023, The SARS-CoV-2 RT-PCR positivity rate was 3.7% and the seroprevalence rate was >90% among the unvaccinated. Detailed analysis on longitudinal seroprevalence across pregnancy is in progress. As the sample size for analysis of pregnancy outcomes like preterm birth, stillbirth, and abortion is very small, this analysis is being carried out with the larger ORCHESTRA group involving other European cohorts.

Evaluating interventions to reduce burden of early life morbidity and mortality-Randomized Controlled Trials

The neonatal mortality rate (NMR) in India is very high at 24.9 deaths per 1000 live births (NFHS-5). The United Nations Sustainable Development Goal 3.2 aims to reduce neonatal mortality to 12 deaths per 1,000 live births by 2030. Seventy per cent of neonatal deaths occur among low birth weight (LBW) babies constituting 15% of all newborns.

The MCH group has a two-pronged strategy for approaching the problem of preterm birth, low birth weight and adverse pregnancy outcomes. The interventions that the MCH team are investigating constitute an important research priority area for improving newborn survival.

Preventive interventions for early life morbidity and mortality

i. iKMC neurodevelopment follow-up study

Investigator: Nitya Wadhwa

Collaborators: VMMC and Safdarjung Hospital, New Delhi; School of Public Health, Kwame Nkrumah University of Science and Technology, Ghana; Queen Elizabeth Central Hospital Malawi; Faculty of Medicine, Obafemi Awolowo University, Nigeria; Muhimbili University of Health and Allied Sciences, Tanzania; Department of Mental Health and Substance Use, World Health Organization

The immediate kangaroo mother care (iKMC) trial in low-birth-weight infants reported a significant 25% reduction in neonatal mortality with iKMC (NEJM, 2021). Whether the survival advantage with iKMC would have a long-term beneficial effect on cognitive development also or lead to higher rates of neurodevelopmental morbidity in infants, has not been investigated. The team initiated a multi-country multi-site follow-up study of the newborn cohorts enrolled in the iKMC trial, to additionally study the risk of neurodevelopmental impairments. The hypothesis being that new-borns who were provided continuous KMC initiated immediately after birth will experience a reduced risk of neurodevelopmental impairment, including the risk of cerebral palsy, hearing impairment, vision impairment, mental and motor impairments, epilepsy, by the age of three years compared with a similar group in whom KMC was initiated only after stabilization. The target sample size of 2200, was achieved and the study was completed in July 2022. Additionally, the research study provided opportunities to enhance clinical care provision at the hospital

site. The infrastructure and processes that were set up for the conduct of the follow-up research study have been continued with the establishment of a child development center in VMMC & SJH hospital which provides comprehensive child neurodevelopmental care as a clinical service. The protocol paper titled "Evaluation of impact of continuous KMC initiated immediately after birth compared to KMC initiated after stabilization, in newborns with birth weight 1.0 to <1.8 kg on neurodevelopmental outcomes: protocol for a follow-up study" was published in the open access BMC Trials journal in April 2023. The analysis of the study is going on for primary publication.

Relevance: If the results show a reduced risk of neurodevelopmental impairment with iKMC, it will strengthen the recommendations on iKMC to improve preterm birth outcomes.

ii. iKMC Implementation Research (IR): The next step for taking forward the story of immediate and continuous KMC towards integration in the health systems:

Investigators: Nitya Wadhwa, Shinjini Bhatnagar

Collaborators: Centre for Health Research and Development, Society for Applied Studies (CHRD-SAS), Delhi, India; Community Empowerment lab, Lucknow, India; Obafemi Awolowo University, Nigeria; Addis Ababa University, Ethiopia; Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh; ICDDR, Bangladesh; World Health Organization (WHO); Government partners from each participating country

Background and rationale: The evidence of the efficacy of immediate KMC (iKMC) in low birth weight (LBW) babies is clear as it reduces the risk of neonatal death by 25%. The number needed to treat is 27, which means that the intervention provided to 27 LBW babies will save one life. It is estimated that globally if all eligible LBW babies (approximately 4 million babies) received iKMC, about 150,000 lives would be saved every year. While there is sufficient evidence to develop an implementation strategy for the conventional KMC after stabilization, evidence and experience are still lacking about the optimal ways to scale up iKMC and its potential impact on key outcomes in the target population under programme conditions.

Implementation research (IR), is a powerful supplement and systematic approach to standard RCT methods for evaluating effective coverage and addressing health systems, identifying optimal options and promoting the research findings into policy and practice. Implementation research on iKMC provides an opportunity to learn how to improve the coverage and effectiveness of iKMC in reducing newborn mortality and improving the health of the most vulnerable babies in LMICs. Thus, the iKMC IR study aims to support implementation research, focused on learning how to scale up immediate KMC within program conditions in the district and higher-level health facilities. This is proposed as a multicountry study in 6 sites across four countries: India, Bangladesh, Nigeria and Ethiopia. Development of a standardized protocol is complete.

iii. ACTION-III trial- Antenatal corticosteroids for late preterm birth:

Investigators: Nitya Wadhwa, Shinjini Bhatnagar, Antara Sinha, Deepika Murugesan

Collaborators: World Health Organization (WHO); VMMC and Safdarjung Hospital, Delhi

Background and relevance: Antenatal corticosteroids (ACS), a glucocorticoid, have long been regarded as a cornerstone intervention in preventing neonatal deaths and severe morbidities due to preterm birth. Previous trials have established the usage of ACS in the early preterm period (26 to <34 weeks' gestation), however the benefits for the same for the late preterm period (34 to <37 weeks' gestation) lack clarity, especially in low-resource settings. Thus, we initiated a multicountry multicentre (5 countries; 7 sites: 2 in India: India-Delhi and India-Belgaum) individually randomized, three-arm, parallel-group, double-blind, placebo-controlled trial to evaluate the benefits and possible harms of two regimens of antenatal corticosteroids (ACS) (dexamethasone phosphate 4x6mg IM q12h and betamethasone phosphate 4x2mg IM q12h) compared to placebo when administered to women with a high probability of birth in the late preterm period to improve neonatal outcomes. After intensive training and standardization of the research

staff, the site started recruiting at the Delhi-India site in August 2022. Till March 2023, the SJH site in India pre-screened 16320 pregnant women, screened 648 and enrolled 420 eligible pregnant women and their newborns. The trial is being conducted with the highest quality standards in compliance with the national ethical guidelines and other regulations.

Therapeutic interventions for early life morbidity and mortality

i. Adjunct zinc for young infant sepsis

Investigators: Nitya Wadhwa, Shinjini Bhatnagar, Antara Sinha

Collaborators: VMMC and Safdarjung Hospital, New Delhi; Maulana Azad Medical College and Lok Nayak Hospital, New Delhi; Chacha Nehru Bal Chikitsalaya, Delhi; Kalawati Saran Children's Hospital, New Delhi; Kasturba Hospital, Delhi; Patan Academy of Health Sciences, Nepal; Kanti Children's Hospital, Nepal; Department of Child Health, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal; Centre for International Health, University of Bergen, Norway.

Background and relevance: Zinc deficiency is known to affect multiple aspects of the immune function in children making them more prone to infections. Zinc supplementation has been proven to be effective in diarrhoea and is part of the treatment recommendations for diarrhoea in children up to 5 years of age. For other infections like sepsis, the team has initial evidence that adjunct zinc given to young infants with sepsis carries a 40% efficacy against treatment failure (Bhatnagar S et al, Lancet, 2012). There was also an observed effect of zinc on death but the study was not designed or powered to measure an effect on death. Providing additional evidence for the effect of zinc could have implications for treatment recommendations for sepsis among young infants.

A study powered to test the effect of adjunct zinc on death from young infant sepsis was planned. This large multi-country (India and Nepal) multicentre trial concluded in March 2022 (The details are mentioned in Annual Report 2021-22). The data analysis is completed and currently, the final report and manuscript writing process is ongoing.

Sub-studies embedded within this trial are summarized below:

Sub-study 1: Biological mechanisms that explain clinical effects of zinc supplementation

Investigators: Shailaja Sopory, Nitya Wadhwa

The team is studying the changes in frequencies and numbers of different immune cells and their intracellular zinc levels at baseline, within 48-72 hours of initiating treatment and at discharge, between the zinc/placebo-supplemented groups. This is being investigated in a subset of 350 enrolled infants from whom blood was collected and PBMCs isolated. Standardization for the use of a 14-colour cocktail panel that includes activation markers for various immune subsets is ongoing. An interim analysis of the plasma zinc concentrations between the zinc and the placebo group revealed no significant difference, across the three time points. However, one could see a significant difference in zinc concentrations when the infants were divided into two groups, based on their age. Neonates (Age $\leq$ 28 days) showed increased plasma zinc concentrations when compared with infants from 29 days to 59 days of age).

Sub-study 2: Stool enteropathogens and characterization of intestinal microbiome/ metagenome

Investigators: Nitya Wadhwa, Bhabatosh Das

Initiated in 2021, the study investigates the intestinal microbiome/ metagenome of young infants with sepsis with or without diarrhoea. The sample acquisition is complete. Data acquisition and analysis are ongoing.

Sub-study 3: Health gain, financial risk protection and cost-effectiveness analysis

Investigators: Nitya Wadhwa, Shinjini Bhatnagar, Kjell Arne Johannson, Tor Strand, Sudha Basnet

This study evaluates the health and economic consequences of adjunct zinc in young infant sepsis with a focus on health gains, financial risk protection and equity impact. This study was conducted as an equity RCT design within the main zinc for sepsis trial. The data cleaning and analysis are going on.

EQUIFINANCE Program

Investigator: Nitya Wadhwa, Shinjini Bhatnagar, Ramachandran Thiruvengadam, Deepika Murugesan, Antara Sinha

Collaborators: VMMC and Safdarjung Hospital, New Delhi; Gurugram Civil Hospital, Gurugram; Bergen Centre for Ethics and Priority Setting (BCEPS)-University of Bergen, Norway; Centre for Intervention Science in Maternal and Child Health, Department of Global Public Health and Primary Care (CISMAC), Norway; Centre for Health Research and Development, Society for Applied Studies (CHRD-SAS), Delhi

The EQUIFINANCE program aims to measure health gains, financial risk protection and equity impact of neonatal and child health care interventions to identify optimal pathways towards universal health coverage. The program is embedded in five studies being implemented in India.

The overarching objectives of the program are to evaluate the effect of neonatal and child health interventions on the household economy, inequality in health and financial risk of households. Three of five work packages are being led and coordinated by Dr Wadhwa's group in THSTI. Two of the three studies are clinical trials that will implement the equity RCT design. The other study implemented within the program is the equity cohort design embedded within the birth cohort study where the team will measure the equity and financial household impact of high-risk infant follow-up at a secondary health care level hospital. This novel design will evaluate financial challenges with implementation, patterns of utilization of programs and association of such patterns with overall health and non-health expenditures to families. The study was initiated after the ethics approvals were obtained and the research staff was trained. Currently, 531 participants have been enrolled and the recruitment is ongoing. The follow-up rate for the study is more than 90%.

The following platforms have been created under the MCH umbrella catering to different aspects of the MCH mandate:

I. Creation of a biorepository and imaging data bank for accelerating evidence generation to facilitate children to thrive.

Investigator: Pallavi Kshetrapal, Savita Singh

A biobank of longitudinally collected varied biospecimens of women enrolled in the GARBH-Ini pregnancy cohort with well-characterized information on environmental, clinical, social and epidemiological determinants at different time points has been established. It is now a national resource, situated at the NCR Biotech Science Cluster and is one of the largest and most varied research bioresource centres in India. Currently, this facility archives > 1.4 million varied biospecimens (maternal blood, serum, plasma, urine, saliva, high vaginal swab, placental tissue, DNA and neonatal heel prick blood) that are being used to answer various research questions in the field of fundamental and translational research on areas of maternal and child health and infectious diseases on the state-of-the-art agnostic platforms for genomics, transcriptomics, metabolomics, proteomics, immunology and many more. Specific protocols have been developed and implemented to maximize efficiency, accuracy and consistency during processing and archival. Access to biospecimens is based on the priority of research questions committed in GARBH-Ini and beyond that through a rigorous peer review process.

II. Establishment of a state-of-the-art robust data management centre.

The Data Management Centre (DMC) at THSTI has undergone a remarkable evolution, growing from a three-member team supporting limited intramural studies to a 21-member interdisciplinary team with state-of-the-art capabilities, extending their support beyond THSTI. A significant accomplishment is the curation of the GARBH-Ini database, encompassing longitudinal clinical data, histopathologic, ultrasound images, and videos from over 10,000 women, providing a valuable resource for research in pregnant women in the country. The DMC now offers comprehensive support throughout the research cycle, including data management plan development, CRF design, data monitoring, validation, and timely backups, with real-time monitoring through interactive dashboards. With expertise in various analytical platforms (Stata, R, and Python), as well as nurturing talent through the Aryabhata Data Science Centre, the DMC has successfully supported a diverse range of studies including 7 PhD student theses. Additionally, the DMC played a crucial role in supporting THSTI's pandemic response through its established data management pipeline. The DMC's capabilities have been recognized on an international scale, leading to the establishment of a WHO Data Management Center for Multi-Country Studies, enabled by the acquisition of a grant for data management of the multicountry iKMC Implementation research program coordinated by WHO.

III. Multiple clinical research methodology courses

Several courses have been developed and conducted both at THSTI and outside medical institutions for a diverse group of students. These courses were crystallized and have evolved into MSc Clinical Research (with clinical trials specialization) coordinated by Clinical Development Services Agency, THSTI where the faculty from MCH, THSTI play lead roles in the development of various learning modules.

IV. Advanced platforms training for young researchers

1. Maternal and child health program at THSTI has successfully implemented young investigators programmes such as the Early Career Medical Research Awardee program and supported independent fellowships like the Wellcome-Trust DBT India Alliance fellowship and Dr M K Bhan Young Investigator and Ramalingaswami fellowship.
2. MCH team has conducted training and workshops titled 'The role of AI in transforming healthcare' between 10th to 14th June 2022 in Goa. This workshop was jointly organised by THSTI & the University of Oxford. A major part of the funding was from the CALOPUS grant with additional contributions from the Centre for Integrative Biology and Systems Medicine (IBSE), IIT Madras and DBT/Wellcome Trust India Alliance. The workshop discussed details on technical challenges and potential solutions as well as challenges in implementing AI algorithms on a large scale in public health. The topics included explainability, generalizability, data bias and data sharing (federated learning) along with keynote presentations, discussions, and demonstrations of the key algorithms. The workshop also focussed on the implementation themes and included talks on the successful implementations of AI algorithms and learnings from those experiences. Both days featured poster presentations by young investigators and students on the relevant topics.

Way ahead

Current Achievement/Progress	Outcomes to be achieved
Confirmed rates: Preterm birth: 13.4%; still-birth: 2.61%, small for gestational age: 38.4 %	Complete external validation of dating tools in other regions of the country
Developed India-specific pregnancy dating tools using ultrasonography for the first time in India	Data-driven phenotyping of preterm to identify subsets of preterm with a higher risk of morbidity and mortality to inform preterm care at secondary-level hospitals

Developed Indian population-specific gestation weight gain (GWG) charts. Evidence from this data shows that in early pregnancy 1 in 4 pregnant women are underweight (BMI <18.5), 12% are either overweight or obese (BMI ≥ 25); the significant predictors of GWG are maternal age, height, first trimester BMI, parity, type of family, & use of clean fuel for cooking.	Study associations between serial GWG with birth outcomes, metabolic disease and child growth in the birth cohort
Increase in exposure to ambient air pollution >110µg/mL in the first trimester reduces the duration of pregnancy.	Longitudinal descriptive centile charts for Fetal Growth
Identified putative molecular signatures associated with PTB, (i) single nucleotide polymorphisms and DNA methylation alterations, (ii) proteomic and metabolomic markers	Identify biological mediators of adverse effects of air pollution on preterm birth
Validated distinct vaginal Lactobacillus species and non-commensal taxa in PTB	- Validate genetic and multi-omics markers for risk of PTB - Validation of diagnostic dipstick kits that contain signatures of the preterm birth-specific vaginal microbiome

Other programs under Maternity and Child Health

Mechanisms in lean muscle mass development

Investigator: Dr Suchitra Gopinath, Anamica Das (NII), and Aneeshkumar Arimbasseri (NII)

This research is focused on identifying molecular mechanisms mediating lean muscle mass development and how the deprivation of vitamin D can affect lean muscle growth. These investigations are foundational studies for exploring the consequences of vitamin D deficiency in pregnant mothers and an assessment of vitamin D deficiency in fetal muscle development.

The team along with researchers from National Institute of Immunology (NII) examined how defects in vitamin D signalling affect metabolic pathways in muscle using a murine model lacking the vitamin D receptor (vdr-/ -). In initial experiments, it was observed that proteolytic mechanisms were increased along with the decreased activity of the mammalian target of rapamycin (mTORC1), a key mediator of cellular growth in vdr-/ - muscles compared to wild-type muscles. An energy deficit in vdr-/ - muscles characterized by reduced fasting blood glucose and hyperlactatemia induced the activation of Foxo1 transcription and the AMPK pathway resulting in muscle atrophy (Das et al., 2021). More importantly, dysregulation of glycogen synthase and glycogen phosphorylase activities were observed resulting in increased glycogen storage in vdr-/ - muscles suggesting an impairment in glucose utilization in the absence of vitamin D signalling in skeletal muscles and critical for determination of fuel choice in the generation of energy. To test this hypothesis, the team designed further experiments to analyse whether energy homeostasis could be restored by providing a carbohydrate-alternate choice to vdr-/ - mice. Our teams observed that the muscles of the vdr-/ - mice adapt by utilizing the available pool of free fatty acids as a preferred choice of energy source. To enable fuel choice and bypass the metabolic impairment of vdr-/ - mice, fat-enriched diets were administered to these mice, similar to the diet composition at the suckling stage during which

muscle atrophy effects are not visible. Vdr-/- mice on a milk-based diet were characterized by high-fat content, restored energy balance, lean mass, glucose tolerance and increased insulin sensitivity. These results suggest that the body uses a toggle mechanism to switch between a vitamin D-based signalling system in a carbohydrate-rich diet, versus a vitamin-D-independent mechanism to utilize fatty acids to maintain energy homeostasis (Das et al, 2023, *manuscript under revision*).

Translational impact of the work done

1. The mouse model lacking vitamin D receptors and investigations into molecular mechanisms downstream of systemic deprivation of vitamin D suggest that carbohydrate-rich, fat-deficient diets promote loss of muscle mass and strength. Diet alteration models suggest that vitamin D signalling systems may be part of a metabolic adaptation from milk-based diets to carbohydrate-dominant diets during infancy. Deficiency of vitamin D in human infants in these early years (6-9 months onwards) might pose serious consequences on the metabolic and growth trajectories of individuals because of the inability to utilize carbohydrates as an energy source, thereby creating systemic energy deprivation.

Understanding the clinical nuances of the SARS-CoV-2 pandemic

Investigator: *Shinjini Bhatnagar, Nitya Wadhwa, Dr Ramachandran Thiruvengadam, Mudita Gosain, Sreevatsan Raghavan, Ayushi*

To create a biorepository of COVID-19 patients, a total of 8673 suspected COVID-19 participants were enrolled out of which 4,962 tested positive. The Biorepository houses clinical data and samples from hospitalised as well as home-isolated individuals hence giving scope to understand clinical spectrum to its full extent. The follow-up rate of the consortium is 87.64% at 10-28 days, 84.5% at 6-10 weeks and 70% for the last follow-up visit scheduled after 12 months from enrolment.

Progress of work in 2022-23

1. A large database of over 33,000 vaccinated and naturally infected participants was systematically developed over the three years of the pandemic. These participants are still being monitored telephonically and clinically (as per need) for re-infections with newer variants possessing greater immune potential and the development of de novo systemic illnesses like diabetes mellitus, hypertension etc., i.e., long COVID syndrome.
2. This large research database allowed for the longitudinal assessment of humoral immune response to heterogeneous antigenic exposure (natural and/or vaccination) against the SARS-CoV-2 virus; it was noted that the omicron variant which emerged in this geographical region in January 2022 caused a widespread immune boost to existing antibody levels. This immune boost was preserved by 60% even after 1 year of follow-up and helped explain clinically why this region reported lower severe infection outcomes despite the higher infectivity of the omicron variant.
3. The database has recently completed a comprehensive review of its participants to understand the determinants and risk factors for SARS-CoV-2 reinfection. The review also allowed the team to document the development of any new diagnoses post-COVID-19 infection to understand the prevalence and characteristics of "long COVID syndrome" as well. 11% of our participants reported a new systemic diagnosis at the 1-year follow-up period.

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The centre is dedicated to understanding the biology and pathophysiology of virus infections such as SARS-CoV-2, Influenza, Dengue, Hepatitis E and HIV. One of the key areas of research is to understand virus biology and the effort is to develop therapeutics and vaccine candidates against viral infections.

Dengue

India is hyperendemic to dengue and over 50% of the adults are seropositive but there is no information on the association between neutralizing antibody profiles from prior exposure and

disease outcomes. In addition, there is limited information on pediatric dengue cases and the factors that associate with disease severity and recovery. **Dr Guruprasad R Medigeschi** and his team are trying to fill this gap by focusing on the correlates of protection for dengue in the population and also in identifying the host factors that associate with disease progression and recovery. In addition, the group also focuses on antiviral development by drug repurposing strategies.

Dr. Medigeschi's team has established hospital-based and community-based cohorts to understand the role of circulating dengue viruses, inflammation and immune response in primary and secondary dengue infections. The aim is to characterize the clinical isolates of circulating dengue viruses in India and identify the factors that determine viral fitness. They use a variety of approaches including flow cytometry, quantitative proteomics, genomics, deep sequencing and cell culture models of infection to address some of the fundamental aspects of flavivirus biology and generate ideas and identify targets for translation.

Translational Research Consortium (TRC) on Dengue virus research

Dr Medigeschi and his team has generated a biorepository of 74 low-passage clinical isolates of dengue virus as a national resource for academic research and vaccine development. All these isolates have been sequenced that have been deposited in the NCBI database. This resource will help in assessing the conservation or divergence of B and T cell epitopes in circulating dengue serotypes in India. In addition, the vaccine trials can utilize this repository to demonstrate the neutralization of Indian isolates in human samples collected from Phase III trials. An in-depth analysis of these sequences is underway. Presently they are carrying out experiments to test the replication fitness of these isolates in cell culture models. The isolates will also be tested in animal models. A high-throughput virus neutralization assay was established using the four serotypes of clinical isolates from India. As part of the dengue TRC, these assays will now be utilized to test the human monoclonal antibodies isolated by the collaborators at ICgeb.

Dr. Medigeschi and the team have initiated a quantitative proteomics study to identify biomarkers of severe dengue using samples from their previous studies. This pilot study will generate further information that will help to plan large validation studies

Under this project, **Dr. Sweetly Samal's** team has developed an acute, lethal, neurotropic AG129 preclinical animal model, using AG129 mouse which is deficient in IFN- γ and α -receptors on 129/Sv genetic background. This model has been validated as a suitable model for antiviral drugs, vaccines, and biotherapeutic testing. The model is now available against DENV 1,2,3 and 4 serotypes to evaluate new therapeutics or vaccines in a fee-for-service mode. Upon request, technical sheet may be provided for the same.

Dr. Samal's team has further evaluated the effect of aging in the AG129 mouse model in the DENV infection. A comparative study between adult and aged mice infected with DENV mouse-adapted challenged viruses showed aged mice are highly susceptible to the DENV infect as compared to the adult mice. There was significant downregulation of the TLRs in aged AG129 mouse as compared to the adult AG129, where the



Dr Guruprasad R Medigeschi

TLRs expression have shown to be upregulated. Metabolomic analysis of sera from mice challenged with mouse-adapted viruses by using mass-spectrometry showed dysregulation of 18 metabolites which might be playing a significant role in the disease progression (the experiment was conducted by Dr. Yashwant Kumar's team).

Antiviral development

Dr. Medigeshi's group has been funded by DBT to generate novel derivatives of Fluoxetine and Salmeterol which were identified as dengue inhibitors by screening a pharmacologically active compound library. In collaboration with CSIR-IICT Hyderabad, they have now tested a number of derivatives of these FDA-approved drugs and show potent anti-dengue activity for some of the new derivatives and a patent has been filed for these new compounds. The group is now performing animal studies to validate the parent compound its derivatives.

The drugs for neglected diseases initiative (DNDi) approached Dr. Medigeshi to establish a dengue alliance which is a network of dengue researchers from Brazil, Thailand, and Malaysia for antiviral development. Dr. Medigeshi's group has performed a pilot study with 24 FDA-approved drugs using *in vitro* assays and identified six drugs that showed potent anti-dengue activities with EC_{50} in the low micromolar range. These drugs are now being validated in animal models across multiple sites including THSTI.

Dr. Sweety Samal along with Dr. Guruprasad Medigeshi and Dr. Dinesh Mahajan is working towards identifying drugs alone or in combinations of repurposing candidates suitable for entry into proof of concept (PoC) clinical studies based on solid preclinical data packages. They have short-listed a set of pan-serotype dengue antiviral drug candidates and profiled within the collaboration network by DNDi. One of the short-listed drugs has been evaluated in the AG129 mouse model against the DENV-2 challenge viruses along with the positive control Janssen JNJ-1802 anti-viral drug for Dengue showing protection and promising results. Further *in vitro* and *in vivo* studies are ongoing to evaluate dose-response studies and establish the proof-of-concept.

Way ahead

Dr. Medigeshi and the group have established a mouse model for mild dengue using AG129 mice used for testing Fluoxetine and Salmeterol for anti-dengue activity. This mouse model will now be used for new drug-screening projects for dengue. In future, Dr Medigeshi plans to focus on viral polymerase inhibitors and establishing *in vitro* assays for drug-screening.

His group has now initiated animal studies to characterize representative clinical isolates of dengue in AG129 mouse model. Full genome sequences will provide information on the mutations in structural and non-structural regions of the virus. This will help to assess if these mutations affect replication fitness in cell culture and animal models, affect the ability of antibodies to neutralize Indian isolates compared to International isolates and provide insights into vaccine development.

Dr. Medigeshi's clinical research program will further explore the role of pre-existing immunity in protection vs enhancement of disease and will focus on understanding the correlates of protection. He plans to identify and validate some of the biomarkers that associate with severe dengue.

Dr. Samal's team has expanded the collaboration with academics to facilitate both Dengue basic biology and translational research. In collaboration with DNDi and CDRI, Dr. Samal plans to continue her efforts in finding promising anti-viral drugs *in vivo* against Dengue 1-4 serotypes to quickly establish the PoC. In collaboration with RCB, she plans to use the acute, lethal preclinical animal model to recapitulate the DHF/DSS like clinical signs to understand Dengue innate responses. She plans to expand the usage of this model for *in vivo* assessment of novel vaccine candidates, drugs or monoclonal antibodies both with academia and industry.

Targeting host ROS pathway genes to attenuate Dengue virus infection

Thrombocytopenia associated with Dengue virus infection is suggested to be the result of multiple mechanisms that affect either the biogenesis or stability of platelets. Platelets are produced from Megakaryocyte mother cells, infection of which has a suppressive effect on platelet biogenesis. Additionally, megakaryocytes have been suggested to be one of the principal cellular sites of high viral replication, and therefore responsible for high viremia in Dengue patients. **Dr Sankar Bhattacharya** and his team studied the effect of Dengue replication on the progress of Megakaryocyte differentiation and vice versa i.e. the effect of differentiation on viral replication using human K562 cell lines which differentiate into megakaryocyte-type cells when treated with phorbol esters. Dr Bhattacharya had earlier shown that the replication of Dengue virus is promoted by the process of megakaryopoiesis, which also inhibited crucial steps in the differentiation process. Analysis of the transcriptome in differentiating cells showed significant upregulation of inflammatory genes, which interestingly did not seem to have any negative effect on the replication of Dengue virus in these cells. Further, the accumulation of reactive oxygen species (ROS) in uninfected differentiating cells was found to be suppressed in infected differentiating cells. Interestingly a comparison of the PMA-induced transcriptome changes between differentiating cells that were either uninfected or Dengue-infected, showed upregulation of genes which are positively controlled by the transcription factor NFE2L2. This suggested that Dengue infection in differentiating megakaryocytes upregulated NFE2L2 to suppress ROS. In support of this hypothesis, pharmacological super suppression of ROS increased viral replication, while pharmacological inhibition of NFE2L2 transcription activity drastically inhibited Dengue replication in these cells. The results suggest that NFE2L2 transcription factor is a potential target approach to reduce Dengue replication.



Dr Sankar Bhattacharya

Way ahead

Dr Bhattacharya plans to investigate the potential of inhibiting Dengue replication through administration of NFE2L2 inhibitor, in the AG129 Dengue mice model.

Dengue vaccine immunogen development

In the past year, **Dr Supratik Das's** group has purified and characterized tag-less, triple mutant, stabilized DENV3 and DENV4 sE(envelope) protein dimers. His group has shown that they have been purified to apparent homogeneity and exclusively form dimers. These proteins have been antigenically characterized and structural characterization is ongoing. His work is an improvement on the design and purification method previously used to purify and characterize DENV E protein dimers. His DENV E protein dimers have been purified to apparent homogeneity and initial work has shown that they are in the correct conformation. Further studies are ongoing.



Dr Supratik Das

Dr. Tripti Shrivastava's group had earlier designed DENV2 ED3 construct computationally. They have now mutated the exposed residues to minimally conserved amino acid conformation. The resurfacing of the loops was done and the broadly neutralizing monoclonal antibody site 4E11 was introduced. The resultant conformation was docked with the 4E11 fab coordinates to validate the binding parameter. Dr.

Shrivastava's lab has also developed DENV E protein cysteine-cysteine stabilized dimers which have been well characterized for their binding towards dimeric interface-directed broadly neutralizing antibodies.

Way ahead

Dr. Supratik Das plans to generate DENV1 and DENV2 sE protein dimers and carry out immunization studies in mice using all four DENV serotypes sE dimers in order to study the neutralizing response and T cell-mediated immune response.

Dr. Shrivastava plans to evaluate the DENV E protein cysteine-cysteine stabilized dimers for immunogenicity, neutralizing efficacy, ADE and vascular permeability following virus challenge from all four serotypes. For the ED3-based constructs, the other broadly neutralizing epitopes will be introduced into the same 4E11 harbouring synthetic construct. This will then be evaluated for binding towards the broadly neutralizing antibodies, immunization studies will be evaluated, along with humoral, cellular and protective responses towards all four serotypes as well as disease pathologies during secondary infection

Hepatitis E

Dr. Milan Surjit and team have been investigating the role of host-pathogen interactions in Hepatitis E virus (HEV) pathogenesis and exploring the mechanism of viral translation and replication. They are also investigating the significance of endogenous retroviruses in HEV pathogenesis and manifestation of the disease symptoms.

Notably, they have identified the RNA-protein interactome of HEV, identified a novel factor that controls HEV replication and demonstrated its mode of action at molecular level. They have shown the co-occurrence of both cap-dependent and cap-



Dr. Milan Surjit

independent translation in HEV and characterized a novel IRES (internal ribosome entry-site) element. They identified and characterized the molecular details of the proviral activity of the HEV protease and showed that HEV protease association with the host stress-sensing kinase eIF2AK4 results in the inhibition of self-association and concomitant loss of kinase activity of eIF2AK4. Site-directed mutagenesis of the 53rd phenylalanine residue of PCP abolishes its interaction with the eIF2AK4. Further, a genetically engineered HEV-expressing F53A mutant PCP shows poor replication efficiency. Collectively, these data identify an additional property of the g1-HEV PCP protein, through which it helps the virus in antagonizing eIF2AK4 mediated phosphorylation of the eIF2, thus contributing to the uninterrupted synthesis of viral proteins in the infected cells.

In collaboration with scientists at the Technical Physics Division, Bhabha Atomic Research Center, Mumbai, Dr Surjit's group synthesized ZnO nanoparticles [ZnO(NP)] and tetrapod-shaped ZnO nanoparticles [ZnO(TP)] and evaluated their antiviral activity. Both ZnO(NP) and ZnO(TP) displayed potent antiviral activity against Hepatitis E and Hepatitis C viruses, the latter being more effective. Measurement of cell viability and intracellular Reactive Oxygen Species levels revealed that both ZnO(NP) and ZnO(TP) are non-cytotoxic to the cells even at significantly higher doses, compared to a conventional Zinc salt (ZnSO₄). This study paves the way for the evaluation of the potential therapeutic benefit of ZnO(TP) against HEV and HCV.

In partnership with Vaxfarm Life Sciences (Faridabad), AIIMS (New Delhi), PGIMER (Chandigarh) and RCB (Faridabad), Dr Surjit's group has established a "HEV vaccine translational research consortium" that is performing the preclinical evaluation of the recombinant virus-like particle-based HEV vaccine candidate as well as conducting hospital-based and community-based surveillance to identify the potential vaccine recipient population.

Way ahead

In the area of basic virology, Dr. Surjit's group is working towards developing an integrated RNA-protein interactome of the HEV to decode the molecular mechanism of viral replication. In the future, they plan to identify novel, specific antiviral targets from the interactome study. With regard to the development of vaccines, his group is performing a preclinical evaluation of the HEV vaccine formulation in mice and non-human primates (Monkey).

HIV

Dr. Jayanta Bhattacharya and his group are working to understand the association between genetic and neutralization properties of currently circulating HIV-1 clade C compare with the ones that are circulating globally, particularly in Africa.

Genetic and neutralization diversity of currently circulating HIV-1

Broadly neutralizing antibody (bnAb) based interventions, both prophylactic and therapeutic are promising and potentially

transformative candidates to effect potent antiviral activity. bnAbs are an important complementation towards antiretroviral therapy amongst HIV-1 infected patients where ART treatment fails or is less effective. Dr. Bhattacharya's team examined the extent of effectiveness (breadth) and efficiency (potency) of lead bnAbs with multiple and distinct specificities against HIV1 subtype C that is currently circulating in India. The team collected samples from nine clinical sites across India and extensive genetic characterization of bnAb epitopes was done on the near full-length genome next-generation sequencing data from these samples. Furthermore, envelope gene pseudoviruses were generated from 58 contemporary sequences and their sensitivity towards 10 broadly neutralizing antibodies targeting distinct epitopes of HIV-1 envelope gene through *in vitro* neutralization assays done. These bnAbs targets 5 distinct epitopes of HIV-1 envelope gene namely CAP256-VRC26.25, PGDM1400 (V1V2 loop specific); VRC01, VRC07 and 1-18 (CD4bs specific); PGT121, 10-1074, BG-18 (V3 glycan supersite targeting); 10E8 and VRC34.1 (MPER and Interface targeting).



Dr. Jayanta Bhattacharya

Design and development of HIV envelope antigens towards informing next-generation germline targeting immunogen design in partnership with a large network of African institutions under South-South collaboration

To elicit the matured broadly neutralizing antibody (bnAb) responses against HIV-1 viruses, it is important to activate the B-cell to secrete germline antibodies in response to a germline targeting priming immunogen. Recently, a human trial has been initiated to test the safety and efficacy of a nanoparticle-based germline targeting immunogen eOD-GT8 capable of eliciting GL-VRC01 class responses as a prime. Dr Bhattacharya's team designed 10 HIV-1 envelope (Env) trimer constructs that are sensitive to VRC01 class bnAbs and 4 HIV-1 envelope trimer constructs which are resistant to VRC01 class bnAbs, but sensitive to other classes of bnAbs. The group has developed, purified and characterized seven Env trimers out of these 14 designs. These trimers were tested for their antigenicity, structural stability and conformations. The team is continuing the preparation, purification and characterization of the remaining env constructs. This is an IAVI-coordinated project in collaboration with Indian and African partners.

Influenza

Supporting Influenza vaccine and biotherapeutic research and development

Under the ENDFLU project (Horizon 2020 DBT-EU Next Generation Flu vaccine), **Dr. Sweety Samal's** team has developed preclinical mouse challenge model for Influenza A IAV/Puerto Rico/8/1934, IAV/California/04/2009 (H1N1) pdm09, IAV/Phillipines/2/82/X-79, IAV/X-31 (H3N2), IAV/Guangdong-Maonan/SWL/1536/2019 and for influenza B; IBV/Washington/02/2019 (Victoria), IBV/Phuket/3073/2013



Dr. Sweety Samal

(Yamagata) and IBV/Brisbane/60/2008 viruses. The team has evaluated > 30 different antigens in seven different studies to evaluate the protective efficacy by using in-house developed influenza challenge animal challenge models. The readouts include body weight, viremia, clinical scoring, survival rate, virus load measurement in organs by qRT-PCR and microneutralization titers.

Dr. Samal's team has extended support to Kyntox Private Limited, Bangalore (Start-up) in assessing the *in vitro* efficacy of IgY biotherapeutics. The team has evaluated two IgY (powder and liquid formulations) provided by Kyntox private limited, specific to Inf A and Inf B viruses by the microneutralization assay in vitro against the viruses; IAV/California/04/2009 (H1N1) pdm09, IBV/Victoria/2570/2019, IBV/Phuket/3073/2013 (Yamagata) and IC50 values were calculated, which showed promising results.

Under the project INDIGO (a five-year consortium between DBT, India and EU partners) for next-generation influenza vaccine development, Dr. Samal's team has developed and optimized the serological assays, ELISA, hemagglutination inhibition (HI) assay for measuring the influenza vaccine efficacy as a correlation of protection.

Indigenously designed and developed pentameric form of M2e-based immunogen provides sub-optimal protection against lethal Influenza virus challenge

In order to design a novel broad-spectrum vaccine candidate to combat the yearly hustle of vaccine re-formulations, Dr. Samal's team focused on the Influenza virus Matrix 2 ectodomain protein (M2e) which is highly conserved across Influenza strains. Previously, the team had engineered three repeats of the M2e (M2e-3x) protein coupled with the tGCN4 tetramerizing domain and found it to be highly stable and efficient in addressing the immunogenic potential of the M2e protein (JBC, PMID: 32817314). To further assess the immunogenic potential of the M2e protein with a gradual increase in repetitive units, the team generated M2e-5x and M2e-7x immunogens with five and seven repeats of M2e epitopes. The pentameric M2e-5x was expressed in Expi 293f suspension mammalian cells and found to be stable, with a good yield of ~6–8 mg/L. The comprehensive analytical characterization of synthesized M2e-5x protein showed high stability and narrow size distribution of the protein as measured by DLS. Following the assessment of immunogenicity in the BALB/c mouse challenge model through intramuscular immunization of M2e-5x immunogen along with Addavax adjuvant with the prime-boost regime elicited high antibody titres and IgG1-dependent immune response but failed to show completed protection against a lethal dosage of mouse-adapted PR8/X-31 virus challenge. However, there was significant virus clearance in the immunized lung tissue as compared to the virus-infected group, suggesting M2e's potential to be used as a conserved component in the Influenza multivalent vaccine development.

Way ahead

Dr. Sweety Samal plans to transfer the technology of their vaccine candidate, Influenza trimeric HA soluble subunit protein, as a single-dose vaccine candidate. She also plans to initiate novel microneedle patch formulation for HA vaccine candidate under the INDIGO project.

Validation of structurally occluded conserved epitopes as the novel addition towards universal Influenza vaccine development and implementation towards respiratory viruses

Next-generation influenza vaccine development is an unmet medical need of today's world. An Influenza HA based universal influenza vaccine candidate, showing complete protection against the challenge towards X31 (mouse adapted H3N2 virus; A/X-31(H3N2) and PR8 (mouse-adapted H1N1 virus; A/PR8(H1N1)) viruses, was developed by **Dr. Tripti Shrivastava's** group. Further, the conservation of the epitopes displayed by the



Dr. Tripti Shrivastava

candidate towards the other virus subtypes H5N1 and H7N9, was confirmed through sequence analysis, biochemical and structural approaches. The antibody FluA-20, proven to interact with H1N1, H3N2, H5N1 and H7N9, targeting the occluded surface, was designed and produced, its binding to the candidate was evaluated using various biochemical methodologies; ELISA, Octet. Additionally, non-competitive binding of FluA-20 was observed when compared with stem-directed monoclonal antibodies CR6261 and CR9114 and head-directed antibody C102. Further, the SAXS data were collected for various complexes characterizing the different antigenic sites displayed by the candidate; stem, head and occluded interface (HA-CR6261-FluA-20, HA-FluA-20, HA-CR9114, HA-CR9114-FluA-20 and HA-FluA-20), validating the accessibility epitopes characterizing the broad reactivity indicating them as a potential candidate for universal influenza vaccine.

Way ahead

Dr. Shrivastava plans to do the production of structurally occluded conserved epitopes as vaccine candidates through baculovirus and CHO-based expression systems to comply with regulatory approval compliances for further development. Also, she plans to use the MVA vector-based system to produce the HA candidate followed by its comparative evaluation of response with protein subunit-based expressed candidates. She plans to evaluate similar study designs for designing and evaluating potential candidates for other respiratory diseases. Dr. Shrivastava also plans to do studies to investigate the phenomenon of binding of depleted monomeric sera on viral surface targeting other subgroup of viruses that are focused towards understanding and characterization of breathing concept of influenza virus

Respiratory Syncytial Virus (RSV)

Epitope-focused vaccine candidate development of Respiratory syncytial virus (RSV)

RSV is the leading cause of respiratory tract infection among the paediatric population and is responsible for 6.7% of all deaths in the infant age group. The licensed RSV vaccine "Arexvy" is recommended to be used for the elderly population only; its applicability towards pediatric population is still under approval. Hence, in order to develop a safe, efficacious and broad-spectrum RSV vaccine, Dr Shrivastava's group is working towards epitope focused vaccine-designing approach, where the candidates have been designed using B and T cell epitopes. The immunogenicity of the candidate was tested in two adjuvant formulations: alum and addavax, in BALB/c animals. Further studies are ongoing.

Way ahead

Dr. Shrivastava plans to evaluate the neutralization assays, humoral and T cell responses for the RSV vaccine candidate.

SARS-CoV-2

Isolation and characterization of Monoclonal Antibodies (mAbs) from a SARS-CoV-2 infected convalescent donor

In continuation to the last year's report on the discovery of anti-SARS-CoV-2 neutralizing monoclonal antibodies (mAbs), **Dr. Jayanta Bhattacharya** and the team isolated two additional monoclonal antibodies (THSC20.HVTR11 and THSC20.HVTR55) by RBD-specific single B cell sorting and cloning method from the same convalescent donor who was infected during ancestral SARS-CoV-2 wave from whom the team had previously reported the isolation of five SARS-CoV-2 and its variants neutralizing potent mAbs (Hingankar et al., PLOS Pathog. 2022, Deshpande et al., Microbiol.Spectr. 2023). Interestingly, all the seven mAbs isolated from this donor belong to the distinct class of germline genes with varied neutralization potencies and specificities. Out of the seven mAbs, four (THSC20.HVTR04, THSC20.HVTR06, THSC20.HVTR11 and THSC20.HVTR26) were found to variably neutralize the Omicron variants tested both in pseudovirus and authentic live virus-based neutralization assays. THSC20.HVTR04 (IGVH3-30) though found to have lost its activity against BA.1 but was found to potently neutralize BA.2, BA.4 (pseudovirus) and BA.5 (authentic live virus) with IC₅₀ values of 0.29, 0.21 and 0.19 µg/mL respectively and for these assays LY-CoV016, REGN10933, REGN10987, and CC12.3 mAbs were used for comparison as known controls. On the other hand, THSC20.HVTR06 (IGVH7-4-1) could neutralize all the BA.1, BA.2 and BA4/BA.5 variants but with low potencies, while THSC20.HVTR11 could neutralize BA.1 and BA.2 with comparable potency as THSC20.HVTR04 but failed to neutralize BA4/BA.5 Omicron subvariants. A unique neutralization diversity conferred by the antibody repertoire developed in this particular individual through natural infection was observed. THSC20.HVTR04 was found to be one of the broadest and most potent antibodies of all.

Way ahead

Dr. Jayanta plans to examine the diversity of SARS-CoV-2 specific B cell repertoire diversity in this particular donor post-vaccination by the deep sequencing of B-cell receptor (BCR) to understand correlates of enhanced neutralization potency and breadth of antibody response through deep analysis of single B cell genomics and their functional properties.

Investigating the longevity of anti-SARS-CoV-2 humoral immune responses following vaccination and omicron infection

In continuation to the last year's report on the assessment of humoral immune response against SARS-CoV-2, Dr. Gaurav Batra's team further studied the durability of humoral immune responses to SARS-CoV-2 in the Indian population following vaccination and infection with the Omicron variant. After 8 months of receiving the second vaccine dose, it was observed that 87% of participants had detectable anti-RBD IgG antibodies, highlighting the persistence of vaccine-induced immunity. The introduction of the Omicron variant resulted in a significant number of asymptomatic infections within the first 4 months. This exposure to the Omicron variant served as a booster for the vaccine-induced immune response, leading to a substantial increase in anti-RBD IgG levels from 114 BAU/ml to 594 BAU/ml ($p < 0.001$). Remarkably, 97% of participants had detectable antibodies during this period. Moreover, participants with a history of prior natural infection and vaccination exhibited higher antibody titers, which were further enhanced following the Omicron surge. These findings suggest a synergistic effect of natural infection and vaccination in boosting the immune response. However, strong immune-imprinting was observed for the ancestral viral strain. There was a 41% decline in antibody levels over time, but the overall duration of elevated antibody levels lasted for an

average of 10 months, demonstrating the durability of the humoral immune response to SARS-CoV-2.

Way ahead

Dr. Batra intends to carry on with the assessment of humoral immune response against newly emerging SARS-CoV-2 variants. This research is aimed at providing guidance for future vaccine development against SARS-CoV-2.

Role of envelope protein of human endogenous retrovirus-R (HERV-R) against SARS-CoV-2

Dr Milan Surjit's group has investigated the cross-talk between human endogenous retroviruses (HERVs) and SARS-CoV-2. HERVs represent retroviral elements that were integrated into the ancestral human genome. HERVs are important in embryonic development as well as in the manifestation of diseases, including cancer, inflammation and viral infections. Envelope proteins of HERVs are known to modulate host-pathogen interactions. Expression analysis of envelope protein of several HERVs in SARS-CoV-2 infected cells revealed increased expression of HERV-E, HERV-V, HERV-FRD, HERV-MER34, HERV-W and HERV-K-HML2 envelope proteins. In contrast, the HERV-R envelope was downregulated in cell-based models of SARS-CoV-2 infection and PBMCs of COVID-19 patients. Overexpression of HERV-R inhibited replication of SARS-CoV-2, suggesting its antiviral activity. Further studies demonstrated the role of the extracellular signal-regulated kinase (ERK) in regulating HERV-R antiviral activity. Overall, these data suggest that the crosstalk between ERK and p38 MAPK controls the synthesis of HERV-R envelope protein, which in turn modulates the replication of SARS-CoV-2. These findings establish the importance of the HERV-R envelope as a prosurvival host factor against SARS-CoV-2 and illustrate the advantage of integration and evolutionary maintenance of retroviral elements in the human genome.

Indigenous multivalent self-assembled nanocage (MSN) vaccine platform

Dr Sweety Samal and her team have developed a multivalent self-assembled nanocage (MSN) vaccine platform that can be used to generate vaccine candidates against various viruses.

A novel, low cost affordable multivalent pancorona vaccine

Here, in collaboration with Panacea Biotec Ltd (PBL), India, Dr. Samal and Dr. Amit Awasth's team developed a novel, subunit protein-based vaccine against SARS-CoV-2 variants of concern using the MSN platform. The team has developed a tagless vaccine candidate in which the highly conserved and immunogenic epitopes from SARS-CoV-2 RBD were stapled into the NSP, purified in E Coli expression system with a high yield which is stable at 2-8oC, forming 220 nm to 350 nm nanoparticulate structure. In vivo assessment of the drug product in the BALB/c mouse elicited potent humoral and T cell responses and showed neutralization breadth against Omicron VoC. Further challenge studies in k18-hACE2 mouse model showed complete protection against ancestral Wuhan-1 and Omicron BA.5 VoC. The process development and stability studies of the drug substance are being carried out at PBL.

Betacoronavirus vaccine development (Panacea Biotec Ltd and CEPI partnership program)

Using the MSN platform, Dr. Samal's team have designed 20 antigens consisting of the conserved or

immunogenic regions of SARS-CoV-1, SARS-CoV-2 VoC and MERS receptor binding domain epitopes stapled to the NSP nanocage. The bioinformatic and molecular docking simulation studies have been conducted by Dr. Shailendra Asthana's team. Upto 14 antigens were expressed and purified in the E.Coli expression system and the antigens showed stability, ease in expression and good yield. These antigens were further evaluated for their immunogenicity in the BALB/c mouse along with MF-59-like adjuvant. The results are promising and few antigens elicited antibody responses to SARS-CoV-1, MERS and SARS-CoV-2 ancestral and Omicron strains thus demonstrating wider breadth. The best down-selected candidates have now been transferred to PBL for process development and formulation. Challenge studies are planned at THSTI to be conducted by Dr. Amit Awasthi's team.

Way ahead

Dr. Samal plans to take forward the SARS-CoV-2 VoC for human Phase-I trial in collaboration with Panacea Biotech. She plans to conduct challenge studies for betacoronavirus vaccine candidate at THSTI in collaboration with Dr. Amit Awasthi.

SARS CoV-2 RBD based vaccine candidate's science and immunomodulatory parameter

In order to understand the science and immunomodulatory effect of vaccination, **Dr. Tripti Shrivastava's** group analyzed their RBD based vaccine candidate for immunological and proteomics profiling of the protein present in the sera of vaccinated and recovered animals in comparison to non-vaccinated animals. It was observed that the animals who received the vaccine candidate had an upregulated immunological component along with Ras GTPase activating protein in comparison to the control group. A similar set of upregulated proteins was observed in animals challenged with Wuhan and Delta variants of SARS-CoV-2. Additionally, her studies show a significant set of downregulated proteins whose role has been shown to support viral replication. Further, the neutralizing potency of the immunized sera was tested with the emerging variants of Omicron; BA.1, BA.2 and BA.5 and it was found that this candidate neutralized all the emerging and circulating key variants of Omicron. On analysing the reason behind this neutralization, Dr Shrivastava's group concludes that the observed phenomenon may be due to the conserved glycan N331 and N343 in all the variants that have emerged so far. The group has now designed a differentially expressing glycans form of RBD and proposes to study its immunological parameters and neutralization response in future.

Establishment of SARS-CoV-2 Virus Culture and Assays

During the SARS-CoV-2 pandemic, **Dr. Shailendra Mani** and his team established SARS-CoV-2 culture and assays that supported many vaccine manufacturers. Recently, they have developed variant-specific including Omicron XBB.1.16 virus neutralization assays. Dr Mani's team has also developed a multiplex bead-based platform for the detection of SARS-CoV-2 virus in serum samples. This platform can also be used to detect Dengue and Chikungunya virus in serum samples. These developed assays will be instrumental in large-scale community screening,



Dr. Shailendra Mani

identification of potential plasma donors, and evaluation of future vaccine and antiviral candidate trials.

Way ahead

Dr. Mani plans to delve into the detection of antibodies in humans across diverse vaccinated populations. He aims to evaluate the efficacy and longevity of vaccine-induced antibody responses by analyzing their levels, specificity, and neutralizing capabilities in animal models.

Genomic surveillance of SARS CoV-2

Dr. Bhabatosh Das's group at the Advanced Nucleotide Sequencing Facility, carries out genomic sequencing of the SARS CoV-2 variants as a part Indian SARS-CoV-2 Genomics Consortium (INSACOG) programme. The institute played an active role in the genomic surveillance of the SARS CoV-2 samples from Haryana state and samples from international or domestic travelers of the Indira Gandhi International Airport. A total of 578 samples from the community surveillance study were sequenced last year. The team is a part of the SARS CoV-2 genome sequencing study of the hospital network samples across India and 731 samples were processed under this project. To date, the sequencing facility of THSTI has submitted 1969 sequencing data in the INDA-CA and in the GISAID. The SARS CoV-2 surveillance programme further extends with the viral load and variant detection in sewage water from different regions of Faridabad. The sequencing facility played a critical role in the development of the in-house vaccine against the omicron variant of the SARS CoV-2.

Monkeypox

Scaffold - multiple antigen based Monkeypox vaccine candidate

The recent emergence of monkeypox is a disease of concern caused by Orthopoxvirus. In order to mount ideal immune response a vaccine candidate should contain contributions from both virus forms: mature virions (MV) and enveloped virions (EV). Dr. Tripti Shrivastava and group have designed and expressed expressed multiple antigens of MV and EV virus with the help of a scaffold protein. Various combinations of MV and EV antigens expressing scaffold construct were designed based of structural and immunological parameters. One scaffold-epitope expressing A33/L1R with scaffold was expressed and purified using bacterial expression system. The purified protein immunogenicity assessment is ongoing in BALB/c

animals. Additionally, an eGFP-BHK-21 cell-based neutralization assay was established by her group to evaluate the neutralization potential of the immunogens.

Way ahead

Dr. Shrivastava plans to design and synthesize different combinations of antigen and scaffold constructs and characterize its biochemical, biophysical and immunological parameters so as to identify and validate the most promising vaccine candidate.

Chikungunya

Dr. Supratik Das has purified and antigenically characterized tag-less and stabilized CHIKV sE1-sE2-E3 trimers. Structural characterization is ongoing. He has developed a novel design to generate stabilized CHIKV sE1-sE2-E3 trimers. These trimers have been purified to apparent homogeneity and antigenically characterized. Further studies are ongoing.

Way ahead

Dr. Das plans to use CHIKV sE1-sE2-E3 trimers for immunization in mice to study the neutralizing response and T cell-mediated immune response.

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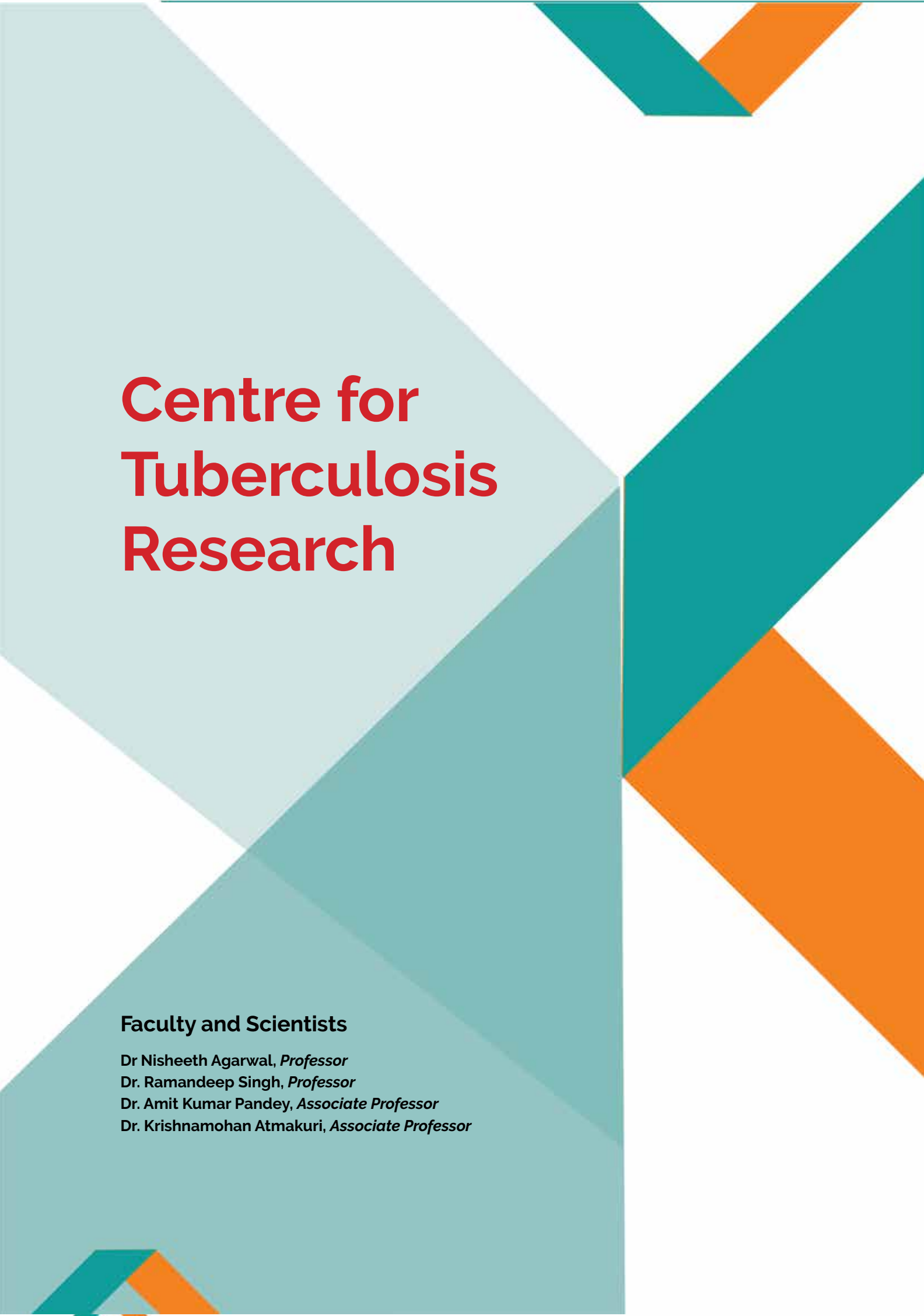
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Tuberculosis (TB) affects about a quarter of the global population and about 1.5 million people die from TB every year. India accounts for more than one-quarter of the global burden. The emergence of drug-resistant strains urgently warrants the development of newer and more effective drugs to control the increasing burden of TB. Tuberculosis is a key focus area of research at THSTI.

Understanding the mechanisms of pathogenesis of *Mycobacterium tuberculosis*

Toxin antitoxin (TA) systems are mostly bicistronic genetic modules that encode for an antitoxin and toxin. The ectopic expression of toxins belonging to TA systems leads to growth inhibition in either a bactericidal or bacteriostatic manner. As part of the India Alliance Project, **Dr. Ramandeep Singh** and his group have functionally characterized toxins belonging to Type IV TA systems from *M. tuberculosis*. In addition to Type II TA systems, *M. tuberculosis* genome also encodes for 4 homologs of Type IV TA systems, MenAT1, MenAT2, MenAT3 and MenAT4. MenT toxins belonging to type IV subfamilies are characterized by the presence of four highly conserved motifs and a highly conserved nucleotidyl transferase (NTase) like domain. Using inducible vector expression systems, the group has shown that ectopic expression of toxins belonging to Type IV TA systems inhibits bacterial growth in a static manner. Using temperature-sensitive mycobacteriophages, they generated $\Delta menT2$, $\Delta menT3$, $\Delta menT4$ and $\Delta menT4\Delta T3$ strains of *M. tuberculosis*. They also observed that in comparison to parental strains, $\Delta menT2$ and $\Delta menT4\Delta T3$ strains are attenuated for growth in guinea pigs. Bacterial RNA-sequencing showed that the levels of transcripts encoding for proteins involved in either in vitro growth or intracellular survival were reduced in mid-log phase cultures of $\Delta menT4\Delta T3$ strains of *M. tuberculosis* relative to the parental strain. RNA-sequencing of total RNA isolated from lung tissues of naïve and $\Delta menT4\Delta T3$ infected animals revealed that the expression of proteins involved in antimicrobial pathways was significantly reduced in the lung tissues of animals infected with $\Delta menT4\Delta T3$ strain. It was found that immunization with toxin-deficient strain, $\Delta menT4\Delta T3$, was able to impart protection against *M. tuberculosis* in mice and guinea pigs. The team has also identified correlates of protection in toxin-deficient strains immunized animals. Dr Singh's group has shown that MenT2, MenT3 and MenT4 are essential for pathogenesis of *M. tuberculosis* and toxin-deficient strains can be explored further for the development of auxotrophic vaccines.



Dr. Ramandeep Singh

Function Characterization of GntR family of transcription factor from *Mycobacterium tuberculosis*

GntR family of transcription factors are widespread among prokaryotes and is involved in various processes including virulence and pathogenesis. Despite the presence of GntR homologs in the genome of *M. tuberculosis* their biological functions have not been well established extensively. Using temperature sensitive mycobacteriophages, Dr. Singh's group constructed various GntR-deficient strains of *M. tuberculosis*. They have characterized the Rv0792c protein (GntR homolog belonging to HutC subfamily) from *M. tuberculosis*. Using sedimentation ultracentrifugation and SEC-MALS it was shown unambiguously that Rv0792c exists as a dimer in solution. The mutant strain was compromised for survival upon exposure to oxidative stress *in vitro* and in guinea pigs compared to the parental strain. In aerosol-infected guinea pigs, the bacillary loads in the lungs and spleens of wild-type infected animals were significantly higher in comparison to the mutant strain. RNA-seq analysis revealed that Rv0792c regulates the expression of a

subset of genes that enable bacteria to adapt and persist in host tissues. Using SELEX, they have identified ss aptamers that are able to bind to Rv0792c protein. SAXS was performed to determine the structure of Rv0792c. The group has identified I-OMe-Tyrphostin as a small molecule inhibitor against Rv0792c. The identified molecule was able to inhibit Rv0792c binding to its native promoter and also inhibited the intracellular growth of *M. tuberculosis*. Experiments are in progress to characterize FadR homologs from *M. tuberculosis*. The group has generated mutant strains of *M. tuberculosis* deficient in either Rv0043c or Rv0586 or Rv0165c or Rv3060c. The ongoing experiments include comparing the growth patterns of parental and FadR deletion strains *in vitro*, upon exposure to stress conditions and *in vivo*.

Identification of small molecule inhibitors against *M. tuberculosis*

Dr Singh and his team have standardized high throughput screening assays (phenotypic, target and macrophage) to identify small molecules with anti-tubercular activity. They have recently validated MetA (an enzyme involved in L-methionine biosynthesis) and PPK-1 (an enzyme involved in inorganic polyphosphate biosynthesis) as drug targets. Using standardized HTS assays, they identified small molecules that are able to inhibit the enzymatic activity of MetA and PPK-1 enzymes. These molecules were able to inhibit the activities of these enzymes in a dose-dependent manner and were able to inhibit enzymatic activity from other bacterial homologs. The identified small molecules were able to inhibit the growth of intracellular *M. tuberculosis* and also enhance the activity of known TB drugs. Taken together, these findings validated MetA and PPK-1 as attractive targets for the development of new broad-spectrum anti-bacterial agents that should be effective against drug-resistant bacteria. In addition to target-based screening, they also performed phenotypic screening to identify small molecules with novel mechanisms of action. One of the small molecules identified, MMV687254 was found to be as active as INH in a macrophage model of infection. MMV687254's mechanism of action was also identified. The group has performed a detailed structure-activity relationship for these molecules and identified small molecules that are more potent than the parent compound. The optimized molecules show activity against both drug-susceptible and drug-resistant bacteria. These molecules are also able to shorten the duration of therapy. Dr Singh and team screened small molecule libraries in macrophage-based screens and have identified small molecules that are either FDA-approved or in clinical studies to possess anti-tubercular activity. Experiments are in progress to evaluate the activity of these compounds in mice models of infection and also to delineate the mechanisms by which these small molecules are able to inhibit the growth of *M. tuberculosis*.

Way ahead

Dr Singh and the group have identified novel drug targets for *M. tuberculosis*. They have also identified small molecules that are active in the mice model of infection and presently are performing experiments to understand the mechanism of action for the other identified small molecules. Dr. Singh also plans unmarking of mutant strains for further development of these strains as vaccine candidates.

Understanding the pathogenesis of TB and developing novel TB therapeutics and diagnostics

A thorough analysis of the genome sequence of TB pathogen *Mycobacterium tuberculosis* reveals multiple genes of unknown functions, several of which are predicted essential for the pathogen's survival. With the help of CRISPRi-based gene silencing technology, **Dr. Nisheeth Agarwal's** group is involved in creating a repository of mutants and studying unknown genes, emphasizing those associated with the protein homeostasis machinery. His ultimate goal is to explore some of these genes as novel drug targets. In addition, Dr. Agarwal's research group is also involved in phenotypic and target-based screening of small molecule inhibitors against *M. tuberculosis* to identify novel anti-TB drugs.

Characterization of the function of Mtb genes of unknown functions

A few years ago, Dr. Agarwal's group created a novel CRISPRi-based gene silencing tool which was found highly effective in mycobacteria. One of the goals of his group is to employ CRISPRi for characterizing the function of a defined set of unknown genes involved in protein homeostasis. They have shown the importance of caseinolytic protease in Mtb pathophysiology. Subsequently, they targeted a few other genes such as an unknown transcription



Dr. Nisheeth Agarwal

regulator, Rv1830; an unknown Hsp90 annotated as HtpG; a membrane protease, LepB; and a signal recognition particle, Ffh. Rv1830 has recently been shown to impart drug resilience in Mtb pathogen. Dr. Agarwal's group has shown that it is highly essential for bacterial growth *in vitro* as well as in animal models of infection. Further, the group has characterized the function of *HtpG* and showed that it plays an important role in the regulation of protein folding by an essential chaperonin, DnaK. It was identified that knockout of *htpG* results in the upregulation of Clp machinery components, thus maintaining cellular homeostasis. Their study suggested that simultaneous inhibition of both HtpG and Clp machinery may be lethal. They have also identified that silencing of *lepB* does not cause as much lethality as expected. Subsequently, the group attempted to knock out this gene by CRISPR-Cas-based editing. Interestingly, they were able to edit *lepB* and are now in the process of characterizing its effect on mycobacterial pathophysiology. Recently, Dr. Agarwal's group has also started to characterize a protein known as Ffh, which is supposedly involved in protein translocation. Using various approaches, the group is trying to obtain mechanistic insight into the role of Ffh in the translocation of proteins on the cell envelope.

Establishing the CRISPR-Cas-based genome editing in mycobacteria

Recently, Dr. Agarwal and his team developed the CRISPR-Cas9-based editing tool for the disruption of genes in mycobacteria. Their early attempts showed that the system is efficient for causing insertion/deletion mutants in the fast-growing *M. smegmatis* and *M. marinum*, but not in *Mtb*. Subsequently, they improvised the tool by co-expression of the NHEJ pathway genes and found a marked increment in the editing efficiency as evaluated by targeting a few genes such as *lepB* and *htpG*. Although the system works in *Mtb*, it seems to be influenced by gene sequence and locus as certain genes such as *groEL1* could not be edited. Moreover, the efficiency varies from 0-50%. Hence, the group is trying to explore other Cas proteins and test their efficacy for obtaining better editing frequency in comparison to that observed with Cas9.

Development of a novel TB diagnostic tool with the help of CRISPR-Cas-based gene editing

Dr. Agarwal and his team have developed a Cas9/gRNA coupled with a quantitative real-time polymerase chain reaction (qRT-PCR) strategy to discriminate Mtb strains with point mutations leading to drug resistance against first-line drugs such as RIF. They designed guide sequences that can distinguish mutations in *rpoB* leading to S531W and H526C substitutions in the RRDR, resulting in differential cleavage of the DNA fragment by Cas9/gRNA ribonucleoprotein complex and subsequent change in the Ct values. The group has demonstrated that this strategy is highly robust and can detect RIF-resistant Mtb with a high level of specificity in a short span of time.

Identification of small molecule inhibitors against ClpC1 by screening and SAR studies

ClpC1 is an unfoldase which plays a major role in controlling protein homeostasis, also known as proteostasis. For the last few years, Dr. Nisheeth's group has been trying to decipher how proteostasis is maintained in Mtb by the chambered Clp proteolytic machinery, and what is the regulatory role of ClpC1 in it. Using animal models, they identified that ClpC1 is critical for mycobacterial virulence and could be explored as a drug target.

In collaboration with Dr. Ramandeep Singh, THSTI and Dr. Sandeep Sundriyal, BITS, Pilani, Dr. Agarwal's group identified a molecule inhibiting the ClpC1 at the sub-micromolar level, which was also found to be active against Mtb. Since this molecule showed a cytotoxic effect against mammalian cells, the group synthesized a few derivatives of Mtb ClpC1 inhibitor and identified a few top hits that retain anti-ClpC1 and anti-TB activities. Studies are ongoing to test these molecules against mammalian cells for cytotoxicity.

Screening of FDA-approved library of small molecule inhibitors against TB pathogen

To identify novel anti-TB inhibitors, Dr. Agarwal and his team are screening a library of ~3500 molecules against Mtb to identify the hit molecules which inhibit growth at the sub-micromolar level.

Building up a repository of CRISPRi mutant strains of mycobacteria

Dr. Nisheeth's group has been building a repository of CRISPRi mutants for TB researchers in the country. In the last year, they added more CRISPRi plasmid constructs and created ~250 knockdown strains of Mtb. His is the only laboratory in India having such a vast collection of CRISPRi strains against a variety of genes from different species of mycobacteria. Several of these plasmid constructs, as well as bacterial strains, have also been shared with TB researchers at various institutes such as IISC, NII, NIPER Mohali, CSIR IMTECH, NCBS, South Asian University, Bose Institute, BITS Pilani, Hyderabad etc.

Way ahead

Dr. Agarwal's group plans to characterize the role of Rv1830, *lepB*, *ffh* and a gene encoding for P-loop GTPase in Mtb pathophysiology. These targets are unique as some of these are absent in humans and can be used for the screening of inhibitors. His group is anticipating to identify a few hit molecules which inhibit Mtb growth at a sub-micromolar level and have potential to further screen against intracellular pathogen. In addition, they plan to establish the CRISPR-Cas-based genome editing tool using a novel Cas protein to assess its editing efficiency in comparison to the Cas9. Their effort on building the CRISPRi repository will be continued by targeting additional set of genes that are predicted essential by Transposon based screen.

Shortening anti-TB regimen by targeting antibiotic- and disease-persistence

Shortening anti-TB regimen by targeting antibiotic- and disease-persistence

Dr. Amit Kumar Pandey's lab work on the hypothesis that the differentially regulated critical metabolic pathways triggered by intracellular nutrient availability and requirements contribute significantly towards the generation of *Mycobacterium tuberculosis* (Mtb) persisters. The group had earlier demonstrated that Mtb could metabolize and survive on media containing cholesterol as a sole carbon source and that cholesterol metabolism is very critical for Mtb persistence. This indicates that Mtb actively modulates the host biosynthetic machinery for the generation of nutrients required for its own survival. Utilizing genetic

and high dimensional bioinformatic approach the group is trying to identify differentially regulated metabolic pathways both in Mtb and its host, which could lead to (i) a better understanding of host-pathogen symbiosis and thus Mtb pathogenesis, and (ii) designing of novel intervention strategies targeting persisters.

Dr. Pandey's lab has identified host pathways that could potentially be involved in long-term disease persistence in tuberculosis. They have also successfully identified genes belonging to different Mtb pathways (i) transcription factors (*Rv1719*, *mce3R*), (ii) nutrient storage and utilization (*Rv3068*, *Rv2668*) and (iii) metal

ion, pH and redox homeostasis (*Rv0391*, *Rv1906*, *Rv0495c*) that modulates antibiotic and disease persistence in tuberculosis. Further, the group has performed studies to decipher the mechanism and understand the role of these genes in triggering antibiotic persistence in Mtb.



Dr. Amit Kumar Pandey

Identification of host correlates of persistence during tuberculosis infection

Cholesterol is an enriched carbon source and its degradation is known to be critical for mycobacterial persistence. Dr. Pandey's lab have demonstrated that activation of RNase toxin (VapC12) results in cholesterol-specific growth modulation that increases the frequency of generation of the persisters in a heterogeneous M. tuberculosis population. Based on the above findings, they hypothesize that differential protein expression profiling between the mutant and the wild type strains would help identify critical proteins/pathways involved in the downregulation of host immune response. Using vapC12 gene deletion strain, the group had successfully developed an animal model in mice that will help us decipher host network and pathways critical for disease persistence in tuberculosis. Host immunoprofiling data suggests that Mtb actively modulates innate immune pathways critical for establishing long-term disease persistence. Currently, his lab is trying to identify proteins critical for the host-pathogen interaction essential for disease and antibiotic persistence in tuberculosis.

Way ahead

With a long-term goal vision of designing intervention strategies directed at the host pathways (HDT) to prevent long-term disease persistence during Mtb infection, Dr. Pandey's group plans to continue exploring new potential anti-persister targets by further their understanding on the generation and evolution of antibiotic- and disease-persistence during Mycobacterium tuberculosis infection. The group is interested to design HTS strategy to actively screen for anti-persister molecules using FDA-approved chemical libraries. Based on the in-vitro studies few of these molecules will be tested using animal models of tuberculosis infection.

Identifying and evaluating novel therapeutic strategies for reducing anti-TB therapeutic regimen and total drug intake

Despite the availability of several anti-TB drugs, because of the continued extended therapeutic regimen (6-24 months), at least 80% of TB patients experience one or more side effects including liver damage, gastritis, vomiting, heartburn, reduced appetite, visual impairment and rashes. Consequently, >60-70% of such TB patients dropout of the DOTS-TB program triggering possible relapse in them. To curtail this behavior, **Dr. Krishnamohan**



Dr. Krishnamohan Atmakuri

Atmakuri's group is exploring novel strategies, the first being targeted delivery of the therapeutic molecule to the site of the pathogen.

Earlier, Dr. Atmakuri in collaboration with Dr. Jonathan Pillai, Orbees Medical Pvt. Ltd., Bengaluru reported had initiated exploration of mEVs as potential nanocarriers of Rifampicin (RIF) drug. Drs. Atmakuri and Pillai hypothesized that mEVs can act as nanocarriers for RIF and slowly release it at the site of the pathogen, thus aiding in the quick reduction of pathogen numbers. During the previous year, they reported efforts to encapsulate RIF within mEVs; characterization of recombinant mEVs^{RIF+}; slow release of RIF post its encapsulation; and on pathways that macrophages exploit to internalize mEVs and mEVs^{RIF+}. This year, they further characterize mEVs^{RIF+} interaction with mycobacteria *in vitro* and *ex vivo*.

Native and RIF-loaded EVs of mycobacteria specifically bind to surface of only mycobacteria.

Dr. Atmakuri's lab has well standardized and published a protocol for efficient enrichment of mEVs from axenic cultures of pathogenic, attenuated and avirulent mycobacteria. Utilizing their protocol, they first enriched the mEVs from 2 L of mid-logarithmic axenic cultures of *M. smegmatis* (Msm; mEVs yield approx. 80-100 µg protein equivalent). After (i) evaluating the quality (by transmission electron microscopy); (ii) determining the quantity (by nanoparticle tracking analysis), and the sterility (no contaminating bacteria) of the enriched EVs, they employed a passive diffusion strategy to load Rifampicin (RIF) (details reported in the last year annual report). They removed the unbound/undiffused RIF by ultra-centrifugation, and washed thrice the RIF-loaded mEVs (mEVs^{RIF+}; ultra-centrifuging every time) to remove the loosely bound RIF. Then they loaded them onto an Iodixanol (Optiprep) density gradient cushion, performed ultracentrifugation and eluted the mEVs^{RIF+} (visible as an orange band). Then, employing a HPLC, they estimated the amount of encapsulated RIF (inside mEVs^{RIF+}). Then, they separately added the mEVs^{RIF+} or mEVs containing mCherry (mEVsm^{Cherry}) to actively growing mycobacteria (*M. tuberculosis* (Mtb) and Msm (both GFP-tagged), *Escherichia coli* (G-ve model organism) and *Bacillus cereus* (G +ve model organism) (both labeled with Alex Fluor 488 through click chemistry). They observed that both mEVs^{RIF+} and mEVsm^{Cherry} specifically associated only with the surface of mycobacteria (Mtb and Msm) but not with the surface of *E. coli* and *B. cereus*. Msm-derived EVs associated with Mtb with comparable efficiency.

mEVs colocalize with intracellular mycobacteria. Given that mEVs associate with mycobacterial surface *in vitro*, and both mEVs^{RIF+} and mEVsm^{Cherry} get internalized by THP-1 macrophages with similar efficiencies when compared to native mEVs (data shown last year), Dr. Atmakuri's group also evaluated if the mEVs^{RIF+} and mEVsm^{Cherry} would similarly associate with infecting mycobacteria in THP-1 macrophages *ex vivo*. Towards that, they infected THP-1 macrophages (PMA differentiated) with Mtb (MOI - 1:10) and then extraneously added (separately) mEVs^{RIF+} and mEVsm^{Cherry} (, 1: mEVs, 100) to the infected macrophages. As expected, a subset (~5-10%) of the mEVs^{RIF+} and mEVsm^{Cherry} associated with infecting mycobacteria. A significant portion (~30%) of them also localized to the vicinity of the infecting mycobacteria indicating potential targeting/co-localization of mEVs to mycobacteria. RIF-loaded mEVs were visualized with DiO, a green fluorescent lipophilic dye.

RIF-loaded mEVs exhibit 8-fold reduction in MIC *in vitro* on mycobacteria. Given the slow release of RIF from mEVs^{RIF+} and their association with mycobacteria *in vitro*, Dr. Atmakuri's group assessed if RIF within mEVs^{RIF+} would exhibit any altered MIC. Towards that, in a 96-well plate setting, seeding 5 X 10⁵ Mtb, they added different numbers of mEVs

such that it equates to known concentrations of RIF. For comparison, they used similar concentrations of free RIF and evaluated MIC with Alamar Blue dye as reporter. Interestingly they observed mEVs^{RIF+} to exhibit 8-fold lower MIC when compared to free RIF alone. Interestingly, when the entire contents of the 200 µL reaction from Alamar Blue 96 well assay plates were plated for CFUs, though all bacteria were killed by equal amount of RIF (~0.5 µg/mL; from either free RIF or encapsulated RIF (mEVs^{RIF+}) containing wells), at least 10-fold less bacteria were found in ten-fold RIF dilutions (viz. 0.005 and 0.05 µg/mL) indicating superior efficiency of killing by encapsulated RIF over free RIF. Drs. Atmakuri and Pillai speculate that free but not encapsulated RIF inactivates with time.

RIF-loaded mEVs kill infecting mycobacteria in THP-1 macrophages with comparable efficiency to free RIF.

Since, (i) RIF from mEVs^{RIF+} gets released gradually; and (ii) the encapsulated RIF exhibited lower MIC and superior killing, Dr. Atmakuri's group tested if encapsulated RIF (in mEVs^{RIF+}) exhibit superior killing of mycobacteria when in THP-1 macrophages *ex vivo*. They infected THP-1 macrophages (PMA differentiated) with Mtb (MOI -1:10) and added different concentrations of free RIF or encapsulated RIF. Over 72 h, they observed comparable killing of infecting mycobacteria indicating that *ex vivo*, encapsulated RIF is as efficient as free RIF in killing mycobacteria.

Way ahead

If Dr. Atmakuri's group receives sufficient funding support, the group will perform: (i) A comparative PK and PD analyses of free and encapsulated RIF in a mice model of TB; and (ii) Evaluate if encapsulated RIF achieves superior killing of infecting mycobacteria in the same mice model of TB.

Development of a small molecule-based new drug leads for MTB infection

Dr Dinesh Mahajan's group, in collaboration with Tuberculosis research group of THSTI, focuses on identification and development of small molecules. The group uses two approaches for new drug discovery. One is based on repositioning of the approved drugs or drug leads evaluated in phase 2/3 trials exploiting. The other approach involved, identification and development of a New Chemical Entities (NCEs) focused either



Dr Dinesh Mahajan

on a specific molecular pathway or a drug target. This includes new chemical hit identification followed by generation and understanding of Structure Activity Relationship (SAR) leading to identification of a drug lead. In the last year, the joint efforts of medicinal chemistry lab and TB lab resulted in the identification of drug like leads with sub micro-molar MIC with well characterized SAR. Few of the leads have been evaluated for oral pharmacokinetic studies in naïve mice as well as efficacy studies in infected mice to establish proof of concept. These molecules are under evaluation for further pharmacological characterization and animal efficacy studies using drug-resistant strains of MTB.

List of Collaborators

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Dr. Krishnamohan Atmakuri

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Dr. Tarun Kumar Sharma, Gujarat Biotechnology University, Gandhinagar



Centre for Immunobiology and Immunotherapy

Faculty and Scientists

Dr. Amit Awasthi, *Senior Professor*
Dr. Deepal Kumar Rathore, *Senior Research Scientist*
Dr Ramesh Chandra Rai, *Scientist D*
Dr Zaigham Abbas Rizvi, *Research Scientist*
Dr. Tanvi Agarwal, *Research Scientist*
Dr. Srikanth Sadhu, *Junior Resaerch Scientist*

Dr. Amit Awasthi's lab works on understanding immunological responses against infectious and inflammatory diseases using small animal model (s) and clinical samples. His lab has contributed to the identification and understanding FOXO1 master transcription factor in the induction of IL-9-producing Th9 cells. Previous studies from the lab have characterized the transcription and metabolic regulation of Th9 cells. His lab contributed immensely to COVID-19 biology by establishing pre-clinical animal models for SARS-CoV-2 infection.

Understanding the role of Th9 cells in COVID-19

The lab investigated the role of IL9 cells in COVID-19 and found



Dr. Amit Awasthi

a Foxo1-IL-9 mediated Th cell-specific pathway. They found introducing exogenous IL-9 or Foxo1-sufficient CD4⁺ T cells to Foxo1-deficient mice restores susceptibility, underscoring Foxo1's role in driving airway inflammation through CD4⁺ T cell-derived IL-9 in this model. Pharmacological inhibition of Foxo1 suppresses SARS-CoV-2 infection and associated immunopathology. Foxo1-conditional deficiency in CD4⁺ T cells renders ACE2.Tg mice resistant to SARS-CoV-2 infection by reducing IL-9 production and upregulating anti-viral and ISGs. IL-9 neutralization and Foxo1 deficiency generate similar immunopathological phenotypes, including lung eosinophil and mast cell accumulation. The group has established the role of the Foxo1-IL-9 axis in regulating SARS-CoV-2 infection and associated immunopathology. These studies give mechanistic insight into a critical inflammatory route in SARS-CoV-2 infection and hence serve as proof of principle for designing host-directed treatments to reduce illness severity.

Prophylactic treatment of *Withania somnifera* (WS) mitigates COVID-19 pathology in hamster & hACE2.Tg mice

The team has evaluated the effect of prophylactic treatment of WS against COVID-19 by using hamsters and hACE2.Tg mice. WS showed immuno-modulatory potential and robust protection against loss in body weight, viral load, and pulmonary pathology in the hamster model of SARS-CoV-2 infection. The results obtained indicate that WS promoted the immunosuppressive environment in the hamster and hACE2 transgenic mice models and limited the worsening of the disease by reducing inflammation, suggesting that WS might be useful against other acute viral infections.

Way ahead

In the upcoming years, Dr Awasthi's lab plans to investigate the effector and regulatory T-cell responses in the context of autoimmune and inflammatory diseases using small animal models. Dr. Awasthi's lab will continue understanding the immunopathology of COVID-19 and also investigate the role of CD4⁺ T cells in the context of other infectious diseases such as Influenza, CHIKV, etc. They also intend to explore the role of immunomodulatory potentials of small molecules, metabolites and metal ions in the progression of tumours and the use of cost-effective combinatorial immunotherapy. In addition, the lab also plans to keep working to understand the immune regulation of inflammatory bowel diseases and a possible therapeutic intervention through a dietary regime.





Centre for Microbial Research

Faculty and Scientists

Dr. Bhabatosh Das, *Associate Professor*
Dr. Krishnamohan Atmakuri, *Associate Professor*
Dr. Susmita Chaudhuri, *Assistant Professor*
Dr. Daizee Talukdar, *Research Scientist*
Dr. Jyoti Verma, *Research Scientist*
Dr. Prabhakar Babele, *Junior Research Scientist*

Centre for Microbial Research

The Centre for Microbial Research (CMR) is involved in exploring interactions between microorganisms and humans and to better understand the role and effect of microorganisms in human health and disease. The centre is also involved in Antimicrobial Resistance research for diagnostic and therapeutic development. The major programs of this centre are:

- Human Microbiome Research
- Antibiotic Resistance Research
- Neonatal Sepsis Research

Human Microbiome Research

Dr. Bhabatosh Das and his team work towards understanding the composition, diversity, dynamics and functions of the human microbiome of healthy subjects and people suffering from different diseases such as

Sepsis, NAFLD, Severe Acute Malnutrition (SAM), Type 2 Diabetes (T2D), Inflammatory Bowel Disease (IBD), pancreatic diseases, Preterm birth (PTB), Diarrhea and stomach disorders. The team is working to develop microbiome-based therapeutics for these conditions. They have carried out metagenomic sequences of more than 3000 clinical samples collected from healthy subjects and the above-mentioned patients and identified disease-specific (IBD, T2D, NAFLD, SAM, PTB) differential microbiome signatures that could be used to develop diagnostic tests for the detection of risk factors



Dr. Bhabatosh Das

Comparative genomics and proteomics analysis of different *Lactobacillus* spp. isolated from Indian pregnant women for indigenous probiotic development

Preterm birth (PTB) is a major challenge in obstetric healthcare and the leading cause of perinatal mortality and long-term morbidity. In healthy reproductive-aged women, the vaginal milieu shows a predominance of *Lactobacillus* species, whereas the dominance of non-indigenous microbial taxa substantially contributes to the pathophysiology of PTB. To identify indigenous probiotic strains and understand the genomics signatures of different *Lactobacillus* species isolated from the vagina of Indian pregnant women, the team carried out whole genome sequencing of all the clinical isolates using a next-generation sequencing platform. Proteomic analysis was performed on the culture filtrate of different strains of *L. crispatus* using a TripleTOF 5600 mass spectrometer coupled with microLC. The pangenome-based analysis revealed that *Lactobacillus* species have acquired several unique genes through horizontal gene transfer (HGT). Analysis of the representative genomes of *L. crispatus*, *L. gasseri*, *L. jensenii* and *L. vaginalis* showed the presence of several secretory transcriptional regulators and several ribosomally (ripp-like) and non-ribosomally (NRPS) synthesized antimicrobial peptides, which correlate with the anti-inflammatory condition in the vagina. Besides these, genetic components associated with CRISPR-Cas having Type IIA cas9 genes and TypeIE were also identified in the genome of *L. crispatus*, *L. jensenii* and *L. iners*. The cell-free supernatant of *L. crispatus* was observed to inhibit the growth of urinary tract pathogens (UTI) like *E. coli* and *K. pneumoniae*. Proteome analysis further identified the expression of antimicrobial peptides in *L. crispatus* strains.

Development of dipstick assay for the identification of preterm birth-associated vaginal microbiota

Seven bacterial species, *Lactobacillus crispatus*, *L. jensenii*, *L. gasseri*, *L. iners*, *Sneathia sanguinegens*, *Gardnerella vaginalis* and *Megasphaera* sp. as identified from our previous study (Shakti et. al., 2021) were selected for the development of the assay by Dr. Das and his team. PCR-Dipstick DNA Chromatography

multiplex assay precisely identified the presence of *Gardnerella*, *Sneathia*, *Megasphaera*, *L. iners*, *L. crispatus*, *L. gasseri*, and *L. jensenii* in the HVS samples of pregnant Indian women. The specificity (68.16%) and sensitivity (73.7%) of detection for term and preterm birth-associated bacteria were very high. The assay's positive predictive value, or the likelihood that an individual with a positive screening test has the condition, is 63.3% for preterm birth and 61.4% for term birth, respectively. The assay's negative predictive value, i.e., the per cent chance that a patient having a negative test is a true negative is 80% for preterm birth and 78.46% for term birth, respectively.

Way ahead

In future, **Dr. Das** plans to develop microbial consortia for improving reproductive health, reducing inflammation, and decolonizing allochthonous microbiota from the gastrointestinal tract.

Antibiotic Resistance Research

Antimicrobial resistance in clinically important microbes is today a global challenge. The dwindling antibiotic discovery pipeline has necessitated the discovery of alternatives to antibiotics.

Dr. Bhabatosh Das's lab has decoded whole genome sequences of more than 1000 MDR and XDR bacterial pathogens and identified genetic signatures that confirm AMR in Gram-negative ESKAPE pathogens. The team has also screened more than 4500 compounds (natural and synthetic) to identify antibiotic potentiators, synergistic molecules and novel antibacterial compounds that work specifically by neutralizing drug-modifying resistance enzymes.

Antimicrobial resistance heterogeneity among multidrug-resistant Gram-negative pathogens: Phenotypic, Genotypic and Proteomic analysis

The study included 2720 Gram-negative bacterial genomes including 203 Gram-negative strains collected from 5 different participating sites covering the North (n=2), South (n=2), and East-Central (n=1) India regions during 2019 to 2022. This predominantly comprised MDR Gram-negative extracellular pathogens such as *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*; and *Salmonella enterica* and *Serovar Typhimurium*, an intracellular pathogen. It was observed that the majority of the isolates (n=188/203) were resistant to at least one of the tested antimicrobial agents. To understand the regional variations within the Indian collection, WGS was performed on 203 isolates. Furthermore, the total cellular proteome of MDR pathogens in the presence and absence of routinely used antibiotics was studied.

Development of a 3 in 1 reporter strain assay for *in-vitro* high throughput screening of novel antibiotic potentiators to re-sensitize MDR pathogens

Dr. Das's team developed a 3 in 1 reporter strain assay for *in-vitro* high throughput screening of compounds to identify their antibiotic potentiation, synergistic or antimicrobial activity. The reporter strain library was constructed by cloning different resistance genes individually into an integrative vector under a constitutive promoter and transferring it into *Vibrio cholerae* N16961, an isolate more than ten times sensitive to most of the antibiotics as compared to the canonical *Escherichia coli*. The genetically engineered resistant reporter strains were used to screen Selleckchem natural compound library (n =803) and MedChemExpress FDA-approved compound library (n =3614) to identify antibiotic potentiators. Seventeen beta-lactam potentiators, eight aminoglycoside potentiators and thirty-four chloramphenicol potentiators with varying degrees of activity were identified through this reporter strain assay. Currently, the team is testing the identified potentiators for different antibiotics against MDR clinical isolates.

Way ahead

Dr. Das plans to develop biotherapeutics against MDR bacterial pathogens to reduce the burden of Sepsis, urinary tract infection (UTI), and Sexually transmitted infections (STI).

Neonatal Sepsis Research

Sepsis is a life-threatening multi-organ dysfunction syndrome caused by dysregulated immune responses to any bacterial/viral/fungal infection. Among newborns, pre-term neonates with 28-34 weeks gestation are most susceptible. India alone accounts for ~40% of the global burden of sepsis-related neonatal deaths. In India, the incidence of neonatal sepsis is at least 4-10 fold higher than reported by high-income countries.

Given the neonatal sepsis situation in India, **Dr. Krishnamohan Atmakuri's** group works towards a better understanding of neonatal sepsis, its pathogenesis by G-ve pathogens (prominent sepsis players), and

superior diagnosis of culture-negative sepsis. Towards that, recently in collaboration with the neonatal group of AIIMS, New Delhi (as nodal centre), four different Government Tertiary Hospitals in NCR and four other basic research Institutions of NCR, he and the neonatal group at AIIMS, New Delhi established a neonatal sepsis network (funded by DBT – referred to as Sepsis Program). In this program, Dr. Atmakuri's group evaluates (i) transmission dynamics that drive culture-positive sepsis (in collaboration with Dr. Bhabatosh Das); (ii) SNPs that associate



Dr. Krishnamohan Atmakuri

with neonatal sepsis (in collaboration with Dr. Rajesh Pandey, IGIB); and (iii) 18 gene host-specific transcripts for superior evaluation of culture-negative sepsis. In addition, his group is involved in identifying *Acinetobacter baumannii*-, *Klebsiella pneumoniae*- and *Escherichia coli*-specific secreted virulent proteins that reach the host's lung epithelial cells for establishing their niche. The sepsis program also involves Dr. Bhabatosh Das's group evaluating the progression and changes in the neonatal gut microbiota (bacteria, fungi and viruses) that are associated with their susceptibility or tolerance to sepsis. THSTI Biorepository team (led by Drs. Pallavi Kshetrapal and Shailaja Sopory) is making a repository of the clinical samples collected in this sepsis program.

Evaluation of transmission dynamics that drive blood culture-positive neonatal sepsis:

To evaluate the dynamics of transmission of the sepsis-causing pathogens especially among hospital-born neonates (in LMIC settings), investigators have been enrolling (from April 2022) pregnant women and their cognate neonate(s) who are born with a gestation period between 28-34 weeks and admitted to NICUs. While the clinical teams identify suspect cases for sepsis and sub-classify them into blood culture-positive and -negative cases, the microbiology teams at the hospitals, have been (i) swabbing the rectal and vaginal tracts of the pregnant mothers to culture pathogens of interest; (ii) culturing the suspected neonate's blood for pathogens of interest; and (iii) swabbing and culturing the immediate hospital environment of the neonates (54 distinct locations – NICUs, labour rooms and maternity operation theatres) for pathogens of interest. A set of rectal, vaginal (both mothers) and environmental swabs and pathogens isolates (of interest) were processed for DNA in Dr. Atmakuri's lab and metagenomics and whole genomic analyses (library preparation; metagenomics sequencing and bioinformatics analyses) at Dr Bhabatosh Das's lab. Out of a total of 146 blood culture-positive cases, 46% of the blood culture-positive cases were found to be infected with *Acinetobacter* sp. Similarly, 21%, 19% and 6% of the blood culture-positive cases were infected with *E. coli*, *Klebsiella pneumoniae* and *Pseudomonas* sp. respectively. There were a total of 524 blood culture-negative (clinically sepsis-positive) cases.

From the ongoing study, some of the findings are:

- Around 555 environmental reservoir samples and 195 pathogen(s) isolates have been processed for DNA extraction that would be subjected to either metagenomics and/or PCRs and/or whole genome sequencing.
- 50% of the thus far processed hospital reservoirs contain quantifiable levels of DNA indicating a lack of sterility.
- 1/3rd of immediate hospital environmental reservoirs (thus far processed) contain bacteria (by 16S rDNA PCRs).
- Preliminary metagenomic analyses indicate reservoirs rich with Proteobacteria dominated by Enterobacteriaceae family of pathogens including the four pathogens of interest.
- Microbiological cultures indicate immediate environments such as NICU, Labor room and Maternity OT replete with bacteria. Approx. 1/4th of all reservoirs contain one or more opportunistic pathogens. 1/3rd of these +ve reservoirs have either *Acinetobacter* sp., or *Klebsiella pneumoniae*, or *Pseudomonas* sp., or *E. coli*.
- NICUs' predominant reservoir for bacterial pathogens includes the four pathogens of interest.
- Despite 2/3rd of all rectal and vaginal swabs of pregnant women being positive for *E. coli*, maternity OT barely houses *E. coli*.
- Most mothers harbour *E. coli* in their rectovaginal tract (more so in the rectal tract).
- Antibiotics-resistant genes are most abundant and diverse in *Acinetobacter baumannii* (environmental isolates).
- NO neonate of mothers with Acb/Kp/Pa/*E. coli* (in the rectovaginal tract) are blood cultures +ve for the same pathogens.
- NO mother whose neonate is blood culture +ve for Acb/Kp/Pa/*E. coli* carries the same pathogen in their rectovaginal tracts.
- PREGNANT women/MOTHERS more often carry Acb/Kp/Pa/*E. coli* in their rectal than vaginal tracts.
- Data thus far indicates very poor vertical transmission (for now, presuming C-ves do not harbour these pathogens; confirmation: comparative genome analyses in progress).
- Horizontal transmission predominant (confirmation: comparative genome analyses in progress).

Way ahead

Drs. Atmakuri and Das labs will continue to process the blood isolates, evaluate the environmental, rectal and vaginal swabs for pathogens of interest and perform comparative whole genomic analyses to decipher the routes of transmission and hospital reservoirs for pathogens of interest.

Developing solutions for controlling surface bacterial contamination to curb hospital-associated infections

A combination therapy using Guanidinium derivative and nanoparticulate Ag(0) with biofilm inhibition and dispersion activity

Healthcare-associated infections (HAIs) are the most critical category of infections with the highest emergence of multidrug resistance. Surgical site infections (SSIs) are one of the most common causes of HAIs and are largely associated with biofilm-dominant infections. Inhibition and dispersion of biofilms are linked to addressing the issues associated with therapeutic challenges imposed by biofilms.

Dr. Susmita Chaudhuri and her team developed a self-assembled guanidinium–Ag(0) nanoparticle (AD-L@Ag(0))



Dr. Susmita Chaudhuri

hybrid gel composite for executing a combination therapy strategy for six difficult to treat biofilm-forming and multidrug-resistant bacteria. Improved efficacy was achieved primarily through effective biofilm inhibition and dispersion by the cationic guanidinium ion derivative, while Ag(0) contributes to the subsequent bactericidal activity on planktonic bacteria. Minimum Inhibitory Concentration (MIC), Minimum bactericidal concentration, Minimum Biofilm Inhibitory Concentration at 50% and 90% reduction (MBIC₅₀ and MBIC₉₀, respectively), and Minimum Biofilm Eradication Concentration (MBEC) for ESKAPE pathogens were demonstrated to show its potency in inhibition of biofilm formation, as well as eradication of mature biofilms. The observed efficacy of this non-cytotoxic therapeutic combination (AD-L@Ag(0)) was found to be better than that reported in the existing literature for treating extremely drug-resistant bacterial strains, as well as for reducing the bacterial infection load at a surgical site in vivo (BALB/c model). Thus, AD-L@Ag(0) could be a promising candidate for anti-microbial coatings on surgical instruments, wound dressing, tissue engineering, and medical implants. This study resulted in two peer-reviewed publications and a patent application for the same has been filed.

List of Collaborators

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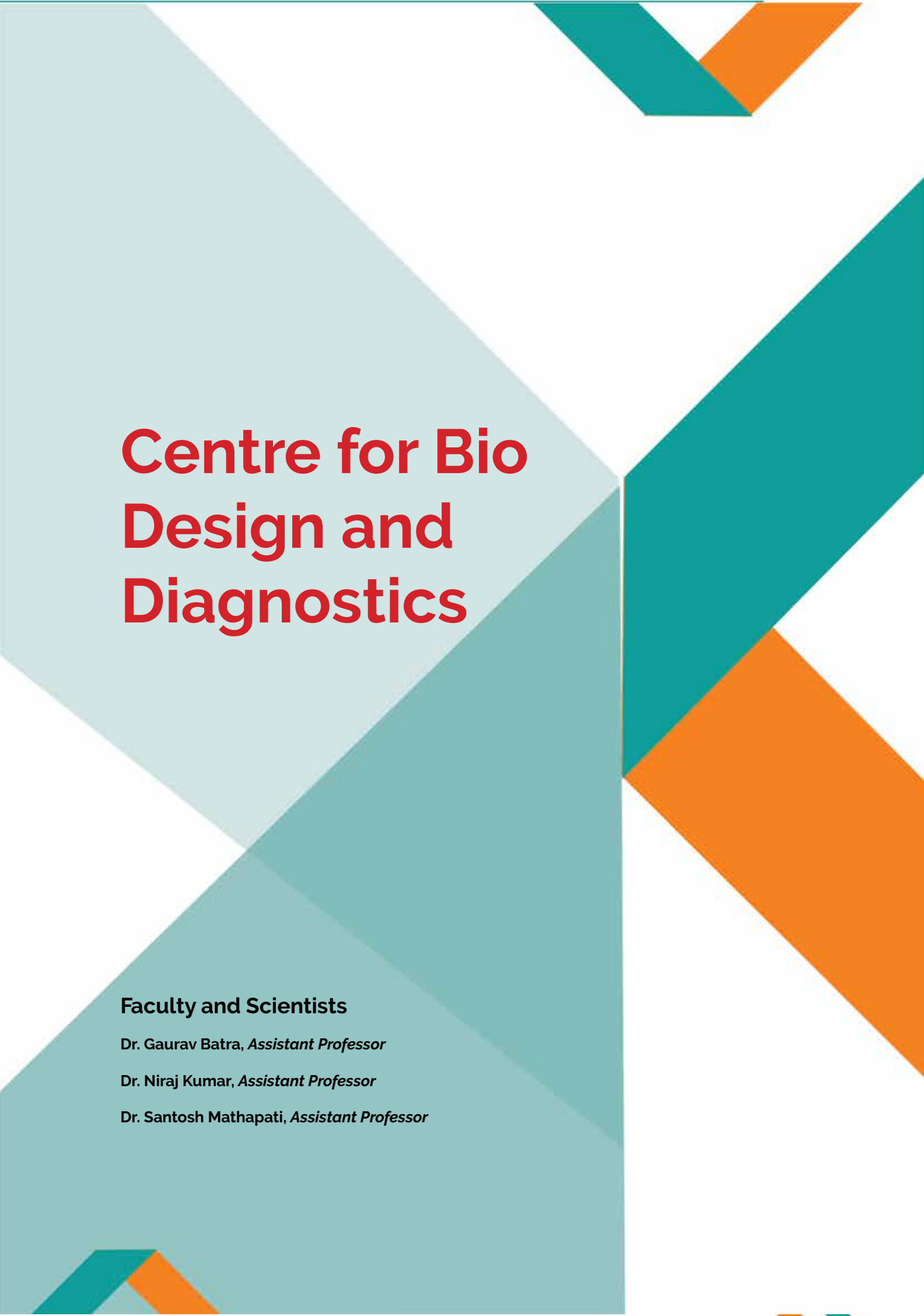
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Hospitals involved in the Sepsis program.

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Centre for Bio Design and Diagnostics

Faculty and Scientists

Dr. Gaurav Batra, *Assistant Professor*

Dr. Niraj Kumar, *Assistant Professor*

Dr. Santosh Mathapati, *Assistant Professor*

The Centre for Biodesign and Diagnostics (CBD) is engaged in developing innovative in vitro diagnostics assays. CBD is also involved in the development of biomaterial-based tissue implants, particularly engineering extracellular matrix and synthetic polymer-based surgical patches and injectable hydrogels for tissue repair.

Development of newer SARS-CoV-2 ELISAs to study the humoral immune response

During the reporting period, **Dr. Gaurav Batra's** research team made significant advancements in the development of newer ELISAs to study the humoral immune response against SARS-CoV-2. Recognizing the global concern surrounding the emergence of the Omicron variant, they successfully developed an Omicron-specific quantitative IgG ELISA. This innovative assay allows for the quantification of IgG antibodies specifically targeting the Omicron variant. By utilizing this assay, valuable insights into the immune response elicited by Omicron infection and its impact on vaccine-induced immunity were gained.



Dr. Gaurav Batra

Development of novel immunoassays for the detection of anti-dengue antibodies without cross reactivity with antibodies induced by non-dengue flaviviruses

Dr. Batra's team has developed innovative immunoassays for the detection of anti-dengue antibodies (IgG and IgM) that do not exhibit cross-reactivity with antibodies induced by non-dengue flaviviruses. The IgG and IgM immunoassays are meticulously designed to accurately identify antibodies specific to the dengue virus, ensuring no interference from antibodies triggered by non-dengue flaviviruses. These assays hold significant value in terms of their application in diagnosis, surveillance, as well as vaccine trials and studies.

Anti-Microbial Resistance (AMR) Diagnostics

The unavailability of rapid diagnostics for pathogen identification and antimicrobial- susceptibility-testing (AST), has been a significant factor for the emergence/spread of AMR. **Dr. Niraj Kumar** and his team have been working to develop rapid, user-friendly and cost-effective diagnostics for pathogen identification and AST profiling. They are also working to identify predictive biomarkers of the emergence of AMR among pathogens so that the antibiotics can be marked for their selective regulation before they become completely ineffective for the purpose. Over the last year, Dr. Kumar's team have focused on pathogen identification. They have developed PCR-based singleplex and multiplex assays for the identification of ESKAPE pathogens and are currently working to validate them. They have also developed a panel of resistant cells of the blood-stream pathogen, *K. pneumoniae*, representing early-, mid- and late-stage antimicrobial resistance emergence using gradually increase doses of last-resort antibiotics. Presently, they are also focusing to identify early biomarkers for the emergence of AMR using OMICS-based approaches.



Dr. Niraj Kumar

Way ahead

Dr. Kumar plans to validate the developed single/multi-plex PCR assays for ESKAPE pathogen identification. He also plans to identify early-biomarker for the emergence of AMR.

Mammalian bioprocessing

Nearly 70% of all recombinant therapeutics are produced in Chinese Hamster Ovary (CHO) cells. However, the cost of such therapeutics remains high. **Dr. Niraj Kumar** and his team have been working towards improving yield from CHO cells. They have fetched a number of potential master-orchestrator gene-of-interest (GOIs) from published literature and evaluated the expression of potential master-orchestrator GOIs to regulate improve the performance of CHO-cell factories.

Way ahead

In future, Dr. Kumar plans to validate the impact of identified GOIs on cell growth and recombinant protein productivity.

Biological, medical devices using human and animal tissues and polymeric scaffolds, and Pluripotent stem cell (PSC)-derived organoids

Dr. Santosh Mathapati and his team work towards developing biological and medical devices using human and animal tissues and polymeric scaffolds. His team is also working on developing Pluripotent stem cell (PSC)-derived organoids.

Placental hydrogels for soft tissue repair

Placental tissue presents minimal ethical concerns when used, making it a promising source of materials for tissue engineering and regenerative medicine applications due to its accessibility and resemblance to fetal origin tissue. To facilitate constructive and functional tissue remodelling in various clinical applications, extracellular matrix (ECM) bioscaffolds prepared from decellularised tissues are used. Dr Mathapati's team carried out



Dr. Santosh Mathapati

the decellularisation of placental tissue (full term, devoid of amniotic membrane (AM) and umbilical cord) and characterised it. They have also completed the synthesis and characterisation of pregel, needed for hydrogel synthesis. The preparation of pregel to hydrogel and its characterization is currently in progress.

Biocompatible amniotic membrane patch for soft tissue repair

The processes of tissue growth and remodelling are closely associated with the generation, construction, and alteration of the extracellular matrix (ECM) and other proteins that are transiently up-regulated. Dr Mathapati's team developed different strategies to enhance the biocompatibility, mechanical strength, and antimicrobial properties of AMs. Sodium deoxycholate and Triton-X 100 were used to decellularize AM and cross-linked with glutaraldehyde (GA). The cross-linked AM tissues were further treated with detoxifying agents. The cross-linking efficiency was evaluated through various methods, including uniaxial tensile testing, enzymatic degradation, and quantification of free amine groups. The detoxification treatment showed a significant reduction in free aldehydes and cytotoxicity, thereby significantly improving the safety and efficacy of the AM tissues. The findings of this study suggest that an acellular-crosslinked-detoxified AM has the potential to serve as a promising scaffold for regenerative medicine and tissue engineering applications.

Pluripotent stem cells derived hepatocytes for drug discovery and disease modelling

The utilisation of experimental modelling of human disorders is an effective way to define the cellular and molecular mechanisms underlying diseases, leading to the development of effective therapies. However, traditional animal models have limitations. Dr. Mathapati's team has successfully differentiated pluripotent stem cells into hepatocytes and characterized them. Currently, they are in the process of establishing a hepatic organoid model derived from pluripotent stem cells. The researchers plan to utilize this model for disease modelling, such as nonalcoholic fatty liver disease.

Way ahead

Dr. Mathapati plans to develop commercially viable and value-added products for soft tissue repair. He also plans to develop pluripotent stem cells based hepatic organoids for drug testing and disease modelling.

List of Collaborators

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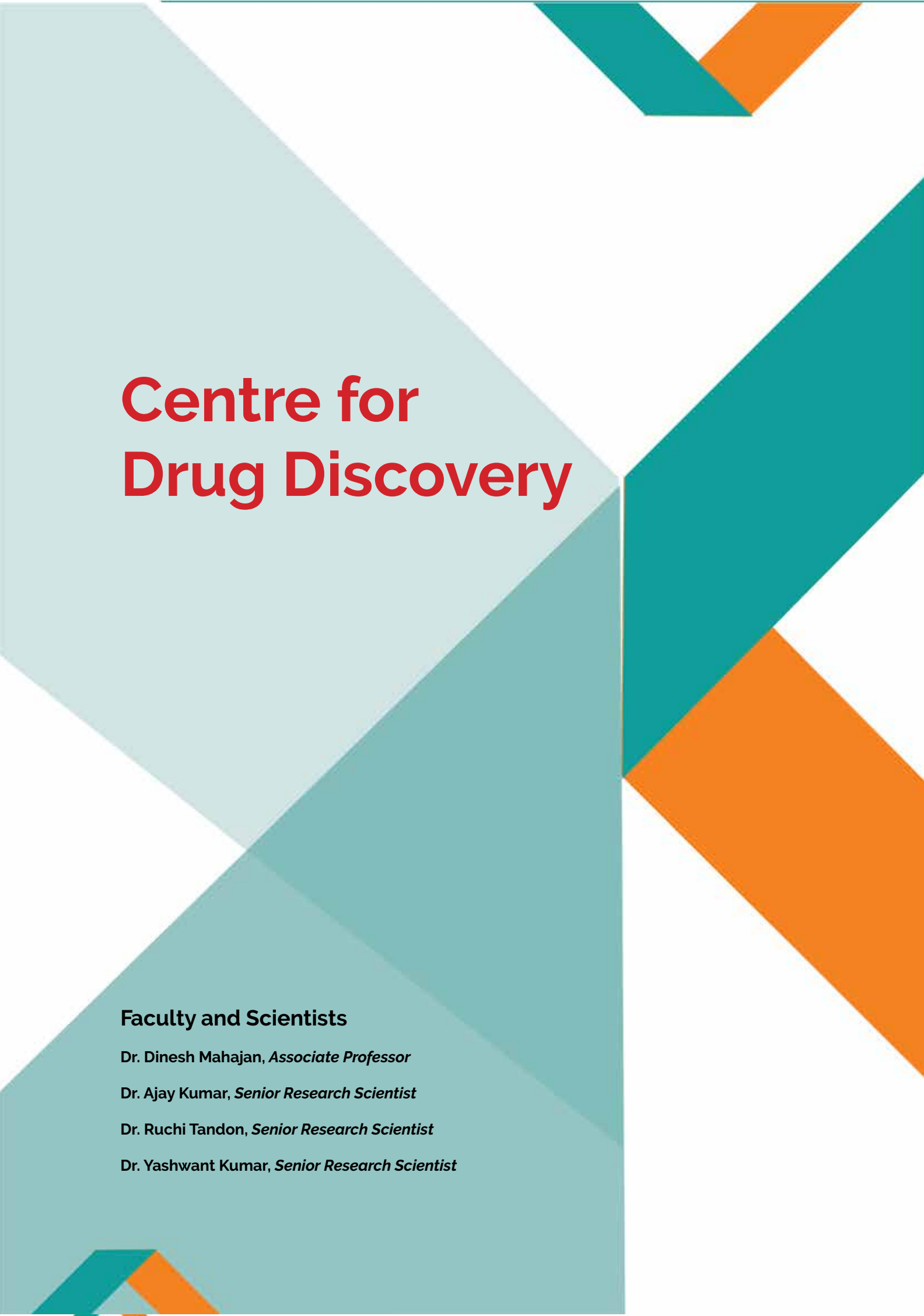
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Centre for Drug Discovery

Faculty and Scientists

Dr. Dinesh Mahajan, *Associate Professor*

Dr. Ajay Kumar, *Senior Research Scientist*

Dr. Ruchi Tandon, *Senior Research Scientist*

Dr. Yashwant Kumar, *Senior Research Scientist*

The major focus of this centre is to translate the findings of disease biology research groups to the development of new drug leads for therapeutic development for clinical evaluation.

Dr. Dinesh Mahajan and his group work in the area of pre-clinical drug discovery with a major emphasis on medicinal chemistry and DMPK (Distribution, Metabolism and Pharmacokinetic) studies. The group is also focused on the establishment of a non-alcoholic fatty liver disease (NAFLD) based mice model to study disease progression as well as to facilitate drug discovery efforts.

Therapeutic development for non-alcoholic fatty liver disease (NAFLD)

Non-Alcoholic Steatohepatitis (NASH) is a liver manifestation of NAFLD characterized by liver steatosis, inflammation, and injury of liver cells with or without fibrosis. There is no FDA-approved treatment for NASH and for preventing/ halting the progression of fibrosis, except for India-specific approval of Saroglitazar. Dr. Mahajan's group has established high-fat diet-induced NAFLD phenotype in mice at THSTI. The established animal model is being used to study the efficacy of identified small molecule drug lead(s) as well as herbal extracts with an aim to develop a new therapeutic for NAFLD. For development of herbal extracts, the team has established a collaboration with Dabur India Pvt Ltd. Under this joint collaboration, team has identified few herbal extracts for detailed efficacy and safety studies in animal models.

Way ahead

Dr. Mahajan's group is working towards understanding the mode of action and pharmacology of the newly identified drug lead(s) and generating more analogues around the lead to understand Structure Activity Relationship (SAR) and pharmacokinetic profile. Dr Mahajan plans to continue the team's efforts in performing detailed efficacy and safety studies of the selected herbal extracts in mice.

Phenotypic Drug Discovery in NAFLD/NASH

Dr. Ajay Kumar and his group have screened small molecule libraries and molecules that have been designed and synthesized in-house at THSTI, using either phenotype-based or target-based approaches.

Using preclinical phenotypic models of NAFLD/NASH, the team identified two small molecules from the NCE library using a phenotype-derived approach (DR62 and DR176) and another couple of promising small molecules using a target-based approach (C04 and C06). These selected hit candidates showed no detrimental effect on cell viability in the hepatocytes and were tolerated by the cells at saturating concentrations. They showed promising efficacy to mitigate LPS-induced inflammation in the PMA-differentiated macrophage-like cells. When evaluated in

the stellate cell line for their efficacy to resolve the TGF- induced fibrotic phenotype, the expression of the collagen gene was significantly corrected in the treatment group as compared to TGF- induced compared to the control group. As compared to Saroglitazar, the shortlisted small molecules revealed comparative efficacy for resolving both inflammation and fibrosis phenotypes.



Dr. Dinesh Mahajan



Dr. Ajay Kumar

In a collaborative effort between THSTI and Dabur India limited, Dr. Kumar and his team investigated nine well-characterized herbal extracts (Mustak, Bhumiamalika, Haritaki, Pippali, Guduchi, Haridra, Sharpunkha, Chirayta and Kalmegha) and a herbal formulation (Hepano) in a preclinical mice model of NAFLD. While Pippali, Haritaki and Bhumiamalika showed some effect on insulin resistance developed in the HFHFD-fed group, haridra presented efficacy to mitigate liver TG levels. Histochemical analysis of liver tissue from mice treated with Sharpunkha, Chirayta and Kalmegha highlighted the significant mitigation of steatosis as well as hepatocyte ballooning when compared to their HFHFD-fed but untreated counterparts. Findings from this study were approved for further investigations by DBT-BIRAC to understand the MoA of Sharpunkha, Chirayta and Kalmegha in a chronic and better-characterized rodent model of NAFLD/NASH. Characterization of mice model is currently underway where Dr Kumar's group is evaluating the development of disease phenotype in mice after feeding them with different fat rich diets (high fat diet, HFD; high fat choline deficient diet, HFCDD; high fat high fructose diet, HFHFD).

Drug repurposing for NAFLD Drug Discovery

Dr Kumar's group screened a commercially available FDA-approved compound library (n = 3614) in hepatocyte cell lines for their anti-steatotic efficacy. Anti-steatotic efficacy was observed for 54 compounds which will be further investigated for other disease phenotypes (inflammation and fibrosis) and subsequently taken up for validation in rodent models of NAFLD/NASH.

Way ahead:

Dr Kumar plans to explore the shortlisted small molecules including DR62, DR176, C04 and C06 for a proof-of-concept study in the CDHF-fed mice model to titrate their dosage and evaluate their tolerance/toxicity in animals. Efficacy studies to evaluate Sharpunkha, Chirayta and Kalmegha (alone as well as in combination) will be conducted in a mice model of NAFLD using a fat-rich diet. The group will continue to screen the FDA-approved drug candidate library for other NAFLD/NASH phenotypes including inflammation and fibrosis.

Establishment of Human Liver Organoid and 3D Spheroid Platforms

Dr. Ruchi Tandon's lab has established human liver organoid platform to understand the pathophysiology and to conduct drug discovery research on NAFLD. Her lab has developed liver organoids using hepatocytes derived from the liver tissues of healthy humans. This model has been standardized by gene expression and immunofluorescence studies to validate the expression levels of markers of hepatocyte function and stem cell properties. Her lab has established a model of steatohepatitis using organoids as an *in vitro* screening platform to identify potential therapeutic options for the management of NAFLD. In order to understand the pathophysiology and identify stage-specific molecular signatures of NASH and its progression to hepatocellular carcinoma, Dr Tandon's group has developed organoids using liver biopsy tissues from patients. Dr. Tandon's



Dr. Ruchi Tandon

lab has also established a multilineage 3D spheroid model using Hep-G2 and LX2 cells to evaluate the effect of test substances on key hallmarks of NAFLD such as steatosis, inflammation and fibrosis. Several plant extracts and small molecule compounds from current discovery programs have been evaluated

in this model. Dr Tandon's group has identified the potential of novel FXR modulators, C04, C05 and C06 in inhibiting the palmitic acid(PA)-induced mRNA expression levels of markers of fatty acid uptake, inflammation and fibrosis using the 3D spheroid model. Using Seahorse XFp technology, C06 showed an improvement in the PA-induced decline in OCR and ECAR parameters associated with mitochondrial health using Hep-G2 cells.

Drug-Repurposing Approach to Identify Small Molecules Hits

In order to identify compounds for the management of NAFLD using the drug re-purposing approach, Dr Tandon's group screened a commercially available library of >3200 compounds that are either approved by the FDA or are in some stage of clinical evaluation. 32 new hits were identified in this assay for their anti-steatotic potential using Hep-G2 cells. Detailed pharmacological evaluation of these hits is in process.

Identification of a Gut Microbiota-derived Metabolite for Improvement of the NAFLD Parameters in an NLRP3 Dependent Manner using C57 mice fed with HF-HF Diet

Dr Tandon's group has conducted *in vitro* and *in vivo* studies to validate the role of inflammasomes in the pathophysiology NAFLD. Increased mRNA expression of NLRP3 and its downstream family members were observed in the liver tissues of mice fed with high fat-high fructose and methionine-choline deficient diets. The group has identified a gut microbiota derived metabolite of a dietary component in modulating the key phenotypes of NAFLD in NLRP3 dependent manner in C57/BL-6 mice fed with high fructose and high-fat diet.

Anti-inflammatory Potential of Ayush herbal extracts using in vitro and in vivo models of inflammation

Aqueous extract of *Withania somnifera* (WS) was found to show amelioration of LPS-induced inflammatory changes in the in vitro cell-based and mice models of inflammation in a TLR 4 dependent manner. The results indicate the potential of clinical evaluation of WS extract in COVID-19 patients with a high propensity for lung inflammation.

Way Forward

Dr. Tandon further plans to utilize the potential of liver organoid model in conducting the basic and translational research including regenerative therapy. To understand the pathophysiology of NAFLD, Dr. Tandon plans to conduct multi-OMICS studies using organoids derived from liver biopsy tissues of NAFLD patients and to identify key molecular signatures for drug discovery and biomarker studies. Her group also plans to conduct detailed pharmacological profiling of 32 hits identified as a result of high-throughput screening of library compounds *in vitro* using organoids and 3D spheroid models followed by their efficacy studies in mouse models of NAFLD. She also plans to establish a humanized mouse model of NAFLD using organoids derived from liver tissue samples from NAFLD patients.

Biomarker discovery and pathogenesis of NAFLD

Dr. Yashwant Kumar's lab is working on the discovery of a non-invasive biomarker and understanding dyslipidemia, inflammation, and fibrosis associated with non-alcoholic fatty liver disease (NAFLD) in humans and animal models. He uses cutting-edge mass spectrometry metabolomics, lipidomics, and data analysis approaches to understand altered pathways.

They used multi-omics approaches and found significant increases in bile acids, inosine, and 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF) in patients with NASH compared to healthy controls. In a lipidomics study, they found

altered phospholipids, lysophospholipids, and ceramides in NASH. The results provide insights into the differences between control and NASH patients and the underlying pathophysiology, which could aid in the development of therapeutics aimed at altered metabolic processes. In addition, Dr. Yashwant's group is actively working on developing tools and databases for interpreting large amounts of data generated from metabolomic and lipidomic studies.

Way ahead

Dr. Kumar plans to apply Systems Biology and Omics technologies in NAFLD research that may offer a transformative opportunity to unlock the complexities of the disease.



Dr. Yashwant Kumar

List of Collaborators

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Dr. Shalimar, AIIMS
Dr. Sanjay Banerjee, NIPER, Guwahati
Dabur India Pvt Ltd

Dr. Ajay Kumar

Dabur India Pvt. Ltd.

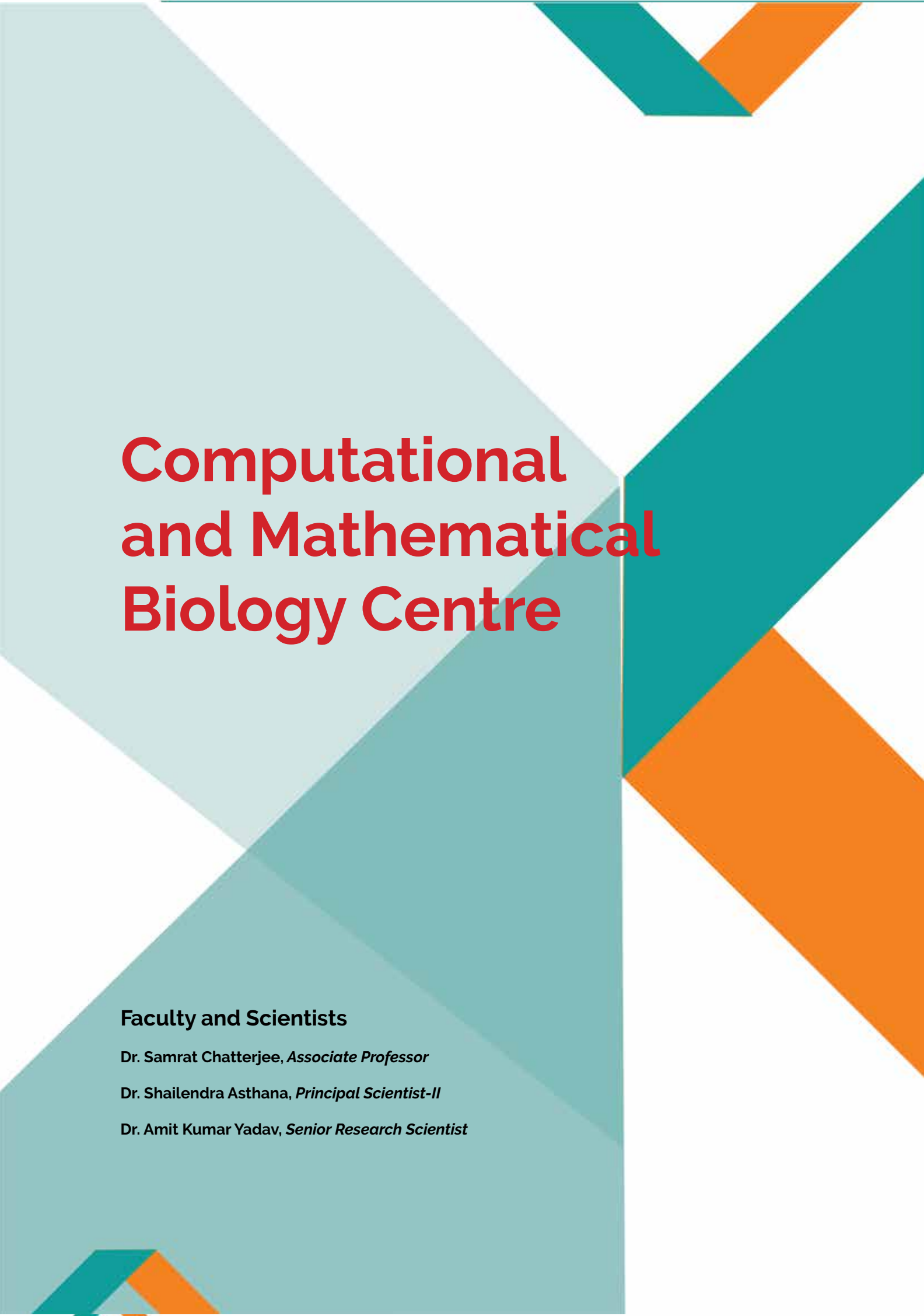
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Dr. Yashwant Kumar

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Computational and Mathematical Biology Centre

Faculty and Scientists

Dr. Samrat Chatterjee, *Associate Professor*

Dr. Shailendra Asthana, *Principal Scientist-II*

Dr. Amit Kumar Yadav, *Senior Research Scientist*

The Computational and Mathematical Biology Center (CMBC) works on big data analysis, fundamental problems and method development in omics research, structural bioinformatics, and mathematical modelling towards network and systems biology. The centre applies these breakthrough developments towards translational outcomes in infectious and non-communicable diseases. The group also develops novel algorithms, tools and pipelines for disease research and has forged strong collaborations within and beyond THSTI with biologists as well as clinicians attacking challenging problems of data deluge and problems of national importance.

Mathematical Modelling and Systems Biology

Using mathematical and computational tools, **Dr. Samrat Chatterjee's** lab works towards understanding the mechanism of a biological phenomenon. One of their research areas is to capture the underlying mechanisms of disease progression and identify potential drug targets. Another area of research involves the identification of molecular signatures associated with a disease and its progression using machine-learning (ML) algorithms.



Dr. Samrat Chatterjee

Understanding disease dynamics using mathematical models

A minimal model of glucose-stimulated insulin secretion process explores factors responsible for the development of type 2 diabetes (T2D)

Dr. Chatterjee's team analysed the GSIS process through a six-dimensional model incorporating calcium and ATP key factors responsible for the progression of diabetes in insulin resistance (IR) conditions. The team has established a model by simulating both the normal and the insulin resistance-induced hyperglycemic conditions. Their analysis revealed the possible factors responsible for the impaired GSIS process in IR, whose dysfunction can lead to T2D. Finally, using the parameter recalibration analysis, they uncovered the potential therapeutic strategies for compensating the insulin secretion-reducing alterations that could eventually help prevent the disease progression.

Bistability regulates TNFR2-mediated survival and death of Tregulatory cells

Dr. Chatterjee and team constructed an ordinary differential equation (ODE)-based model to capture the mechanism of cell survival and apoptosis in T-regulatory (Treg) cells via tumour necrosis factor receptor 2 (TNFR2) signalling. The sensitivity analysis reveals that the input stimulus, the concentration of tumour necrosis factor (TNF), is the most sensitive parameter for the model system. The model showed that the cell goes into survival or apoptosis via bistable switching. In order to understand how stimulus strength and feedback strength influence cell survival and death, they computed bifurcation diagrams and obtained cell fate maps. The results indicate that the elevated TNF concentration and increased c-Jun N-terminal kinase (JNK) phosphorylation are the major contributors to the death of T-reg cells. Finally, the system was studied under stochastic perturbation to see the effect of noise on the system's dynamics. They observed that introducing random perturbations disrupts the bistability, reducing the system's bistable region, which can affect the system's normal functioning.

Developing tools for identifying potential drug targets

Understanding noise in cell signalling in the prospect of drug-targets

The introduction of noise to signals can alter central regulatory switches of cellular processes leading to

diseases. Dr. Chatterjee's group works to understand the noise tolerance of motif structures in the cell signalling processes. The vulnerability of a node to noise could be a significant factor in causing signalling error that needs to be controlled. They developed stochastic differential equation (SDE) based mathematical models for different network motifs with two nodes and studied the association between motif structure and signal-noise relation. A two-dimensional parameter space analysis on motif sensitivity with noise and input signal variation was performed to classify and rank the motifs. The team has proposed a theoretical framework to identify nodes from a network as potential drug targets. They applied this mathematical formalism to three cancer networks to identify drug targets and validated them with existing databases.

konnnect2prot: a web application to explore the protein properties in a functional protein-protein interaction network

Dr Chatterjee and his team have developed a web application, 'konnnect2prot' (k2p), which can generate context-specific directional PPI networks from the input proteins and detect their biological and topological importance in the network. They pooled together a large amount of ontological knowledge, parsed it down into a functional network, and gained insight into the molecular underpinnings of the disease development by creating a one-stop junction for PPI data. k2p contains both local and global information about a protein, such as protein class, disease mutations, ligands and PDB structure, enriched processes and pathways, multi-disease interactome and hubs and bottlenecks in the directional network. It also identifies spreaders in the network and maps them to disease hallmarks to determine whether they can affect the disease state or not. This application was launched in 2021. It was further refined and has now been published in a highly reputed journal 'Bioinformatics' by Oxford Press.

Big data analysis through network study and machine learning tools

The present study used an ML-based approach to analyze RNA-Seq data in cancer. Dr Chatterjee's team started with the basic principles of ML-based analysis and later enacted the understating on a breast cancer dataset. Among the rabble of available methods for identifying disease-associated genes, they opted for the ANN method which helped to capture 158 deeply associated genes (DAGs) that are possibly playing a role in breast cancer's pathophysiology. The choice of a neural network-based method for identifying DAGs provided the advantage of extracting condition-specific associations, which is not possible in molecular interaction network-based approaches. To signify the importance of DAGs, the team opted for a PPI network analysis approach. They extracted the human interactome information from the STRING database and constructed a network of the genes obtained from the feature selection method. The interaction of this network was both physical and functional. Topological analysis was carried out in the network to study the degree of centrality and clustering affinity. The analysis revealed that the DAGs are among the topologically strong proteins in the network and thus very important in disease progression and possess high spreading power in the network. A significant association was observed between the DAGs and breast cancer, hypothesizing that these genes are possibly responsible for the disease's pathology.

Way aheadl

Dr Chatterjee plans to validate the mathematical model of the glucose-stimulated insulin secretion process with experimental evidence in collaboration with Biologists. With regard to understanding noise in cell signalling, Dr. Chatterjee plans to do a more in-depth study to get more mechanistic insights and do experimental validation. He plans to increase more updated versions of k2p which will enhance the analysis part by providing other centrality measures and structural insights and expanded for advanced users, where they could upload their own transcriptomic/proteomic data, which would be analysed by the k2p to identify triggers/targets.

Computer-assisted Drug Discovery, Computational Biophysics and Structural Bioinformatics

Dr. Shailendra Asthana and his team use high-performance computing and theoretical approaches (molecular dynamics simulations and computational chemistry) in close collaboration with experimental groups to provide meaningful insights by interpreting complex molecular data to guide future experiments and design and discover therapeutics. His lab works to understand the protein structures and their conformational changes at the atomic level to underscore the microscopic critical recognition processes and their types. They have established a standard pipeline for the discovery of therapeutics against different disease-oriented drug targets by using conventional and advanced computational tools which encompasses computational biophysics, structural bioinformatics and Computer-aided drug discovery (CADD) techniques.



Dr. Shailendra Asthana

FXR targeted drug discovery for partial agonist designing

Using molecular docking simulations and residue-wise communication network analysis, Dr Asthana's team has identified the structural regions which are flexible with a partial agonist (PA) but frozen with an agonist. Also, the network analysis identified the considerable changes between an agonist and PA in biologically essential zones of FXR. Furthermore, the thermodynamic profiling suggested the methionine residues seem to be responsible for the recruitment of PA. The team has also discovered agonists belonging to three different chemical classes that have been tested in cell lines in collaborative work with Dr. Ajay Kumar. They are now analysing these compounds in 3-D organoid models in collaboration with Dr. Ruchi Tandon.

Modulating ASK1 activity via protein-protein interactions

Apoptosis-signaling kinase 1 (ASK1) hyperactivity has been identified as a key contributor towards hepatic inflammation, apoptosis, and liver fibrogenesis which is a hallmark of NASH. Dr. Asthana and his team are working towards exploring an alternate approach to modulate ASK1 +ve and -ve regulators via protein-protein interactions (PPIs) to modulate ASK1 activity via an allosteric route to mitigate its biological activity rather than a complete blockage by targeting catalytic site. They are exploring 14-3-3, CFLAR and TRX that allosterically inhibit ASK1. The results showed that 14-3-3 allosterically regulates ASK1 by modulating the catalytic site as it is not available for endogenous substrates for inactive-to-active transition.

Development of Autophagy inducers

Dr. Asthana and his team are working to understand autophagy by targeting autophagy regulatory proteins in a protein-protein interaction (PPI) manner to establish a platform as a broad therapeutic application against multiple diseases. Earlier, the group had mapped Beclin-1 and +ve and -ve regulators and designed 20 peptides. The group observed five peptides viz., P3T, P5T, P7T, P8T and P13T that were found to be active, *mTOR independent* and reduced or minimal toxicity *in vitro*. *In-vivo* experiments were carried out in IBD and salmonella mice models and the results indicated that peptide P7T was the most effective. This peptide was redesigned using computational approaches, followed by experimental assays. Among designed P7T derivatives, P7T_R was found to have improved autophagy induction compared to P7T and also against Tat_D11, a commercially available autophagy inducer from Novus Biologicals (**The US patent filed**).

Conformational-locking antibodies of PD-1 and PD-L1 for the discovery of cryptic pockets to design small molecule inhibitors

Dr. Asthana's lab also works on mapping protein-mABs interaction sites in their static (crystal/co-crystals) and dynamic states using large-scale conventional and accelerated molecular dynamics simulation to monitor the conformations-driven transition states at their bound and unbound states of PD-1/PD-L1 with mABs. The group is working to establish a pipeline to identify small molecules that can effectively bind to either the orthosteric or allosteric pockets of PD-1. They used a guided virtual screening workflow to identify hits from ~7 million compounds library, which were then clustered based on structural similarity and assessed by interaction fingerprinting. The selective and diverse chemical representatives were subjected to MD simulations and binding energetics calculations to filter out false positives and identify actual binders. Advanced methods such as Binding pose metadynamics calculations, confirming the stability of the final hits in the pocket. This study emphasizes the need for an integrated pipeline that uses molecular dynamics simulations and binding energetics to identify potential binders for the dynamic PD-1/PD-L1 interface, due to the lack of small molecule co-crystals. Only a few potential binders were discovered from a large pool of molecules targeting both the allosteric and orthosteric zones. The results suggest that the allosteric site has more potential than the orthosteric site for inhibitor design. The identified "computational hits" hold potential as starting points for in vitro evaluations followed by hit-to-lead optimization. The group established a computational pipeline for exploring and enriching both the allosteric and orthosteric sites of PPI interfaces by mining of antibodies *"a tough but indispensable nut to crack"*

Structural biochemistry to characterize the binding site of Ubiquitin Specific Proteases7 (USP7) for anti-cancer drug discovery

Dr. Asthana's lab also works on Ubiquitin specific protease-7 (USP7) to identify novel anti-cancer molecule(s). They elucidated atomic-level insights from protein–ligand perspective and established a structure–activity link between USP7 inhibitors using classical and advanced molecular dynamics simulations combined with linear interaction energy and molecular Mechanics-Poisson Boltzmann surface area. To identify USP7 inhibitors, the team studied 1) a dynamically stable full-length model of USP7 (1102 amino acids), 2) the binding site architecture of USP7 catalytic domain (USP7-CD), 3) the molecular recognition mechanism of USP7 and its substrates 4) activation/inactivation mechanism of USP7, and 5) variable binding potencies of USP7 inhibitors despite several similarities. Their results demonstrate the critical role of blocking loop 1 in allosteric inhibition and enhanced binding affinity.

Collaborative work for structure-based small molecule drug discovery:

(a) Mycobacterium tuberculosis (MTB)

Dr. Asthana's group is exploring various MTB proteins in collaboration with experimental group of THSTI, Drs. Ramandeep singh, Krishnamohan Atmakuri and Amit Pandey. The group establish the structure-based virtual screening platform to explore multiple targets such as ArgA, PPK-1, LeuA, MetX, HupB and SerB2 using in-house curated compounds for initial identification in form of "hits".

(b) Dengue

Dr. Asthana's group in collaboration with Dr. Prasenjit Guchhait (RCB), Dr. Sankar Bhattacharyya (THSTI) and Dr. Rambabu Gundla (Gitum University) discovered a series of thiazole linked Oxindole-5-Sulfonamide

(OSA) derivatives by targeting RNA-dependent RNA polymerase (RdRp) of Dengue virus. In our previous study, the compound OSA-15 was identified as a hit molecule which was confirmed in ex-vivo studies. Here, in this work, a series of analogues were designed and synthesized by replacing the difluoro benzyl group of OSA-15 with different substituted benzyl groups. The group identified other potential candidates viz., OSA-15-17, OSA-15-DM and OSA-15-17-DM and the latter was observed to be more efficacious. The extensive molecular dynamics simulation studies indicate the possible binding of identified hits to DENV RdRp. The identified oxindole derivatives are novel compound series that can inhibit Dengue replication and work as non-nucleoside inhibitors (NNI) that work is in progress to explore further. (**M. Venkat et. al. 2023, Bio-organic chemistry, and patent PCT/IN2021/050596.**).

(c) Bovine Viral Diarrhoea Virus (BVDV)

The development of potent non-nucleoside inhibitors (NNIs) could be an alternate strategy to combating infectious bovine viral diarrhoea virus (BVDV), other than the traditional vaccination. RNA-dependent RNA polymerase (RdRp), an essential enzyme for viral replication, is one of the primary targets for countermeasures against infectious diseases. The reported NNIs, belonging to the classes of quinolones were analysed computationally. The results indicate that the quinoline inhibitors bind at the template entrance channel of RdRp, which is governed by conformational dynamics of interactions with loops and linker residues. These structural and mechanistic insights will help in designing improved antivirals.

(d) Designing immunogenic peptides against SARS-CoV-2 and Monkey Pox

Dr. Asthana's lab is also working to establish immunoinformatics platform by merging different freely available software and tools using *in-house* scripts. Furthermore, the identified antigenic/immunogenic peptides the molecular recognition was characterized using computational biophysics against SARS-CoV-2 and monkey-pox in collaboration with Dr. Sweetly Samal.

Big data, Multi-Omics and Biomedical Informatics

Dr. Amit Kumar Yadav works on the analysis of omics data using bioinformatics to understand Non-Alcoholic Fatty Liver Disease (NAFLD) and Anti-Microbial Resistance (AMR). His team works on the proteomics data for studying NAFLD and uses Next-Generation Sequencing (NGS) data for detecting and understanding AMR. His team also develops methods for proteogenomics analysis.

Prioritization of Disease Proteins and Metabolites in NAFLD and NASH Using Big-Data Approaches

Dr. Yadav's team is working on big-data analytics for pursuing novel and effective biomarkers for stage-specific NALFD biomarkers. They previously developed and applied algorithms to gain newer insights into disease biology and progression by large-scale identification of posttranslational modifications (PTMs) from shotgun proteomics data.

His team has mined a comprehensive list of genes previously reported to be associated with NAFLD or nonalcoholic steatohepatitis (NASH) and prioritized the list to reveal 18 proteins (12 in NAFLD, 4 common and 2 in NASH), that may be used either



Dr. Amit Kumar Yadav

for disease identification or for therapeutic target purposes. When this list was cross-referenced within known metabolite interactions, they revealed several metabolites like arachidonic acid, palmitic acid, oleic acid which are already being studied for their role in fatty liver diseases. These molecules are now being studied as a priority list for measuring in targeted assays for any expression changes in NAFLD and NASH patients.

MetaResDB: A Comprehensive Meta-Database for Mining Resistome (ARGs) and Accelerating Antimicrobial Susceptibility Testing (AST)

Dr. Yadav's group in collaboration with Dr. Bhabatosh Das, has integrated the antimicrobial resistance genes (ARGs) from many publicly available sources, both computational as well as manually curated, to develop a comprehensive in-house database called **MetaResDB**. The database integrates information from various public databases, including CARD, MegaRes, NCBI, aRG-aNNoT and ResFinder. **MetaResDB** aims to streamline antimicrobial susceptibility testing (AST) by providing a consolidated resource for the rapid identification of pathogens and the detection of resistance to specific antibiotics. They also developed a web server that integrates MetaResDB to provide a comprehensive platform for mining antimicrobial resistance genes (ARGs) from genomics and metagenomics data for users. The web server utilizes an integrated BLAST service to predict ARGs and their associated mechanisms of resistance. MetaResDB provides users with a user-friendly web server interface that allows for the submission of genomics or metagenomics data for analysis. The web server accurately predicts the presence of ARGs and provides valuable insights into the mechanisms of resistance associated with the identified genes in more detail than other ARG databases. This capability makes MetaResDB a valuable resource for studying resistance patterns in clinical settings, environmental samples, and other relevant contexts.

Resolving fine-mapping of brain variant proteoforms using Proteogenomics

Dr. Yadav's team in collaboration with Dr. Debasis Dash's team at CSIR-IGIB is working to resolve the translation of genetic variants by integrating genome/transcriptome and proteome data. The objective of this collaborative project is to achieve fine mapping of brain proteoforms through the implementation of a proteogenomics approach. The collaborative team has developed an advanced proteogenomics pipeline that utilizes the publicly available and assembled transcriptomics database, GENCODE, to create a comprehensive three-frame translated database encompassing all possible translational products. To ensure deep mining of variants, the team leverages the known variants reported in the NextProt database using nextVar module developed in-house. To improve the accuracy and quality of the results, false variant hit filtering is critical, for which the team has developed a dedicated tool called PgxSAVy. This tool is designed to effectively filter out false variant hits in the proteogenomics analysis using multiple features to separate true events from false ones, thus ensuring the reliability and validity of the identified variants.

Way ahead

Dr Yadav plans to monitor the identified PTMs in liver diseases in collaboration with Dr. Shalimar, AIIMS New Delhi. He also plans to integrate metabolomics and lipidomics data and conduct data analysis to discover novel genes associated with liver diseases and identify sensitive biomarkers to develop a comprehensive biomarker panel.

In future, Dr Yadav plans to streamline and expedite the identification of pathogens and determine their drug sensitivity profiles in the meta-resistome database. His team is working on predicting constitutive and inducible resistance genes, as well as accurately predicting minimum inhibitory concentration (MIC) from sequencing data that are needed for more efficient and targeted antimicrobial treatment strategies.

In the field of proteogenomics, Dr Yadav plans to further develop the brain-based proteogenomics map as a platform to assist in biomarker discovery that will help in understanding brain diseases through the integration of multi-omics data.

List of Collaborators

Dr. Samrat Chatterjee

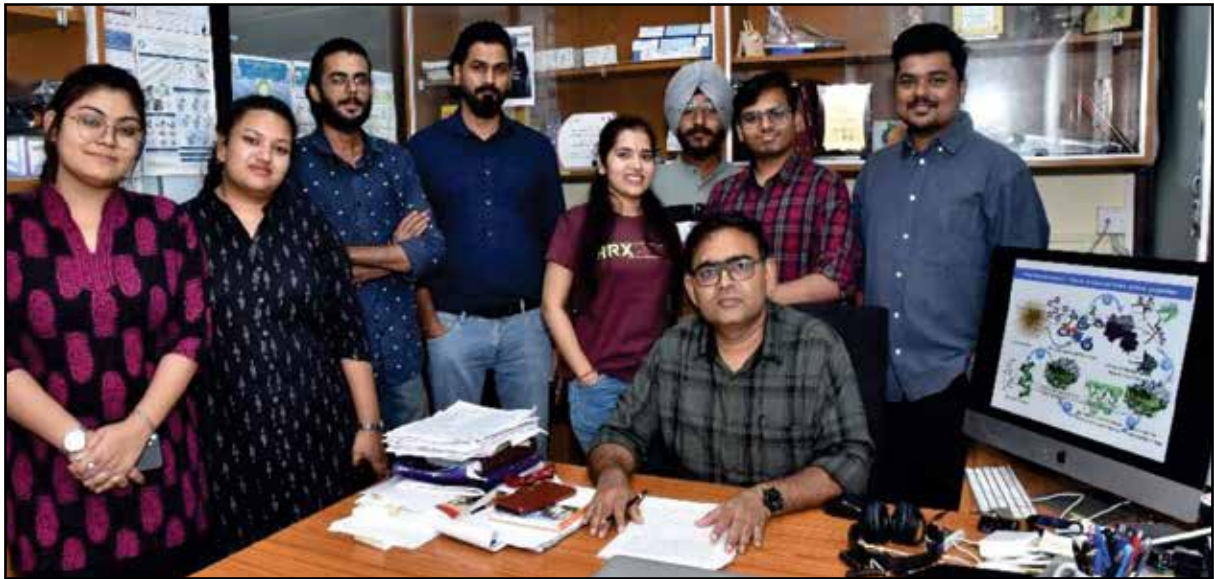
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Prof. Vijay Pancholi, Ohio State University, USA
Dr. Amit Kumar, University of Cagliari, Italy
Prof. Anthony Auerbach, University of Buffalo, USA
Dr. Manjula Kalia, RCB
Dr. Prasenjit Guchit, RCB
Dr. Tushar K Maiti, RCB
Dr. Deepak Nair, RCB
Dr. Rajendra Motiani and Ambadas Rhode, RCB
Dr. Santosh Chauhan, ILS Bhubneswar
Dr. Ravindran, ILS Bhubneswar
Dr. Sharad Wakode, DPSRU, New Delhi
Dr. Dhruv Kumar, UPES, Deharadun

Dr. Amit Kumar Yadav

Dr. Debasis Dash, CSIR-IGIB
Dr. Ramu Adela, NIPER-Guwahati
Dr. Srikanth Rapole, NCCS
Dr. Shalimar, AIIMS, Delhi
Dr. Sanjay Banerjee, NIPER-Guwahati
Dr. Manjula Kalia, RCB
Dr. Arup Banerjee, RCB
Dr. Tarun Sharma, GBU
Dr. Yogita Adlakha, Amity University



Clinical Development Services Agency

Team

Dr. Nitya Wadhwa, *Senior Professor*
Dr. Sucheta Bannerjee Kurundkar, *Head-Training*
Ms. Vineeta Baloni, *Head-Data Science*
Mr. Prashant Bhujbal, *Head-Services*
Ms. Komal Wadhwa, *Team Lead, Clinical Sciences*
Mr. Ashish Das, *Team Lead, Project Management*
Ms. Vandana Chawla, *Administrator, Training*

Clinical Development Service Agency (CDSA), was created with a mandate to support and nurture clinical product development and clinical research capacity in India. CDSA has successfully created a robust institutional platform and a governance structure, recruited high-quality professionals, developed an ecosystem for training and capacity building in clinical research and supported several ongoing projects.

CDSA functions as an academic clinical research unit (ACRU) and provides support services to investigators, sponsors, etc in all stages of a clinical trial/ study including design, planning, set up, training, conduct, data and safety monitoring, data management, analysis and report writing. CDSA also builds research capacity and capability through superior training in clinical research and development/trials and regulations and undertakes other unique initiatives to strengthen the clinical research environment in the country.

Academic Clinical Research Unit (A-CRU)

The activities of the A-CRU are led by the **Clinical Portfolio Management (CPM)** vertical with support from the other teams/ verticals within CDSA. The centre has contributed to writing and reviewing grant proposals with special emphasis on operational aspects, project planning, tracking of milestones, risk identification and efficient implementation.

All documents comply with applicable regulatory and ethical guidelines for each phase of the clinical trial/ study.

Patient safety is at the core of all clinical trials and one of the most critical aspects of trial conduct. The CDSA team has experience and capability to advise / help constitute a Data and Safety Monitoring Board (DSMB), DSMB charter and review of reports and recommendations.

CDSA has established robust clinical trials IT infrastructure, like Clinical Data Management Systems (CDMS), Electronic Trial Master File (eTMF), Clinical Trial Management System (CTMS) and standardized processes to provide support for large multicentre trials/studies.

The ongoing trials/ studies being supported by the ACRU are detailed in **Annexure A**.

Key achievements of ACRU in 2022-23

- Successfully completed eight trials/observational cohort studies including two regulatory and one academic clinical trial.
- Critical role of project coordination and monitoring for a multicenter clinical trial to evaluate the efficacy of Digoxin in reducing mortality in patients with Rheumatic Heart Disease. Initiated in February 2022, this trial with a sample size of 1800 is being conducted across 11 sites in India.
- Vital role in monitoring a large multicenter TB vaccine clinical trial evaluating two indigenous TB vaccines sponsored by ICMR and enrolling 12000 household contacts of TB patients; enrolment and vaccine administration completed in January 2021. The last patient last follow-up is projected for March 2024. Concurrent onsite clinical and safety monitoring is ongoing
- Supported INSACOG in establishing 14 clinical sites (hospitals) under the Hospital Network Study. Phase 1 is completed and the manuscript submitted to IJMR for publication. This crucial pan India

study is designed to evaluate trends and associations of different variants of SARS CoV-2 with disease severity to inform health policy makers on strategy for vaccination and management.

- Effectively supported the project management unit (PMU) at National Biopharma Mission (NBM), BIRAC for establishing community based seroprevalence of acute febrile illness (AFI) across 10 sites, with focus on Dengue and Chikungunya.
- Continued support in monitoring and evaluating performance of 11 DHS sites and 5 clinical trial networks (CTNs), comprising 36 hospitals established by NBM.
- Awarded a prestigious grant for clinical and safety monitoring of the India site trial activities for a global trial SURE: Short intensified treatment for children with tuberculous meningitis. This trial is coordinated by the Medical Research Council Clinical Trials Unit, University College London, UK

The **Data Science** vertical leverages strong capabilities centered in database development, data coordination, data quality control and, management and maintenance of scientific data repository across all its projects.

The data science team utilizes different databases and approaches, including validated and regulatory compliant commercial and open data management systems, based on the study requirement, including commercial data management systems like Promasys, Octalsoft and ODK. The data management systems at CDSA-THSTI are regulatory compliant and installed in a secure and validated IT environment ensuring a quick and smooth transition from database development to database lock with operational cost advantage.

Key achievements of data science vertical in 2022-23

- The ongoing studies are a mix of regulatory clinical trials, academic clinical trials and longitudinal cohort studies with varying sample sizes (70-110000) and data acquisition time points (2-150).
- Supported two doctoral fellows for their research: CRF designing and database programming for electronic data capture and data management.
- Contributed as faculty in the MSc in Clinical Research (with specialization in clinical trials) program at THSTI.
- Developed the 'clinical data management' module for the MSc curriculum.
- Awarded a grant for database designing and data monitoring for a large multicentre study on the Epidemiology of Pancreatitis and GI diseases.

Biostatistics is an important vertical and core strength of CDSA-THSTI. The CDSA biostatistician has extensive ability to provide statistical support across all the stages of a study/ trial from planning to set up to conduct to final analysis, report and manuscript writing.

Annexure A contains the details of the CDSA-Biostatistics support provided in 2022-23.

Key achievements of Biostatistics vertical in 2022-23

- Contributed as faculty in Biostatistics for MSc in Clinical Research (with specialization in clinical trials) program and the PhD program of THSTI.

- Successfully completed the analysis of a multi-country RCT on zinc for young infant sepsis, utilizing Bayesian approaches.
- Provided analytical assistance, including sample size estimation, statistical analysis, and data visualization to intramural MCH-THSTI, and external projects upon request.
- Developed analytical pipelines for improved reporting and analysis.
- Enhanced capabilities for longitudinal data analysis.
- Provided support to nine PhD. students with data cleaning and statistical analysis for their theses.
- Provided support in publication of 6 research papers through the CDSA-Biostatistics unit.

Training

To enhance and strengthen the clinical trial capacity and capability in India, various short-term, face-to-face as well as online training programs were conducted for investigators, ethics committee members, clinical researchers, laboratory team members, on different aspects of clinical research by the training vertical. An online, self-paced, certification course on '*Rational use of Medicines*' has been co-designed and co-developed with World Health Organisation (WHO), and the Pharmacy Council of India. This course is hosted on the CDSA-THSTI state-of-the-art Learning Management System (LMS).

The training program details for 2023-24 are in **Annexure A**.

Major achievements of training vertical in 2022-23

- **MSc in Clinical Research (with specialisation in clinical trials):** THSTI initiated its first master's programme in clinical research with specialisation in clinical trials in 2022. The programme is jointly developed by CDSA-THSTI along with its partners namely Christian Medical College, Vellore; Medical Research Council Clinical Trials Unit at University College London; Center for Health Research and Development, Society for Applied Studies, New Delhi; and other partnering institutes. The MSc degree will be awarded by the Regional Centre for Biotechnology. The first batch of 12 students joined in September 2022.
- **Good Clinical Practice Professional Certification Scheme (GCPPCS):** First-in-globe, the professional certification scheme for evaluation of competence of clinical trial professionals, based on international standard, ISO 17024 announced the first Personnel Certification Body (PrCB) , North Eastern Christian University on 26th January 2022.
- **Regulatory course with Indian Drugs Regulatory Agency, CDSCO:** 5124 participants registered for the 2022-23 online certificate course on '*Current regulatory requirement for conducting clinical trials in India for investigational new drugs (now version 3.0)*' co-developed by CDSA with the Indian drugs regulatory agency, CDSCO (Central Drugs Standard Control Organization). This is hosted on the SWAYAM portal. CDSA runs this online regulatory course with IIT, Madras; NPTEL.
- Awarded a **British Council grant** under an India-UK Going Global Partnership for '*Training the next generation of Indian clinical trialists*'. This one-year collaborative grant between THSTI, MRC CTU, London and CMC, Vellore supported development of the master's programme (M.Sc.) in clinical research with specialisation in clinical trials at THSTI. This included an exchange programme for Indian and UK faculty members.

List of collaborators

National Collaborations

- i. National Biopharma Mission (NBM), BIRAC
- ii. Indian Council of Medical Research (ICMR)
- iii. Central Drugs Standard Control Organization (CDSCO)
- iv. National Programme for Technology Enhanced Learning (NPTEL)
- v. All India Institute for Medical Sciences (AIIMS), New Delhi
- vi. VMMC & Safdarjung Hospital, New Delhi
- vii. National Institute of Mental Health and Neurosciences (NIMHANS)
- viii. Christian Medical College (CMC), Vellore
- ix. Center for Health Research and Development (CHRD), Society for Applied Studies (SAS), New Delhi
- x. International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi
- xi. Pharmacy Council of India (PCI)
- xii. ESIC Medical College and Hospital, Faridabad
- xiii. JSS University, Mysuru
- xiv. KEM Medical College & Hospital, Pune

International Collaborations

- i. Medical Research Council (MRC), Clinical Trials Unit (CTU), University College London (UCL), UK
- ii. World Health Organization
- iii. Public Health Research Institute (PHRI, Canada).
- iv. The United States Agency for International Development (USAID)
- v. Bill and Melinda Gates Foundation (BMGF)
- vi. National Institutes of Health (NIH), USA

Annexure A: Projects supported by Clinical Development Services Agency (CDSA)

Table 1. Summary of studies / trials supported by the Academic Clinical Research Unit (A-CRU) of CDSA in 2022-23

S. No.	Project Title (Funding Agency)	Principal Investigator / Institute	Role of CDSA	Contribution	Remarks
PROJECTS SUPPORTED IN 2022-23					
1.	Genomic Surveillance for SARS-CoV-2 In India: Indian SARS-CoV-2 Genomics Consortium (INSACOG) – Phase II-Component C Study design: Longitudinal cohort study	Prof Nitya Wadhwa, THSTI 14 sites across India	- Site preparation and initiation - Project management and monitoring - Coordination with hospital sites and IGSLs for sample shipments - Financial management of study conduct at hospital sites	- Sites readiness and initiation - Supported sites for their institutional ethics committee (IEC) submissions and coordinated with the sites for the IEC approvals - Project management support: training of site staff for data capture in EDC platform, participant recruitment and retention, etc. - Data management - Coordination of sample shipments and timely receipt of sequencing results from IGSL - Scientific, administrative, and technical support to the sites	ongoing
2.	A Prospective Cohort Study to Evaluate the Severity and Outcomes of SARS-CoV-2 infection and Correlation of Clinical Outcomes with Virus Variants (Phase I) Study design: Longitudinal cohort study	Prof Pramod Garg, THSTI 14 sites across India	- Site preparation and initiation - Project management and monitoring - Coordination with hospital sites and IGSLs for sample shipments - Financial management of study conduct at hospital sites	- Sites readiness and initiation - Supported sites for their institutional ethics committee (IEC) submissions and coordinated with the sites for the IEC approvals - Project management support: training of site staff for data capture in EDC platform, participant recruitment and retention, etc. - Data management - Coordination of sample shipments and timely receipt of sequencing results from IGSL - Scientific, administrative, and technical support to the sites - Manuscript writing	Completed in December 2022
3.	Inter-Institutional Program for Maternal, Neonatal and Infant Sciences-A translational approach to studying preterm birth. (GARBH-INI-Phase 2) (DBT) Study design: Longitudinal cohort study	Prof Shinjini Bhatnagar, THSTI; other collaborating institutes: RCB, NIBMG, General Hospital Gurgaon VMMC & SJH, CDSA, MAMC	- Study start-up support - GCP and GCLP training of the research team - Monitoring: Study processes, clinical data, laboratory and biorepository.	- Monitoring to ensure study is being conducted in compliance with protocol, national ethical guidelines for biomedical research and GCP. - Monitoring of 100% clinical data (critical variables), lab data - Process monitoring of pregnancy cohort and birth cohort including neurodevelopment assessments. - Support for query management - Support delivery of clinical milestones within the stipulated timelines.	Ongoing
4.	A Phase III, Randomized, Double-blind, Three arm Placebo controlled Trial to Evaluate the Efficacy and Safety of two vaccines VPM1002 and Immuvac(Mw) in Preventing Tuberculosis (TB) in Healthy Household Contacts of Newly Diagnosed Sputum Positive Pulmonary TB Patients (ITRC-ICMR) Study design: Clinical trial (regulatory)	Dr Manjula Singh, ICMR-HQ 18 sites across India	- Study start-up support - GCP trainings- every year - Clinical and safety monitoring - Project management support - Data and medical monitoring support	- Supported creation of GCP and CDSCO compliant study documents, ICD, CRF, SOPs and data collection tools. - Monitoring to ensure trial execution as per protocol, GCP and NDCT rules 2019 - Support in medical monitoring - Trial updates to the sponsor and expert committee members in fortnightly meetings - Training on safety reporting, GCP, good documentation practices	ongoing

S. No.	Project Title (Funding Agency)	Principal Investigator / Institute	Role of CDSA	Contribution	Remarks
5.	Translational Research Consortium For Establishing Platform Technologies To Support Prophylactic and Therapeutic Strategies for Dengue Discovery to Proof-of-Concept (NBM, BIRAC) Study design: Longitudinal cohort study	Dr. Chande, ICGEB; Dr. N. Wadhwa, CDSA 3 hospital sites in India and 4 research institutes	- Program management and coordination - Quality control of study conduct at clinical sites including monitoring of clinical sites, sample shipment and biorepository - Data management: clinical and scientific data - Develop and maintain Biorepository management system (BMS) - Develop and maintain a repository of optimized SOPs - Administrative support for program management	- Developed and standardized documents (ICDs, SOPs, CRFs, logs and templates) for the clinical cohort study. - Supported clinical site preparation for cohort study - Conducted training on protocol, GCP, good documentation practices, CRF filling, query management, use of biorepository platform - Study initiation at all participating clinical sites. - Ensure conducting of study in adherence to protocol, national ethical guidelines for biomedical research and Good Clinical Practice (GCP) standards - Developed and implemented quality monitoring plan (QMP) - Monitor clinical & laboratory data, - Support query resolution with sites - Developed data management system for clinical data entry - Developed barcode platform for sample traceability. - Data management of clinical and lab data ensuring data confidentiality, data security and back up and - Developed and ongoing execution of Biorepository Management System (BMS) for sample and biorepository management - Monitoring, facilitating, tracking bio-specimen collection at clinical site. - Support delivery milestones within timelines. - Tracking of financial activities - Facilitate coordination and communication among various stakeholders for seamless conduct of study. - Organize annual meeting of consortia partners	
6.	Digoxin in patients with rheumatic heart disease- a randomised placebo-controlled trial (ICMR) Study design: Academic clinical trial	Dr. G. Karthikeyan, AIIMS, New Delhi 12 sites across India	- Site start-up support - Quality monitoring - IP supply management	- Support sites for institutional ethics committee (IEC) submissions - Coordinate and support sites for completion of codal formalities for ICMR - GCP training of project team. - Site initiation: Trial initiated at 9 sites - Monitoring to ensure trial execution as per protocol, GCP and national ethical guidelines for biomedical research - Project coordination with all sites - Procured Clinical trial insurance policy for sponsor IP supply management: Procured 2nd batch of IP for the trial; coordinated distribution of IP to each site according to the SOP - Supported preparation of DSMB charter and coordination for DSMB meeting	Ongoing
7.	INDIGO: Effective and Affordable Flu Vaccines for the World (DBT as part of a HORIZON 2020 EU-DBT grant) Study design: Phase 1 clinical trial (regulatory)	Prof Pramod Garg, THSTI (Till February 2023) Dr. Remko, AIGHD	- Project Management (Ethical and Regulatory compliance, Quality Monitoring, Data management, etc) - Regulatory support - Clinical trial management - Dissemination, Exploitation, and Regulation.	- Contributed to development of dissemination tools (website, newsletters, press releases) - Initiated process for co-developing phase 1 trial protocol and other process and related documentation for the conduct of phase 1 clinical trials. - Dissemination of project-related information through newsletters and organising periodical project update meetings	ongoing

S. No.	Project Title (Funding Agency)	Principal Investigator / Institute	Role of CDSA	Contribution	Remarks
8.	Sepsis-related mortality in neonates in India: A multi-disciplinary, multi-institutional research program for context-specific solutions (DBT) Study design: Longitudinal cohort study	Dr. M Jeeva Sankar, AIIMS, New Delhi 4 clinical sites in Delhi - NCR and 6 research institutes	- Quality monitoring: clinical, lab and biorepository - Project management support including coordination - Organize Training for clinical site staff - Data management: Clinical and biospecimen data - Clinical sites: Financial and administrative management including procurement	- Developed and standardized documents (SOPs, CRFs, logs and templates) for the clinical cohort study. - Supported clinical site preparation for cohort study: recruitment of staff, procurement of equipment, consumables - Supported setting up harmonized processes for study conduct at each site - Conducted training on GCP, good documentation practices, CRF filling, query management, use of biorepository platform - Study initiation at all participating clinical sites. - Ensure conduct of study in adherence to protocol, national ethical guidelines for biomedical research and Good Clinical Practice (GCP) standards - Developed and implemented quality monitoring plan (QMP) - Monitor clinical & laboratory data, - Support query resolution with sites - Developed data management system for clinical data entry - Developed barcode platform for sample traceability. - Data management of clinical and lab data ensuring data confidentiality, data security and back up and - Developed and ongoing execution of Biorepository Management System (BMS) for sample and biorepository management - Monitoring, facilitating, tracking bio-specimen collection at clinical site. - Support delivery of milestones within timelines. - Facilitate coordination and communication among various stakeholders for seamless conduct of study.	ongoing
9.	SURE: Short intensified treatment for children with tuberculous meningitis (MRC-CTU, London) Study design: Academic clinical trial	Dr Diana Gibb (MRCCTU, London) Dr N. Sankhyani, PGI Chandigarh Dr V Singh (KSCH) 2 trial sites in India	- Clinical monitoring - Support trial coordination at India sites - Regulatory guidance	- Devised India site specific quality monitoring plan - Contribute to India site meetings, trial management (TMC) and trial steering committee (TSC) meetings - Regulatory guidance	Ongoing
10.	Epidemiology of Pancreatitis and Major Gastrointestinal Diseases: A Multi-centre Study Across India – An ICMR Task Force Project Study design: Cross sectional population- and hospital- based surveys and case control study	Dr Pramod Garg	- Project Coordination - Data Management	- Project management for the large multicentre study: study coordination, risk management, trainings - Developed study operation manual, logs, templates - Provided training to all sites on protocol, GCP, CRF filling, data entry, query resolution - Developed database for electronic data capture - Data management and monitoring	Ongoing

S. No.	Project Title (Funding Agency)	Principal Investigator / Institute	Role of CDSA	Contribution	Remarks
11.	Clinical Trial Regulatory Advisory and Data Safety Consultancy Services (National Biopharma Mission, BIRAC) Study design: supporting trial registries & clinical trials	Dr. Nitya Wadhwa, Dr. Monika Bahl	• Site evaluation • Resourcing and planning for clinical site preparedness • Resourcing and planning for site laboratory preparedness • Training • Technical review of study related documents • Quality management and assurance • Monitoring of surveillance study(ies) • Laboratory quality monitoring • Co-monitoring of trials • Safety data monitoring • Regulatory advice • Review of validation data of immunogenicity assays	• Community based seroprevalance of acute febrile illness (AFI) cohort study- with focus on Dengue and Chikunguniya (10 sites), Site feasibility & assessment, Site Initiation, Development of quality monitoring plan • Data and lab monitoring. • Continued support to monitor and evaluate performance of 11 DHS sites which have initiated activities for COVID-19, Dengue and Chikungunya sero-epidemiology studies • Continued support to monitor the 5 clinical trial networks (CTNs), comprising 36 hospitals. The CPM facilitates and supports their outreach programs to reach out to sponsors, and funding agencies. • Independent oversight monitoring of BIRAC funded studies	Ongoing

Table 2: Summary of the statistical support provided by CDSA-Biostatistics vertical and ADAPT-MCH in 2022-23

S. No	Project Title (Funding Agency)	Study design (longitudinal cohort, RCT, etc)	Sponsor/ Principal Investigator	CDSA-Biostatistics unit Role
ONGOING PROJECTS				
1	Zinc as adjunct for treatment of clinical severe infection in infants younger than 2 months: health gain, financial risk protection and cost-effectiveness analysis (Research Council of Norway)	RCT	Dr Nitya Wadhwa	• Statistical analysis • Bayesian analysis
2	Inter Institutional Program for Maternal, Neonatal and Infant Sciences-A translational approach to studying preterm birth. (GARBH-Ini: Interdisciplinary group for advance research on birth outcomes- DBT India Initiative). (GARBH-Ini Phase I)	Longitudinal cohort	Coordinating PI: Dr Shinjini Bhatnagar	• Sample size estimation • Plan of analysis • Statistical Data monitoring • Data cleaning • Exploratory Data Analysis • Statistical analysis • Advanced statistical modeling
3	Inter Institutional Program for Maternal, Neonatal and Infant Sciences-A translational approach to studying preterm birth. (GARBH-Ini: Interdisciplinary group for advance research on birth outcomes- DBT India Initiative). (GARBH-Ini Phase II)	Longitudinal cohort	Coordinating PI: Dr Shinjini Bhatnagar	• Statistical Data monitoring • Data cleaning • Exploratory Data Analysis
4	GIISER: - Global Immunology & Immune Sequencing for Epidemic Response (BMGF)	Longitudinal study	Translational Health Science and Technology Institute	• Sample size estimation • Plan of analysis • Data cleaning • Exploratory Data Analysis • Statistical analysis
5	A "bench to bedside" model for clinical and translational science between academic research institutes and hospitals focused on fetal growth restriction and preterm birth (Department of Biotechnology (DBT), India)	Longitudinal cohort	Translational Health Science and Technology Institute	• Sample size estimation • Plan of analysis • Statistical analysis • Advanced statistical modeling
6	Multi Omics for Mother and Infant consortium (Bill and Melinda Gates foundation through Grand Challenges India, BIRAC)	Longitudinal cohort	Translational Health Science and Technology Institute	• Plan of analysis • Data cleaning • Statistical analysis • Advanced statistical modeling
7	Effects of extreme heat on maternal, placental and fetal physiology, lactation and newborn health in India	Longitudinal cohort	Translational Health Science and Technology Institute	• Plan of analysis

Table 3. Summary of Training programs conducted by CDSA

	2009-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-2020	2020-2021	2021-2022	2022-2023	Total
No. of Training	3	10	14	17	21	29	17	19	18	12	19	4	183
Cities/Countries	2	5	10	10	9	15	12	14	10	58	186	9	340
Faculty	11	112	146	175	233	236	120	149	174	118	163	30	1670
Participants	41	436	894	1241	1906	1510	4476	1344	1851	1549	1959	306	17510
Institutions	10	117	222	428	536	391	409	418	638	315	419	17	3921

Table 4: Details of training programs conducted in 2022-23 by CDSA

S.No.	Date	Workshop/Courses	Funding	Place & City	Faculty	Participants	Attendee Institutions
1	April 22 - April 23, 2022	Clinical Research Concepts, Design, and Conduct	MPMMCC & HBCH	Varanasi (Hybrid modal face-to-face & online, virtual)	13	93	6
2	May 13- May 19, 2022	THSTI-IBSC online Biosafety Training Course	CDSA, THSTI	Online (virtual)	6	105	1
3	January 27-February 10, 2023	Good Clinical Practice	ESIC, NOIDA	Online (virtual)	5	34	1
4	March 29-April 19, 2023	Good Clinical Laboratory Practice	DBT funded Sepsis program	Online (virtual)	6	74	9
				Total	30	306	17





RESEARCH FACILITIES

BIOASSAY LABORATORY

The Bioassay laboratory (BL) of THSTI is the only NABL-accredited (ISO 17025:2017) - cGLP laboratory in a DBT institute. BL has trained manpower and a robust quality management system and generates data from molecular and serological assays for Dengue, Chikungunya, and SARS-CoV-2. The laboratory serves as a national resource platform for the clinical development of vaccines and biologicals by engaging with Indian and global vaccine developers. BL is one of the ten labs of the Centralized Network labs of the Coalition for Epidemic Preparedness Innovations (CEPI) in the world for facilitating COVID-19 vaccine development. The primary objective of this collaboration is to establish a common platform that employs the same protocol, assays, and data analysis methods, to ensure that vaccine candidates are assessed in a manner acceptable to regulators worldwide. The facility is involved in partnerships and collaborations with both national and international organizations such as International Centre for Genetic Engineering and Biotechnology, Institute of Genomics and Integrative Biology, Indian Institute of Science and National Centre for Biological Sciences, Christian Medical College, Manipal Virus Research Centre, IncLEN Trust International, New Delhi, National Institute of Virology, AIIMS, New Delhi and ESIC Medical college and hospital, Faridabad.

Vaccine Development: Under the CEPI network, BL provided testing services for Phase I-III samples to vaccine developers such as Biological E Ltd, India; S K Bioscience, South Korea; The Government Pharmaceutical Organization (GPO), Thailand; Aurum Institute, South Africa and also provided collaborative services for WHO Solidarity Trial, Geneva, Switzerland. BL is actively involved in establishing the standards and controls for CEPI assays for the CEPI network laboratories. Bioassay lab also collaborated with the World Health Organization (WHO) and National Institute for Biological Standards and Control (NIBSC) to establish the 2nd International standard for anti-SARS-CoV-2 immunoglobulin, a reference panel for SARS-CoV-2 variants of concern and to establish the 1st WHO International Standard for SARS-CoV-2 antigen.

New assays: During last year, BL has developed the platform for binding antibody assay and neutralization assay platform for flaviviruses such as Dengue, Zika virus, Japanese encephalitis virus and West Nile virus.

During 2022-23, BL successfully completed NABL assessment and renewed its accreditation for two more years. The accredited assays have supported our collaborators like International Centre for Genetic Engineering and Biotechnology, New Delhi and epidemiological studies led by INCLEN Trust International at Palwal. Bioassay lab successfully isolated the BA.2.75 variant for SARS-CoV-2, developed a Microneutralization assay and demonstrated the compromised ability of antibodies from previously infected or vaccinated individuals to neutralize this new variant of concern.

Bioassay Laboratory had excellent performance in SARS-CoV-2 Antibody Assay Monitoring (SAAM) External Quality Assurance (EQA) Program by Duke Human Vaccine Institute, USA and also participated in 28 proficiency testing programs last year with no discordant results which is a testimony to the quality of data generated by the laboratory. BL has processed around 20,000 clinical samples in FY 2022-2023 for national and international collaborators across the globe.



BIOREPOSITORY

NCR biotech science cluster BioRepository Facility (BRF) is a scientific and biomedical research platform for facilitating global collaborations on fundamental and translational research. With a team of members trained in ISO 9001:2015, ISO 20387:2018, GCP, GLP and GCLP, the facility has successfully archived more than 14 lakh biospecimen as aliquots of blood, urine, saliva, high vaginal swab, placental punches, cord blood, NP/OP swabs, PBMCs and rectal & vaginal isolates and swabs under population and disease-based cohorts. Standard operating protocols (SOPs) and Management Systems protocols (MSPs), have been improvised as per the requirements of the biobank accreditation program ISO 20387:2018. The Facility has maintained its membership status with ISBER (International Society for Biological and Environmental Repositories) since 2020 and has received a proud member badge in 2023 from the society. BRF participated in ISBER BAT (Biobank Assessment Tool) Survey and received a certificate of participation with a score of 99.9% in Nov 2022.

BRF has initiated its participation in ISBER Proficiency Testing (PT) programs to ensure accuracy, reliability and consistency of the DNA quality assessment processes followed at the facility. The facility has established and implemented the quality management system as per the requirement of the ISO 20387:2018 international standards towards obtaining accreditations.

The biospecimen collected, processed and archived at the biorepository facility and shared under the various studies has led to more than twenty-seven peer-reviewed publications and two PhD thesis in the year 2022-23.

Trainings/ workshops, talks and webinars organized

Senior members at BRF have delivered talks and webinars as invited speakers at national and international conferences to disseminate the knowledge and importance of biobanks in research and medicine. The team has been engaged in trainings and workshops to propagate the processes and guidelines of biobanking abiding best practices.

Cohorts/studies supported by NCR Biotech Science Cluster Biorepository Facility

Technical and scientific support to several ongoing projects within the institute and around NCR cluster is being provided as per the mandate of the facility. Currently the facility archives samples collected and processed under the programs summarized below:

S. No	Programs/ Studies	Study design/ Disease/ Type of Biospecimen	Ongoing/ completed If ongoing, what are the next milestones	No of aliquotes /Type of biospecimen archived	Role of BRF
1.	Inter-Institutional program for Maternal, Neonatal and Infant Sciences: interdisciplinary Group for Advanced Research on Birth outcome- DBT India Initiative (GARBH-Ini Phase II)	Longitudinal Study/ Pregnancy & Birth Cohort	Ongoing (participants ~11,000) Collection, processing and archival of additional biospecimen from pregnant women (up to 12000 participants) and their babies	14,00,000 Maternal high vaginal swab, sera, plasma, urine, placental tissue, placental membranes, umbilical cord, cord blood, neonatal heel prick samples, sera plasma and breast milk	Collection, processing, archival and retrieval of Biospecimen Quality assurance and quality control of the processes and biospecimen
2.	Gall Bladder Cancer (GBC) Registry	Cross sectional study/ Cancer Registry	Completed	213 Gall bladder tissue and bile fluid	Archival and retrieval of biospecimen

S. No	Programs/ Studies	Study design/ Disease/ Type of Biospecimen	Ongoing/ completed If ongoing, what are the next milestones	No of aliquotes /Type of biospecimen archived	Role of BRF
3.	Post-Gestational Diabetes Mellitus (GDM) cohort:	Longitudinal study/ Diabetes	Ongoing Archival of follow-up samples	10,000 Sera and Plasma	Archival and retrieval of biospecimen
4.	Pediatric Renal Biology Program: Research on Nephrotic syndrome	Longitudinal study/ Nephrotic Syndrome	Completed Cold chain maintenance of the archived biospecimen and their retrieval as per the study specific SOPs	31,000 Sera, Plasma, DNA, Urine	Archival and retrieval of biospecimen
5.	DBT's Resource of Indian Vaccine Epidemiology Network (DRIVEN 2020)	Longitudinal study/ Community Surveillance	Completed Cold chain maintenance of the archived biospecimen and their retrieval as per the study specific SOPs	92,213 Sera	Archival and retrieval of biospecimen
6.	Indian SARS-CoV-2 Consortium on Genetics (INSACOG)	Cross-sectional study/ COVID-19	Ongoing	4500 NP/OP swabs	Archival and retrieval of biospecimen
7.	Sepsis-related mortality in neonates in India: A multi-disciplinary, multi-institutional research program for context-specific solutions	Longitudinal study/ Neonatal Sepsis	Ongoing	4163 Cord blood, rectal vaginal swabs and isolates	Archival and retrieval of biospecimen
8.	GARBH-Ini India Pregnancy Risk Stratification Platform Alignment (GIPA)	Longitudinal Study/ Pregnancy Cohort	Ongoing	3177 Sera, plasma, placental tissue, placental membranes, umbilical cord, cord blood and neonatal heel prick samples	Archival and retrieval of biospecimen
9.	DBT COVID-19 consortia	Longitudinal Study/ COVID-19	Ongoing Collection, processing and archival of additional biospecimen from 24 months follow up visits	1,50,000 Sera, Plasma, NP/ OP swab, PBMCs Collection, processing, archival and retrieval of biospecimen	Quality assurance and quality control of the processes and biospecimen

Way Ahead

For the upcoming year, the facility plans to obtain the ISO 20387:2018 accreditation. The facility has implemented the revised SOPs as per the requirement of the ISO 20387:2018 standards and gap analysis has been conducted as a part of our internal audits. The facility has procured Biorepository Management Software (BMS) and customization of the same is under process as per the requirements for efficient management of storage space and retrieval. BRF has established the protocols for the assessment of sample quality and integrity for the various sample types archived over the years and is in the process of evaluating the samples using the optimized assays.

List of collaborators:

Regional Centre for Biotechnology (RCB), International Centre for Genetic Engineering and Biotechnology (ICGEB), Delhi University, South Campus, New Delhi, National Institute of Immunology (NII), New Delhi, All India Institute of Medical Sciences (AIIMS) New Delhi, ESIC Medical College Hospital, Faridabad, Lady Hardinge Medical College, New Delhi, Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi, Civil Hospital Gurugram (GCH), Medanta hospital, Gurugram, Civil Hospital Palwal (PCH), Dr. Ram Manohar Lohia Hospital, New Delhi, Makunda Christian Leprosy & General Hospital, Karimganj, Assam, Christian Medical College, Vellore, Tamil Nadu, ICMR-National Institute of Epidemiology (NIE)- Model Rural Health Research Unit, Tirunelveli, Tamil Nadu, Society for Health Allied Research Education India (SHARE INDIA), Medchal, Telangana, SOMAARTH-DDESS, The INCLEN Trust International, Palwal, Haryana, Vadu HDSS, KEM Hospital Research Centre (KEMHRC), Pune, Maharashtra.



BSL-3 FACILITY

A state-of-art BioSafety Level-3 (BSL-3) Facility established in the NCR Biotech Science cluster with financial support from the Department of Biotechnology (DBT), Govt. of India was inaugurated by Dr. Jitendra Singh ji, Hon'ble Minister of State (IC) for the Minister of Science & Technology and Ministry of Earth Sciences, Minister of State for PMO, MoPPP, DAE and DoS, Govt. of India on 15th July 2021. The facility has been built with a mandate to serve as a national resource platform for accelerating vaccine and drug development against existing and future infectious agents

The facility built is as per international norms, covers an area of around 3,800 square feet and is the largest of its kind in India with independent modules for handling bacteria and viruses. It features dedicated lab suites, animal holding areas, procedure rooms and a common instrumentation room to maintain unidirectional workflow. Equipped with all necessary equipment like type II B2 Biosafety cabinets, aerosol inhalation exposure system, multimode readers, trinocular microscopes, CO₂ incubators, deep freezers, roller bottle incubators, incubator shakers, IVC cages, homogenizers, etc., the BSL-3 facility has been calibrated and validated as per the guidelines laid out by DBT. The facility has been approved by the Review Committee on Genetic Manipulation (RCGM) established under the DBT, Ministry of Science and Technology and is fully functional to handle risk group 3 pathogens.

BSL-3 Facility is open to various academia and industry partners involved in vaccine and drug development. During COVID-19, the BSL-3 was utilized actively and responsibly in contributing towards vaccine development. The facility collaborated with various academic organizations like NII, IISER Pune, AIIMS, CSIR-IGIB, TIFR, etc. for serological surveys and various industry partners like Mynvax, Reliance Lifesciences, Intas pharmaceuticals, Hetero pharmaceuticals, Dr. Reddy's, Zydus Lifesciences, Premas Biotech Pvt. Ltd for the development of vaccine candidates by supporting pre-clinical and clinical trials. This involved both in vitro virus neutralization assays and in vivo animal model challenge studies for the development of prophylactic and therapeutic interventions for combating the pandemic. Animal models like the Hamster Challenge model and ACE2 transgenic mice were developed to study the efficacy of vaccine candidates and were extensively used by various academic and industrial partners involved in vaccine development. Through the utilization of the BSL-3 facility, THSTI played a very important role in bringing almost all COVID-19 vaccines (e.g. ZyCoV-D, Corbevax, Nanocovax, Sputnik-V, COVID-Vac, Sputnik Light) to the Indian market.

During the past year, the BSL-3 facility strengthened its governance structure by providing training to various scientific and technical staff.

Currently, the BSL-3 facility is facilitating research on Mycobacterium tuberculosis and SARS-CoV-2 with future plans to expand its scope with respect to additional risk group 3 pathogens.

Way forward

BSL-3 is actively involved in the generation of validated assays (both in vitro and in vivo) with a robust quality management system for facilitating vaccine development.

BSL-3 is currently in the process of developing SOPs to facilitate use by external vaccine developers & manufacturers.

In addition, THSTI is actively collaborating with start-up industries for the development of diagnostics methods for risk-group 3 pathogens as a value addition to combating future pandemics.



DATA MANAGEMENT CENTRE (DMC) & ARYABHATA DATA SCIENCE AND ARTIFICIAL INTELLIGENCE PROGRAM AT THSTI (ADAPT)

The **Data Management Centre (DMC) & Aryabhata Data science and Artificial intelligence Program** at THSTI (ADAPT) serves as a platform to complement the research programs at THSTI and support other academic partners for their research.

Manpower and governance

Operational oversight of the DMC is by THSTI faculty. There is a core team comprising of lead-database development, database programmer, IT architect and data manager. Statistical assistance for data management is provided by the CDSA biostatistician. In addition, each project is managed by dedicated project staff which may include data entry operators, data analysts, statistical programmers and data managers. During the past year, the DMC further strengthened its governance structure and developed a performance-based contract career path, recruited high-quality professionals, and expanded capacity-building efforts.

Robust systems/processes to ensure data management services to the highest standards of quality

Infrastructure and processes for clinical data management

The DMC has robust processes and data management systems (DMS) that ensure validated and secure databases, reliable data quality, audit trail, quicker turnaround, data security, storage and backup. THSTI-DMC uses a number of different data management approaches depending on the need of the study, including in-house designed and developed bespoke database systems (DBS) based on MS SQL Server with frontend development in Dot NET, open source database management systems using REDCap as well as commercial data management systems like ODK. The data management systems at THSTI-DMC are installed in a secure and validated IT environment ensuring quick and smooth transition of database build to database lock with operational cost advantage.

State-of-the-art data management support from data capture to analysis-ready data

- i. THSTI-DMC has successfully supported 11 completed projects. Currently, the DMC is actively providing data management support for 20 studies (**Annexure 1**). The ongoing studies are a mix of randomized control trials (RCTs) and longitudinal cohort studies with varying risks, sample sizes (70 to more than 30,000) and data acquisition time points (2-74).
- ii. Clinical data of >1.5 lakh participants managed, monitored, and stored in a secure environment
- iii. In January 2023, THSTI-DMC was awarded a prestigious grant for data management of a WHO-coordinated multicountry study of 6 sites in 4 countries of Asia and Africa. The WHO Data Management Center at THSTI is for the immediate Kangaroo Mother Care Implementation Research.

QA & QC in clinical data management

The DMC has set up processes for data quality control ensuring a quick turnaround for clean and reliable data. The CRFs are designed to ensure that data is collected in compliance with GCP and the requirements of the study protocol. During database development in-built checks and edits are programmed to run in real-time and ensure data completeness and accuracy. Study data managers perform regular data quality checks as the next level of data quality control. Statistical monitoring is performed periodically to review the quality of the accrued data and take appropriate corrective and preventive action. To enable this process of QA & QC, the DMC has created interactive real-time dashboards and developed analytical pipelines for central statistical data monitoring and reporting. The clinical data management is implemented using systems that have national and international recognition and are compliant to widely used data management standards such as 21 CFR Part 11, FISMA, HIPAA, and GDPR. This has helped in data harmonization and in-

tegration in studies especially involving multiple sites both within the country or across multiple countries

Automation of Data Management Processes

DMC has developed an algorithm for the automation of the implementation of data quality rules on Red-Cap. The tool increases the efficiency in implementation of checks within the data management system. A proof-of-concept for automation of query generation has been developed to enable execution of a large number of checks within seconds.

Other IT systems for trial/clinical research management

The DMC has demonstrated capability to design and develop other clinical trial management systems to support efficient conduct and quality management of clinical studies/ trials. In the past year, the DMC has established an automated process for monitoring the temperature of an investigational medicinal product (IMP) in the THSTI-Intervention Room and at the study hospital site(s) with email alerts in case of temperature excursions.

Methodologically advanced data analysis for intramural and extramural studies

Established epidemiological & trial data analysis proficiencies

The DMC and ADAPT have developed analytical pipelines for analysis and reporting of studies implemented within THSTI and if requested on a case-to-case basis for studies outside THSTI. The analysis of a multi-country trial on zinc for young infant sepsis including the Bayesian approach was undertaken and the manuscript is under preparation.

Statistical support across all stages of clinical trials/ studies including design, planning, conduct, analysis and reporting

Besides statistical support to the clinical research programs coordinated by the MCH domain at THSTI, DMC & ADAPT are currently supporting eight Ph.D. students for data cleaning and statistical analysis for their theses. More than 10 publications have been conceived and supported by DMC and ADAPT.

Annexure 1: Studies Managed under DMC & ADAPT, THSTI in 2022-23

S No	Project title	Study design (longitudinal cohort, RCT, etc)	DMC & ADAPT Role
ONGOING PROJECTS			
1	Inter Institutional Program for Maternal, Neonatal and Infant Sciences-A translational approach to studying preterm birth. (GARBH-INI-Phase 2)	Longitudinal cohort	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks for birth cohort • Data monitoring • Data cleaning • Data analysis

S No	Project title	Study design (longitudinal cohort, RCT, etc)	DMC & ADAPT Role
2	ACTION-III Trial: A multi-country, multi-centre, three-arm, parallel-group, double-blind, placebo-controlled, randomized trial of two doses of antenatal corticosteroids for women with a high probability of birth in the late preterm period in hospitals in low-resource countries to improve newborn outcomes	Academic clinical trial	- Developed an electronic tracker for tracking women who are potential participants. - Developed an electronic automated system to schedule follow-up visits of enrolled participants and send reminder messages to the field staff for the scheduled follow-ups - Developed an automated process for monitoring the temperature of the investigational medicinal product (IMP) in the THSTI-Intervention Room and at the study hospital site with email alerts in case of temperature excursions - Data monitoring - Data cleaning - Data analysis
3	Equity and financial household impact in randomized controlled trials, implementation research and cohort studies in India (EQUIFINANCE)	RCTs and longitudinal cohort	For studies coordinated and implemented by THSTI - Sample size estimation - Plan of analysis - CRF design - Development of database including edit checks - Data monitoring - Data cleaning - Data analysis
4	Hospital Network study: A Prospective Cohort Study to Evaluate the Severity and Outcomes of SARS-CoV-2 infection and Correlation of Clinical Outcomes with Virus Variants	Longitudinal cohort	- Plan of analysis - CRF design - Development of database including edit checks for birth cohort - Data monitoring - Data cleaning - Data analysis
5	Zinc as an adjunct for the treatment of very severe disease in infants younger than 2 months	RCT	- Sample size estimation - Plan of analysis - CRF design - Development of EDC database including edit checks - Data monitoring - Data cleaning and lock - Data analysis
6	The follow-up study to evaluate the impact of continuous KMC initiated immediately after birth compared to KMC initiated after stabilization in newborns with birth weight 1.0 to <1.8 kg on their neurodevelopmental outcomes in low-resource settings	Prospective follow-up study of RCT participants	- Developed an electronic automated system to schedule follow-up visits of enrolled participants. - Data monitoring - Data cleaning - Data analysis

S No	Project title	Study design (longitudinal cohort, RCT, etc)	DMC & ADAPT Role
7	Severe SARS-CoV2 related disease in low- and middle-income country children aged 0-19 years: a multicountry observational study in a network of hospitals.	Longitudinal cohort study	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Shared data dictionary with other partnering country sites • Data monitoring • Data cleaning and lock • Data analysis
8	DBT COVID-19 Research Consortium: Diagnostics, Vaccines, Novel Therapeutics, Repurposing of Drugs or any other intervention for control of COVID-19	Longitudinal cohort study	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning ongoing • Data analysis ongoing
9	Study of association of air pollution and pregnancy outcomes in a semi-urban district of North India (Haryana Air Pollution and Pregnancy (HAPPY) Study)	Cohort study	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning and lock • Data analysis
10	24-hour recall dietary for validation study of "association between dietary patterns in North India Pregnant outcomes-An observational cohort study"	Cohort study	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning and lock • Data analysis ongoing
11	GIISER:- Global Immunology and Immune Sequencing for Epidemic Response	Longitudinal study	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning ongoing
12	Connecting European Cohorts to Increase Common and Effective Response to SARS-CoV-2 Pandemic: ORCHESTRA	Longitudinal cohort	For study coordinated and implemented by THSTI • Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning • Data analysis

S No	Project title	Study design (longitudinal cohort, RCT, etc)	DMC & ADAPT Role
13	"A "bench to bedside" model for clinical and translational science between academic research institutes and hospitals focused on fetal growth restriction and preterm birth."	Longitudinal cohort	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning • Data analysis
14	Maternal micronutrient and genetic associations with pregnancy outcomes in North India	Longitudinal cohort	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning • Data analysis
15	A Prospective Cohort Study to Evaluate the Severity and Outcomes of SARS-CoV-2 infection and Correlation of Clinical Outcomes with Virus Variants)	Longitudinal cohort	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning and lock • Data analysis
16	Vaccine Effectiveness Study	Negative case control	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning and lock • Data analysis
17	Multi-Omics Signatures Of Human Placenta: Real Time Assessment Of Underlying Mechanisms For Prediction Of Birth Outcomes And Development	Longitudinal cohort	For study(ies) coordinated and implemented by THSTI • Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning • Data analysis ongoing
18	Multi Omics for Mothers and Infants	Longitudinal cohort	For study(ies) coordinated and implemented by THSTI • Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning • Data analysis ongoing

S No	Project title	Study design (longitudinal cohort, RCT, etc)	DMC & ADAPT Role
19	Covid-19 Bioresource at the NCR Biotech Science Cluster	Longitudinal cohort	• Sample size estimation • Plan of analysis • CRF design • Development of database including edit checks • Data monitoring • Data cleaning
20	Biological mechanisms that explain clinical effects of zinc supplementation	Sub study within RCT	• Sample size estimation • Plan of analysis • CRF design • Developed lab management system • Data monitoring • Data cleaning and lock • Data analysis



IMMUNOLOGY CORE LABORATORY

Established in 2020, the THSTI's Immunology Core Laboratory (TICL) serves as a pivotal core facility, specializing in incorporating cutting-edge technologies to support immunological assays for both clinical and pre-clinical research. TICL offers invaluable scientific and technical expertise to investigators engaged in fundamental and translational research.

The facility has successfully secured additional grants, enabling the acquisition of state-of-the-art equipment like nCounter® Analysis Systems, BD FACS Aria Fusion, and Fluorescent Microscope. To further enhance its capabilities, TICL has developed infrastructure for the Ferret Facility and Ferret IVC cage unit and cage system. These advancements have further strengthened the establishment of animal models for SARS-CoV-2 challenge studies, crucial for the pre-clinical evaluation of potential vaccine and drug candidates in Syrian golden hamster and the K-18 humanized Ace-2 transgenic mouse.

One of TICL's significant achievements lies in its pivotal role in collaboration with various academic and industry partners for preclinical trials focused on vaccine and anti-viral drug development for SARS-CoV-2. Notable collaborators include Panacea Biotech, Immortalight, Erasmus Institute – The Netherlands, IIT Delhi, IICB - Kolkata, IGIB - Delhi, and BARC - Mumbai.

Beyond pre-clinical studies, TICL has also played a crucial role in determining the SARS-CoV-2 specific T cell memory response in vaccinated individuals. This research has been instrumental in understanding and assessing the immune response to vaccination.

TICL's relentless dedication to advancing scientific knowledge and its close partnerships with both academic and industrial players have positioned it as a leading entity in the fight against the SARS-CoV-2 pandemic. The facility's continuous growth and progress promise even more significant contributions to the field of immunological research and its applications in the future. The facility is open to providing services to academia and industry.

Vaccine pre-clinical trials:

Vaccine Name	Company name	SARS-CoV2 animal model	Study performed	Status
COVID19 vaccine	Erasmus institute	hACE2 transgenic mice efficacy study	Immunization, SARS-CoV-2 challenge, lung viral load, lung histology, cytokine mRNA expression.	International collaboration
CoviWall Vaccine	Panacea Biotech pvt. Ltd.	Challenge study in hamster model Immunogenicity study in C57BL/6 mice	Immunization, SARS-CoV-2 challenge, lung viral load, RBD ELISA, lung histology, cytokine mRNA expression. Immunogenicity of the vaccine candidates.	PoC completed and data provided to PBL
Nanocovax Vaccine	Panacea Biotech pvt. Ltd.	Challenge study in hACE2 mice model	Immunization, SARS-CoV-2 challenge, lung viral load, RBD ELISA, lung histology, cytokine mRNA expression.	Undergoing
VLP candidate	IIT Delhi	hACE2. Transgenic mice	Immunization, SARS-CoV-2 challenge, lung viral load, lung histology, cytokine mRNA expression.	PoC completed and published

Antiviral drug trials:

Drug	Company/ Academ- ic insitute name	SARS-CoV2 animal model	Study performed	Status
Curcumin	Immortalight	Hamster study	Therapeutic dosing, SARS-CoV-2 challenge, lung viral load, lung histology, cytokine mRNA expression.	Report sent to Immortalight
Drug substance	IICB-Kolkata	hACE2. Trans- genic mice	Therapeutic dosing, SARS-CoV-2 challenge, lung viral load, lung histology, cytokine mRNA expression.	Report sent to IICB-Kolkata
Drug substance	BARC-Mum- bai	Hamster study	Therapeutic dosing, SARS-CoV-2 challenge, lung viral load, lung his- tology, cytokine mRNA expression.	Report sent to BARC
PCZ –CPZ compounds	IGIB- Delhi	Hamster study	Therapeutic dosing, SARS-CoV-2 challenge, lung viral load, lung his- tology, cytokine mRNA expression.	Report sent and published

Ongoing Work and Future Plans

- Developing national and international collaborations with academic and industrial partners.
- Designing of T cell epitope-based next-generation COVID-19 vaccine candidate.
- Developing animal models for COVID-19, including the Ferret model.
- Developing animal models for autoimmune diseases and cancer.
- Bringing universality to the antigen-specific T cell assays
- Understanding the magnitude, breadth and functionality of the antigen-specific T cell response in COVID-19 vaccinated individuals.
- Understanding the cross-reactive T cell immune response against the upcoming variants of SARS-CoV-2.
- Understanding the immune response against SARS-CoV-2 in immunocompromised individuals such as patients with HIV-AIDs or Cancer.



MULTI-OMICS FACILITY

The multi-OMICS facility at THSTI is equipped with high-end instruments that provide support for multi-OMICS experimental design and high-end data analysis. The facility also provides training to individuals as a part of skill development and capacity building through regular workshops and seminars. The facility provides support and services in the following areas:

- **Genomics and Transcriptomics**

The facility is equipped with next-generation sequencing systems like Illumina NextSeq 2000 and MiSeq and has established protocols for genomic and metagenomic sequencing from viral, bacterial, fungal, human, etc samples. During the year 2022-23, the facility sequenced clinical and sewage samples surveillance from Delhi-NCR under the INSACOG programme. The facility also carried out whole-genome sequencing of >1960 SARS-CoV-2 clinical samples and submitted them to INDA-CA and GISAID databases. Also, WGS, 16S rRNA, ITS, and Sanger sequencing of >6000 bacterial and fungal samples have been carried out in 2022-23.

- **Proteomics**

The facility has a state-of-art SWATH-MS platform for proteomics services, such as protein identification, label-free and label-based quantification, and targeted proteomics. Also, BONCAT workflow for the analysis of low-abundant newly synthesized proteins has been established in the facility. The facility has developed a well-optimized LCMS method for purified, complex, and targeted proteins. This year, the facility has developed comprehensive in-house spectral assay libraries of protein databases of pathogenic bacteria for high-quality proteomics data generation.

- **Metabolomics and Lipidomics**

The facility has high-resolution Orbitrap, QTRAP, and GCMS mass spectrometers, in-house developed SOPs for metabolomics & lipidomics and data analysis. It has the largest in-house metabolite database of >9000 compounds and has now established targeted metabolite analysis methods for bile acids, fatty acids, short-chain fatty acids etc.



Small Animal Facility

The Small Animal Facility (SAF) at THSTI provides support to the scientific community of NCR Biotech Science Cluster and presently supports the animal related requirements of THSTI and Regional Centre for Biotechnology (RCB). It breeds and maintains quality laboratory animals. SAF has been established in compliance with the guidelines of the Committee for Control and Supervision of Experiments on Animals (CCSEA), Ministry of Fisheries, Animal Husbandry and Dairying, Department of Animal Husbandry and Dairying, Government of India and registered with CCSEA vide registration number 1685/GO/ReRcBi/S/2013/CPCSEA. All the animal experiments are performed only after taking prior approval from the Institutional Animal Ethics Committee (IAEC).

Relevant SOPs are in place to facilitate humane and ethical use of animals and to ensure this, training on animal care, handling and experimental techniques for research staff and students are conducted at regular intervals. The facility has CCTV surveillance monitoring and access control system.

At present the facility houses 43 mouse strains that includes inbred, transgenic, knock-out, knock-in and immune-deficient strains. In the current year two new transgenic strain were added in the breeding colony. Currently, the researchers are actively using the above platform for designing appropriate intervention strategies against Dengue, COVID-19, etc. As a part of the expansion plan, additional biosafety cabinets, cage changing stations and individually ventilated caging systems for mice were procured and installed in the facility to increase the housing capacity.

In order to keep up with the requirement of the research community, the facility is being upgraded with an aim to increase the quality of animals and build up additional support and infrastructure. The vision is to make the facility a nodal center for various animal model platforms to be used for both communicable and non-communicable diseases by researchers and various other stakeholders in a public-private partnership mode.

Ferret Facility

In order to support the research on respiratory viruses such as Influenza viruses, SAF helped design and commission BSL-2 ferret facility at THSTI. The ferret facility is the first such facility in India. Import License for procuring experimental ferrets has already been obtained and the process of importing the same is underway.

Infectious Disease Research Facility (IDRF)

IDRF, a specialized Animal Biosafety Level 3 (ABSL-3) containment facility is available to carry out research on infectious diseases caused by a pathogen that requires a biosafety level 3 (BSL3) facility for their handling such as COVID-19, Tuberculosis and HIV. All the staff working in this facility have been imparted mandatory BSL3 training.

Quality Control Laboratory

Quality control in laboratory animals has become a critical attribute in facility management to ensure production of high-quality animals and generate widely acceptable, reproducible experimental data. The Quality Control Laboratory conducts health and genetic monitoring of laboratory animals bred and maintained in the facility. The team has developed positive controls for the identification of 17 different laboratory animal pathogens and a routine health monitoring program.

Mouse Germplasm Cryopreservation Laboratory

Transgenic mice production is an important tool in biomedical research. There are chances of accidental loss of important mouse germplasms. Mouse Germplasm Cryopreservation Facility at SAF is involved in

transgenic mice production so as to preserve mouse germplasm. Currently, the team is in the process of standardization and validation of protocols for mouse embryo collection, preservation and rederivation.

Histopathology Laboratory

Histopathology is a powerful acknowledged tool with a wide range of applications within almost every domain of life sciences. The histopathology laboratory provides service for fresh, snap frozen and preserved tissue samples. Routine H & E staining as well as different special staining are also done.

Future plans

THSTI is in the process of upgradation of this existing Small Animal facility to achieve the national and international standards related to animal research and animal facility management. THSTI is working on making the ferret facility operational soon. It is also planned to establish a mouse genome engineering laboratory to conserve the germplasm of important mouse strains. Also, these germplasms will be shared with institutes. For maintaining the quality of animals, the future plans include implementing molecular-based diagnostic screening for pathogens.



VACCINE DESIGN AND DEVELOPMENT CENTRE

The Vaccine Design and Development Center (VDDC) is a unique unit facility in the academic setup built to accelerate vaccine product development and bridge the gap between academia and industry. The centre was inaugurated in February 2023 by Dr. Rajesh Gohale, Secretary, Department of Biotechnology (DBT). The centre has pre-GMP-like facilities for the production of subunit protein-based vaccines and biotherapeutics as drug substance and comprehensive analytical characterization instruments. The area of the centre is ~6000 sq ft, with the process development unit consisting of a ~4500 sqft GMP-like facility with ISO 007 grade clean units with regulatory compliances and quality control processes for the development of new sub-unit-based protein vaccine candidates. The centre currently has the following vaccine candidates in pipeline that are at different Technology Readiness Levels (TRLs):

- COVID-19 Variant of Concern candidate: **TRL 6**
- Potent Trimeric Flu candidate: **TRL 5**
- Monkeypox virus candidate: **TRL 4**
- CEPI Boradly protecting beta coronavirus candidate: **TRL 3**

VDDC is open for collaboration with academics, industry, and start-ups as fee-for-services.





ACHIEVEMENTS

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BOOKS AND CHAPTERS

1. Verma R., Raj S., Berry U., Ranjith-Kumar CT., Surjit M. (2022). Drug repurposing for COVID-19 therapy: Pipeline, current status and challenges in *Drug repurposing for emerging infectious diseases and cancer*: pp 451-478DOI: <https://doi.org/10.1007/978-981-19-5399-6>.
2. Sarmah, D T., Kumar, S., Chatterjee, S., Bairagi, N. (2022). Dissecting big RNA-Seq cancer data using machine learning to find disease-associated genes and the causal mechanism in Big Data Analytics in Chemoinformatics and Bioinformatics; eBook ISBN: 9780323857147

Patents granted in the year 2022-2023

S. No.	Title	Country of Grant	Patent No.	Date of Grant	Inventors
1.	Novel Compounds as Anti-Tubercular Agents	European Union	3148518	30-11-2022	Sundeeep Dugar, Dinesh Mahajan, Santosh Kumar Rai, Kanury Rao, Varshneya Singh
2.	Method of improving stability of recombinant protein product in CHO batch culture and uses thereof	India	407401	22-09-2022	Niraj Kumar, Susmita Chaudhuri, Ashutosh Tiwari
3.	Cytolethal distending toxin 8 polypeptide variant and polynucleotide encoding same	India	409520	20-10-2022	Ashutosh Tiwari, Chandresh Sharma, Anurag Sankhyar, Tarang Sharma, Shinjini Bhatnagar, Navin Khanna

Patent Applications filed in the year 2022-2023

S. No.	Title	Application No.	Filing Date	Inventors
1.	Universal microbial sample transport medium for genomic and metagenomic studies	202211023269	20-04-2022	Bhabatosh Das, Shruti Panwar, Nitya Wadhwa, Roshan Kumar
2.	HA monomer based universal Influenza vaccine candidate and its uses thereof	202211065678	16-11-2022	Tripti Shrivastava
3.	A biomaterial and method of its preparation	202211068526	29-11-2022	Santosh Mathapati, Sunil
4.	Novel formulations containing gut microbiota derived metabolites of dietary Tryptophan for the management of Non-alcoholic Fatty Liver Disease	202311016126	10-03-2023	Ruchi Tandon, Phulwanti Kumari Sharma, Yamini Goswami, Ruby Bansal

List of Extramural Projects Sanctioned during the Financial Year 2022-23

S. No.	Project Name	Name of P.I./ Co-PI from THSTI	Funding	Project From	project Upto	Amount Sanctioned for THSTI (₹)
1.	ADVANCE-Accelerate the Development of Vaccines and New Technologies to Combat the AIDS Epidemic	Dr Jayanta Bhattacharya	USAID/IAVI	Jan 2023	Dec 2023	2,93,77,830
2.	Development of high-throughput screening assays to identify antivirals targeting multiple stages of henipavirus life-cycle	Dr Guruprasad R Medigeshi	Good Ventures Foundation, Open Philanthropy	Mar 2023	Sep 2026	8,34,77,726
3.	SARS-CoV2 anti-viral activity testing platform to support the preclinical development of new chemical entities, and natural products from Academia, Start-ups and Pharma companies	Dr. Amit Awasthi	BIRAC	05-09-2022	04-09-2024	2,79,54,000
	Training the next generation of Indian clinical trialists	Dr. Nitya Wadhwa	University College London	01-09-2022	30-09-2023	54,28,000
	SURE: Short intensified treatment for children with tuberculous meningitis	Dr. Nitya Wadhwa	University College London	01-01-2023	31-12-2025	25,32,000
4.	SARS-CoV2 animal challenge model for pre-clinical and translational research	Dr. Amit Awasthi	BIRAC	08-04-2022	07-04-2023	7,52,70,000
5.	Inter-Institutional School of Diagnostic Innovation in Biodesign (SIB) at THSTI	Dr. Jayanta Bhattacharya	DBT	19-12-2022	18-12-2027	5,94,45,000
6.	Identification of lead molecules for development of novel therapeutic strategies against viruses	Dr. Shailendra Asthana	DBT	13-09-2022	12-09-2027	49,06,400
7.	Uncovering the role of essential RNA-binding proteins in transcriptional regulation of genes involved in placental development	Dr. Indira Bag (Ramalingaswami fellow)	DBT/ RCB, Faridabad	31-10-2022	30-10-2027	1,23,60,000
8.	To delineate the survival strategy of mycobacteria through antigenic determinants by inhibiting autophagy via miRNA and its significance in host directed therapy	Dr. Ramandeep Singh	DBT	23-12-2022	22-12-2025	23,63,360
9.	Genomic surveillance for SARS-CoV2 in India: Indian SARS-CoV2 Genomics Consortium (INSACOG)-Phase-II	PI - Nitya Wadhwa, Dr. Bhabatosh Das Co-PI- Dr. Pallavi Kshetrapal, Dr. Komal Wadhwa	DBT	29-12-2022	28-12-2023	4,35,29,280
10.	Immunological responses of Arsenicum album 30C to combat COVID-19: A double-blind, randomized, placebo controlled-clinical trial in the Pathanamthitta district of Kerala	Dr. Amit Awasthi	Central Council for Research in Homeopathy (CCRH)	15-09-2022	14-09-2023	49,00,000

S. No.	Project Name	Name of P.I./ Co-PI from THSTI	Funding	Project From	project Upto	Amount Sanctioned for THSTI (₹)
11.	Exploration of Immunopathogenesis of extra-intestinal organ involvement in patients with Celiac diseases	Dr. Amit Awasthi	ICMR	18-01-2023	17-01-2026	9,09,729
12.	CEPI Centralised Laboratory (Bioassay Lab)	Dr. Guruprasad R. Medigeshi	CEPI	16-02-2023	08-09-2025	69,60,000
13.	MOMI Ideas Fund 2021: N-linked glycosylation in Gestational Diabetes Mellitus	Dr. Shinjini Bhatnagar	BIRAC	07-03-2023	06-03-2024	73,97,900
Total						36,68,11,225

Honors and Awards for the year 2022-2023

- Dr Shinjini Bhatnagar, Distinguished Professor, was elected as a fellow of Indian Academy of Sciences in 2023 under the Medicine section.
- Dr. Amit Awasthi, Senior Professor, was conferred with the Award of Excellence in Research on Immune-Therapies at the 49th Annual Conference of Indian Immunological Society, PGIMER, Chandigarh, November 2022.
- Dr Guruprasad R Medigeshe, Professor, received full membership of European Society for Virology.
- Dr. Bhabatosh Das, Associate Professor, was elected as a fellow to the prestigious West Bengal Academy of Science and Technology (WAST) in December 2022.
- Dr Sucheta Banerjee Kurundkar received the Silver Award in QCI Quality Champion Award 2022.
- Dr Ajay Kumar, Senior Research Scientist, received membership of European Association for the Study of the Liver (EASL)
- Dr Amit Kumar Yadav, Senior Research Scientist, received the best presentation (runners up) award in Virtual Podium Asia Pacific Conference 2022.
- Dr Amit Kumar Yadav, Senior Research Scientist, has been elected as Executive Council member of Proteomics Society of India (PSI).
- Dr. Zaigham Abbas Rizvi, Senior Research Scientist, won the best Oral presentation award, 2022 at the 49th Annual Meeting of Indian Immunology Society (IMMUNOCON 2022) held from 23-26 November 2022 at PGI, Chandigarh.
- Dr. Deepjyoti Paul, MK-Bhan Research Fellow received the Bill & Melinda Gates Foundation Professional Development Award 2022.
- Dr. Lekshmi N., MK-Bhan Research Fellow, was awarded the Best Poster Award at the 16th Asian Conference on Diarrhoeal Disease and Nutrition (ASCODD) at Kolkata.
- Dr. Ashish Kumar Agrahari, MK-Bhan Young Researcher Fellow, was awarded the second prize in "The Bioinformatics Grand Challenge Eduthon" at the 1st Colloquium on Bioinformatics Learning, Education and Training (CoBLET2022), held at Bezmialem Vakif University, Istanbul, Turkiye, from 11th-14th October 2022.
- Dr. Niranjana Shri S and Dr. Suruchi Aggarwal were awarded the M K Bhan Young Researcher Fellowship for the year 2022-23.
- Akshay Binayke, Ph.D. Scholar, won the prestigious G.P. Talwar Young Scientist Award, 2022 at the 49th Annual Meeting of the Indian Immunology Society (IMMUNOCON 2022) held from 23-26 November 2022.
- Ms. Shabnam Ansari, PhD Scholar, won the Best poster award at the International Conference on Virus Evolution, Infection and Disease Control (ICVEIDC) organized by the Department of Biotechnology and Bioinformatics, School of Life sciences, University of Hyderabad, Hyderabad on 15th-17th December 2022.
- Ms. Gazala Siddqui and Ms. Ritika Khatri (Technical Staff) received Best Poster award in VIROCON 2022 conducted by Indian Virology Society.
- Mr. Dipanka Tanu Sarmah, Senior Project Associate won third prize in the poster presentation in the Symposium on Accelerating Biology 2023: Discovery to Delivery in Pune from February 28 - March 02, 2023.



ACADEMICS

Doctoral Program

The Ph.D. program in biomedical and clinical research offered by THSTI is recognized by Jawaharlal Nehru University, Delhi. The institute is also affiliated with the Regional Centre for Biotechnology (RCB), Faridabad, Manipal Academy of Higher Education (MAHE), Karnataka and Jadavpur University (JU), Kolkata for the Ph.D. Program. The thematic areas for research are under the broader areas of Infection & Immunology, Maternal & Child Health, Non-Communicable Disease, Multidisciplinary Clinical & Translational Research and Mathematical and Computational biology.

As on 31st March 2023, 124 students have been enrolled for the THSTI doctoral programs.

S. No.	Name of the Student	Supervisor
1.	Ms. Eeba	Dr. Nisheeth Agarwal
2.	Mr. Aakash Goswami	Dr. Amit Awasthi
3.	Ms. Priya Sehrawat	Dr. Guruprasad R. Medigeshi
4.	Mr. Devvrat Pandey	Dr. Samrat Chatterjee
5.	Mr. Chandra Ratan	Dr. Ramandeep Singh
6.	Ms. Poulomi Chatterjee	Dr. Samrat Chatterjee
7.	Ms. Jaya	Dr. Susmita Chaudhuri
8.	Ms. Priyanka Verma	Dr. Guruprasad R. Medigeshi
9.	Ms. Eram Fatima	Dr. Niraj Kumar
10.	Ms. Kanchan	Dr. Gaurav Batra
11.	Ms. Avika Kalra	Dr. Krishnamohan Atmakuri
12.	Ms. Saima Perween	Dr. Amit Kumar Pandey
13.	Ms. Juhi	Dr. Ramandeep Singh
14.	Ms. Sneha Bajpai	Dr. Krishnamohan Atmakuri
15.	Mr. Aayush Raj Tyagi	Dr. Amit Awasthi
16.	Ms. Sreemoyee Ghosh	Dr. Milan Surjit
17.	Mr. Linus Augustin	Dr. Nisheeth Agarwal
18.	Ms. Kajal Kamboj	Dr. Bhabatosh Das
19.	Mr. Sanchit Singhanian	Dr. Amit Kumar Yadav
20.	Mr. Rakesh Chaudhary	Dr. Tripti Shrivastava
21.	Ms. Gurleen Kaur	Dr. Sweetie Samal
22.	Mr. Jishnu Sankar	Dr. Dinesh Mahajan
23.	Ms. Jyotsna Dandotiya	Dr. Amit Awasthi
24.	Mr. Debapriyo Sarmadhikari	Dr. Shailendra Asthana
25.	Dr. Deepika Rathna Murugesan	Dr. Nitya Wadhwa

Short-term Training Program

Our previous experience with training young students from undergraduate and post-graduate courses from across the country has been an equally enriching experience for our faculty members and PhD students alike. Last year, THSTI hosted and trained 36 students in the fields of Infection & Immunology, Maternal & Child Health, Non-Communicable Disease, Multidisciplinary Clinical & Translational Research and Mathematical and Computational biology.

Students' Achievements

Five of our Ph.D. Students were conferred with doctoral degrees in 2022-23:

- Dr. Aleksha Panwar, JNU
- Dr. Riya Sarkar, JNU
- Dr. Farha Mehdi, JNU
- Dr. Niti Singh, MAHE
- Dr. Deepika Chaudhary, MAHE



Dr. Aleksha Panwar



Dr. Riya Sarkar



Dr. Farha Mehdi



Dr. Niti Singh



Dr. Deepika Chaudhary



External Relations and Institutional Development Office (ERID)

The External Relations and Institutional Development (ERID) office supports researchers at THSTI for grants, regulatory compliance with respect to ethics committees, innovation management, intellectual property management, scientific communications, and outreach. The office supports the investigators and administrators in various institutional meetings and works towards centralization of processes for efficiency. It has been a busy year at the office for international collaboration, industrial partnership, patenting and communication.

Ms. Vidhya Krishnamoorthy, Technical Manager (Grants Coordinator), is responsible for centralizing the operations involving ethics committees and grants support (pre and post-award) for national and international grants and is the point of contact for collaborations with industries. Her profile provides significant support in the pre-award area with a special contribution to the post-award reporting of international grants. She is responsible for the secretariat of the committees for human participation, and stem-cell research and is active in alerting the investigators and updating the institutional compliance with regulatory agencies.

This year, she coordinated the application to a U19 grant application to the National Institute of Health, quarterly reporting to CEPI, annual reporting of the GLISER and sub-grant agreements of the PAD initiative. Approximately, a total of eleven meetings were organized for the review of proposals involving human participants, animal experiments and stem-cell research. Ms. Vidhya Krishnamoorthy was an invited participant in the WHO tool for benchmarking ethics oversight of health-related research with human participants, the workshop conducted by the bio-ethics unit of ICMR, Bengaluru.



Dr. Soma Patnaik, Senior Technical Officer, is the point of contact for Scientific Communications, Outreach activities, Intellectual Property Rights and Technology Transfers of the institute. During the period 2022-23, she conducted many outreach activities under the Science Setu program of DBT and has organized and coordinated science expos such as IISF, Akash for Life and Science Day. She was involved in getting three patents granted and filing four patent applications in the year 2022-23 and filing four international PCT applications. Dr. Patnaik has been involved in preparing and submitting press releases, and official documents and providing scientific inputs such as PPTs and Infographics, as desired by organizations such as DBT, DST, etc. She also coordinated the documentary film on THSTI unveiled by Honourable Minister, Dr Jitendra Singh ji on 22nd Feb 2023 as a part of Unveiling THSTI's Scientific Achievements and Vision, UTSAV, 2023 at THSTI. One of her key roles has been in preparing THSTI's annual reports.



Ms. Vidhya

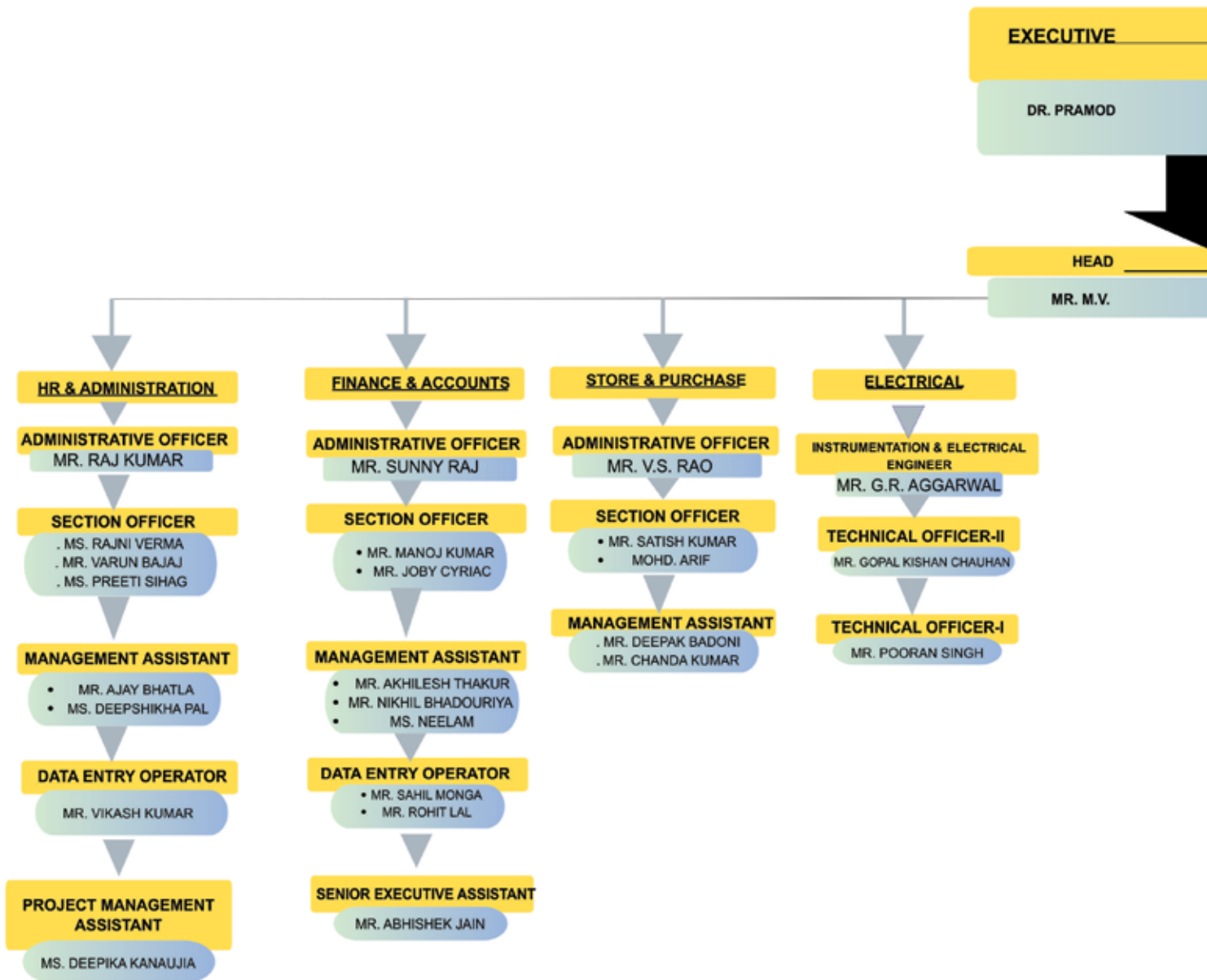


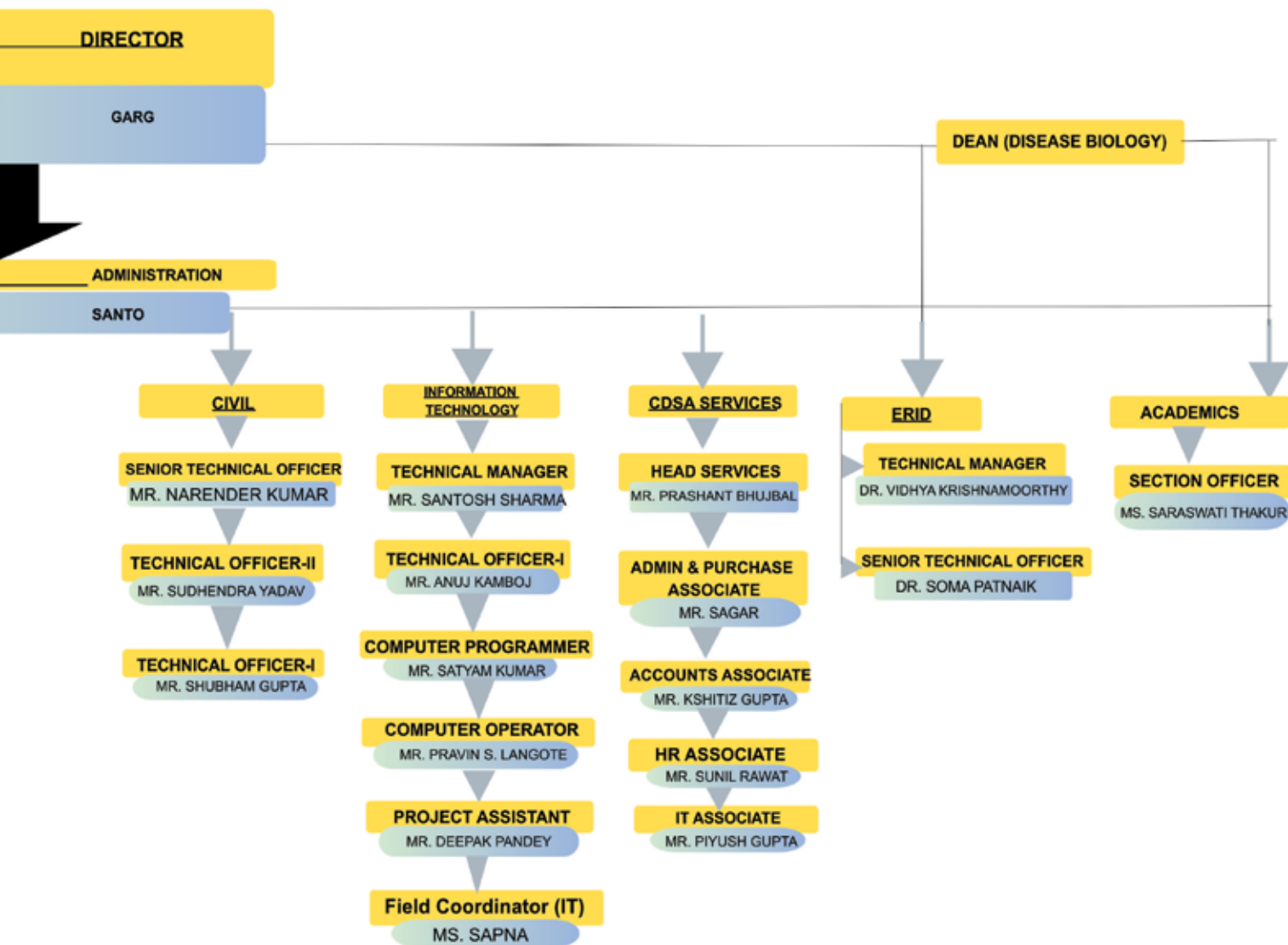
Dr. Soma Patnaik



ADMINISTRATION

ADMIN CHART







The administration of THSTI rendered support through its Officers and staff members who have very professionally and sincerely carried out their duties for making the various activities of the Institute successful in the year 2022-2023. The personnel in administration comply with the Government of India Rules and related guidelines issued by the Govt. of India from time to time in their functioning.

The THSTI Administration comprises several functional sections: General Administration, Human Resources and Legal, Finance & Accounts, Stores & Purchase, Information Technology, Engineering & Estate Management, and Intellectual Property Management. The various sections have functioned effectively under the able leadership of the Executive Director and the Head Administration. The essential activities performed by various sections are detailed below.

General Administration

The General Administration section broadly deals with the constitution of committees, the conduct of meetings of the THSTI Society, Governing body, Finance Committee, Scientific Advisory Committee, and other internal committees, and wherever required, follow-up and implementation of the decisions of these committees, the commemoration of important days, hostel management, front office management, RTI and grievances handling, official language implementation functions, logistics arrangement for the officers / staff / guests, security management, house-keeping services management, and any other functions as and when ordered by the Executive Director / Head-Administration.

THSTI Governance

THSTI conducted one Society, two Governing Body, two Finance Committee, and one Scientific Advisory Committee meeting during the FY 2022-23. Recommendations made by the concerned committees were documented and circulated among concerned individuals/departments for implementation.

THSTI Internal Committees

Various internal committees are constituted to advise and support the Executive Director in decision-making. The various committees and the members of the same may be seen in the later part of this report.

Intellectual Property Protection and Collaborations

During the FY 2022-23, THSTI made significant achievements in patents, technologies developed and commercialized, and national/international collaborations. Our sphere of influence is visible from our productive collaborations with scientific organizations, academic institutions, and industries. During this financial year, THSTI filed a total of 4 patent applications, THSTI was granted 3 patents, and THSTI developed 4 technologies. The institute was a primary part of the 23 research collaborations / MoUs executed with different agencies during the FY 2022-23.

Right to Information

In compliance with the provisions of the Right to Information Act, 2005, THSTI has nominated Public Information Officer and Appellate authority to provide information to the citizens who seek information. To ensure transparency in its functioning, THSTI has regularly made Suo moto disclosures on its website so that the number of RTI applications received is minimized. From 1st April 2022 to 31st March 2023, a total of 38 applications and 2 appeals were received by the institute. All the applications and appeals have been disposed of as per the RTI Act, 2005 within the prescribed time limit.

Every public authority is required to conduct the **'Transparency Audit of Disclosures u/s 4 of the Right to Information Act'**. In this connection, we submitted our request to Central Information Commission (CIC) to map THSTI with the Indian Institute of Mass Communication (IIMC) for conducting the third party transparency audit on the activities of our institute. **In this third party transparency audit, THSTI has obtained an overall marks of 93% for the various aspects of suo motu disclosures.** The auditing agency has submitted its report on the CIC portal.

Public Grievances

Public Grievances received either offline or through CPGRAMS are monitored and disposed of regularly. During the FY 2022-23, one public grievance was received and disposed of within the prescribed time limit.

Special Campaign 2.0 for disposal of pending matters

Special campaign 2.0 was observed in the institute from 02.10.2022 to 31.10.2022. Pursuant to the directions of the Department of Personnel & Training, the institute carried out record management practices in the light of Special Campaign 2.0 which was closely monitored by the Department of Biotechnology. In terms of the provisions contained in Section 5 (1) of the Public Records Act, 1993, Mr. Raj Kumar, Administrative Officer was nominated as the Record Officer in the institute. The record retention schedule for various sections of the administration was prepared. Among many other activities on Special Campaign 2.0, a total of 19780 files were reviewed out of which 19347 were weeded out.

Prevention, Prohibition, and Redressal of Sexual Harassment of Women at the Workplace

The Institute fully complies the policy on prevention, prohibition, and redressal of sexual harassment of women at the workplace. It has an Internal Complaints Committee (ICC) in compliance with the Sexual Harassment of Women at Workplace (Prevention, Prohibition and Redressal) Act, 2013. The members of the ICC are responsible for conducting inquiries pertaining to such complaints. During the year 2022-23, one complaint was received by the ICC and the same was dealt as per rules and guidelines. To ensure equality at the workplace and to create a safe and productive environment for all female employees by protecting their rights, Institute organised three training sessions on "Prevention of Sexual Harassment of Women at Workplace" during the year 2022-23.

Vigilance Activities and Vigilance Awareness Week 2022

The Institute has a Chief Vigilance Officer to look into the complaints with respect to malpractice, corruption or other types of misconduct against the employees of the Institute.

As per the directions of the Central Vigilance Commission, a three-month campaign from 16.08.2022 to 15.11.2022 as a precursor to vigilance awareness week was carried out during which examination of details of land/properties which are not in use was carried out and action plan thereof was made, examination of unused assets was made and the scraps were disposed of duly following the proper procedure. Record management, website updation, guidelines updation and disposal of pending complaints were taken up as part of said campaign during the year 2022-23.

The "Vigilance Awareness Week" (31st October- 6th November) began on 31st October 2022 with an integrity

pledge administered by Dr. Pramod Garg, Executive Director, THSTI, to all the faculty members, scientists, officers, employees, students, and research fellows in the presence of THSTI's chief vigilance officer.

The 31st of October is also celebrated as Rashtriya Ekta Diwas to mark the birth anniversary of Sardar Vallabhbhai Patel. On this day, Dr. Garg administered Rashtriya Ekta Diwas pledge to all the faculty members, scientists, officers, employees, students, and research fellows of THSTI. Addressing the gathering, he encouraged all to adopt the principles of integrity both in the personal and professional walks of life.

In order to encourage the employees and the users, a link to take integrity pledge and be a part of the movement was displayed on the website of the Institute.

An essay writing competition was organized for the employees of the Institute on "Corruption free India for a developed nation". Further, an outreach activity was organised in Government Primary School of Bhakri village wherein approximately 70 students participated in the poster making competition. An awareness Gram Sabha was also organised in the school wherein the local village leaders and parents of the students residing in Bhakri village were invited.

Implementation of the official language policy

The Institute promotes the use of Official Language (Hindi) in the day to day official works to ensure proper implementation of the Official Language Policy of the Government of India. The official language implementation committee of the institute monitors the progress of all the implementation activities. All the letters received in Hindi were replied in Hindi as per the Rule 5 of the Official Language Rules, 1976. All the employees are regularly advised through various means to promote the use of Hindi in official work from time to time.

The name plates of officers, visiting cards, letterheads and rubber seals are ensured to be in bilingual format. The recruitment notices are regularly published in Hindi dailies. The majority of the Institute's website is bilingual in nature.

हिन्दी पखवाड़ा

संस्थान में हिन्दी पखवाड़ा 14 से 29 सितम्बर 2022 को मनाया गया। मुख्य कार्यक्रम 29 सितम्बर 2022 को आयोजित किया गया। इस दिन प्रो. अनिल राय, प्रोफेसर, हिन्दी विभाग, दिल्ली विश्वविद्यालय को मुख्य अतिथि के रूप में आमंत्रित किया गया। इस पखवाड़ा के दौरान हिन्दी सुलेख प्रतियोगिता, हिन्दी निबंध प्रतियोगिता, हिन्दी गीतों की अंताक्षरी प्रतियोगिता आयोजित की गयी। हिन्दी में लिखित प्रश्नोत्तरी प्रतियोगिता भी आयोजित की गयी जिसमें षड्वार्थ, विलोम षब्द और पर्यायवाची षब्द आदि पूछे गए।

इसके अलावा मुख्य कार्यक्रम के दौरान मंच पर हिन्दी कविता पाठन (कविता स्व-रचित या किसी कवि द्वारा रचित) प्रतियोगिता का आयोजन किया गया। इन सभी प्रतियोगिताओं के विजेताओं को मुख्य अतिथि द्वारा पुरस्कार दिये गए।



Other main events organized during the year 2022-23

THSTI observed all the important days / weeks / Pakhwadas as directed by the Government of India, such as Hindi Pakhwada and Vigilance Awareness Week as mentioned above and few others as shown below:

International Yoga Day

The International Yoga Day-2022 was celebrated on 21st June 2022 to spread awareness about the invaluable benefits of yoga. THSTI conducted a yoga session and Rajyog Meditation session for its faculty members, scientists, officers, employees, students, and research fellows with the theme of 'Yoga for Humanity'. Prof. Pramod Garg, Executive Director, led the enthusiastic group of participants for the yoga session.



13th Foundation Day

THSTI celebrated its 13th Foundation Day on 15th July 2022. Dr. Vinod K Paul, Member, NITI Aayog presided over the foundation day function as the chief guest. Dr. Rajesh Gokhale, Secretary, Department of Biotechnology (DBT) delivered the Foundation Day address. Dr. Alka Sharma (DBT), Dr. Jyoti Logani (DBT) attended the event along with other invitees and the faculty members, scientists, officers, employees, students, and research fellows of THSTI.

In the Executive Director's address, Prof. Pramod Garg highlighted the major achievements of THSTI in the past year in various areas such as SARS-CoV-2, Vaccine development, Pregnancy Cohorts, Tuberculosis, Influenza, Non-Alcoholic Fatty Liver Disease, etc. He also gave a brief on the upcoming new facilities at THSTI.

While delivering the Foundation Day address, Dr. Gokhale applauded the work being done at THSTI & emphasized that scientists should not only answer their inquisitiveness but also work with empathy to find solutions for the needs of poor people & make India a great nation.

Dr. Paul delivered the keynote address and urged everyone especially young researchers to make excellence a daily habit so that as a nation we can grow and become more successful.

Prof. Garg read out the message from Dr. Jitendra Singh Ji, Hon'ble Minister of State (IC) for the Ministry of Science & Technology and Ministry of Earth Sciences; Minister of State for PMO, MoPPP, DAE and DoS, Govt. of India, lauding THSTI for its collaborative efforts & building innovation ecosystems.

The celebrations also marked distribution of awards for outstanding performance of faculty, scientists, PhD scholars and staff in their respective fields. The Foundation Day celebrations also included colloquium, poster competition, quiz competition and entertainment programs and winners and participants were felicitated.



Independence Day

THSTI organized several events to mark the Independence Day celebrations. Under the aegis of Azadi Ka Amrit Mahotsav, a campaign "Har Ghar Tiranga" was carried out by the institute wherein the employees were encouraged to hoist the national flag of India in their homes during the period from 13-15th of August 2022. The national flags were distributed among all the employees of the Institute. The employees of THSTI also carried out a rally for promoting #Har Ghar Tiranga along with the Government School students of Bhankri village Faridabad, on 12th August 2022. All the children were given flags and were motivated to hoist them at their homes.

On 15th August 2022, THSTI celebrated the 76th Independence Day with great fervour and pride. During his address, Dr. Pramod Garg, Executive Director, applauded India's achievements during the past 75 years and urged everyone to make their thinking independent and take pride in our country's great heritage. He urged the students, faculty members, scientists and staff of THSTI to take the lead and contribute in making India a developed nation. Dr. Garg lauded the contributions of THSTI to the nation in Science and Technology (S&T) arena.

The school children from the Government School, Bhankri, Faridabad were invited for the Independence Day celebrations at THSTI. They performed group and solo dances to the tunes of few patriotic songs. They also performed a skit highlighting the plights of a girl child from birth to growing up and what should be done by everyone to improve the condition. The skit was very well appreciated by all the members of the institute.

3rd Annual "Dr. MK Bhan Memorial Oration"

Every year, THSTI commemorates Dr. MK Bhan's birth anniversary on 9th November by holding the 'Dr. MK Bhan Memorial Oration'. This year, Dr. Rajiv Bahl, Secretary, Department of Health Research (DHR) and Director General of Indian Council of Medical Research (ICMR) delivered the 'Dr. MK Bhan Memorial Oration'. Dr. Bahl highlighted the excellent work done in India on Rotavirus Vaccine, Childhood Diarrhoea and Kangaroo Mother Care which has significantly reduced neonatal mortality. Dr. Bahl also interacted with the faculty members and scientists of THSTI. The program was organised in hybrid mode, with many participants joining the event online.



Unveiling THSTI's Scientific Achievements and Vision

On 22nd February 2023, Honourable Minister, Dr. Jitendra Singh Ji, Union Minister of State (Independent Charge) Science & Technology; Minister of State (Independent Charge) Earth Sciences; MoS PMO, Personnel, Public Grievances, Pensions, Atomic Energy and Space, visited Translational Health Science and Technology Institute (THSTI) and laid the foundation stone for a 'Medical Research Centre', 'Translational Research Laboratories' and a Hostel in its campus.



The Medical Research Centre (MRC) will be a 50 bedded hospital that will be immensely useful for the conduct of observational cohort studies and phase I and II clinical trials in future. The Translational Research laboratories, Ind-CEPI mission of DBT, will be useful for vaccine development and provide space for Small and Medium-sized Enterprises (SMEs) for their R&D. With the addition of these facilities, THSTI seeks to leverage its strengths to become a leader in translational research.

The THSTI fraternity welcomed the minister and celebrated the occasion as UTSAV 2023 (Unveiling THSTI's Scientific Achievements and Vision).

UTSAV 2023 was marked by an introductory address by the Executive Director, Prof. Pramod Garg who highlighted the major achievements of THSTI in the past years in various areas such as mother and child health (MCH) research, vaccine development, clinical cohorts, Tuberculosis, Influenza, diagnostics, Human Microbiome, Non-alcoholic fatty liver disease, etc. MCH is developing AI powered ultra-sonography tools which will help pregnant women in remote areas. Prof Garg informed that THSTI has developed an anti-TB molecule, two new COVID and pan beta-coronavirus vaccines, and started three important courses in Clinical Research, Vaccinology course and Biodesign. Prof Garg also gave a brief insight into THSTI's collaborations with industry and other organizations.

Dr. Rajesh Gokhale, Secretary, Department of Biotechnology, congratulated THSTI fraternity for its exemplary work done in the past especially in the COVID-19 research, vaccine and diagnostics. Dr Gokhale said that institutions like THSTI bring about transformative changes in the country with the kind of work they do.

The Hon'ble Minister Dr. Jitendra Singh Ji, conveyed his warm wishes to THSTI. Dr. Singh appreciated the scientific achievements of THSTI and lauded the commitment of the organization to work towards biomedical innovations to improve the health of people in India and the world. Dr Singh congratulated THSTI for setting up of Medical Research Centre (MRC) at NCR Biotech Science Cluster. He said MRC is very relevant and needed for the kind of translational work that is being done at THSTI. Lauding the efforts of THSTI, Dr. Singh said people should know the kind of work that THSTI has been doing. He suggested institutionalizing collaborations with industry and academia which is very important for taking bench-side research products to the clinic. He suggested that to further increase its collaborations with academia, THSTI's research work can become a part of PG and DM dissertations of medical students.

During the celebrations, a video highlighting the THSTI's research activities and major achievements was released by the Hon'ble Minister.

National Science Day (28 February 2023)

To commemorate the announcement of the discovery of the 'Raman Effect' by Nobel Laureate C V Raman, every year India celebrates National Science Day on 28th February. This year the theme of National Science Day was 'Global Science for Global Wellbeing'. THSTI celebrated this day with the theme "Global Vaccines for Global Well Being". The under-graduate and post-graduate students from Sri. Venkateshwara College, Delhi University (DU), Maitreyi College, DU, Shaheed Rajguru College of Applied Sciences for Women, DU, Manav Rachna International Institute of Research and Studies, Faridabad and MVN University, Palwal were invited to THSTI. The experts from THSTI and industry delivered talks and interacted with the students. A quiz competition and visit to THSTI's research facilities were organised for the students.

International women's day

THSTI celebrated International Women's Day on 7th March 2023. Ms Kanchan Lakhani, International Para Athlete was the Chief Guest for the event. The students from Government Girls Primary School, Bhankri Village, Faridabad were specially invited to be a part of these celebrations. During the event, Ms. Lakhani shared her story of challenges, grit and determination, inspiring the faculty, scientists, students and staff. Prof. Pramod Garg, Executive Director, THSTI appreciated the role of women in society. He also thanked the chief guest and the young school students for attending the event and presented school bags to students. The young women researchers of the institute were also felicitated during the event. As a part of the celebrations, an essay writing competition was also organized and the winners were given prizes.

Swachhta Pakhwada 2022

The Swachhta Pakhwada was observed by THSTI from 1st May 2022 to 15th May 2022 with utmost zeal and enthusiasm. During this period, both on campus and off campus cleanliness activities were organised. The banners were displayed on the main gate and reception area.

The Pakhwada began on 2nd May 2022 with Dr. Pramod Garg, Executive Director (THSTI) administering the Swachhta Pledge in English and Hindi to all the faculty members, scientists, officers, employees, students, and research fellows. Dr. Garg, Executive Director spoke about the importance of Swachhta and motivated them to actively participate in all the activities scheduled to be conducted and thereby contribute to the fullest to make this campaign a huge success.

On 6th May 2022 a lecture was delivered by Dr. Meenakshi Sharma (HR section) to sensitize the housekeeping staff, gardeners, construction workers and other unskilled staff on the importance of personal and environmental hygiene.

As a part of the "Swachhta Pakhwada", the Institute executed civil works in the Government Primary School for Girls in Bhakri Village, Faridabad to ensure the much-needed hygiene standards. The hygiene of the school premises was below the required level. There was only one toilet for 113 girl students which had no water supply. The following civil works were carried out in the school premises to improve cleanliness :

3 toilets with water points and wash basin were constructed

Painting of school building and cement work in the school assembly area

Construction of drinking water platform and provision of a RO drinking water



The above civil works were completed and handed over by Dr. Pramod Garg, Executive Director, THSTI to the school authorities on 12th May, 2022.

On this occasion, Dr. Garg interacted with the students emphasizing the importance of personal hygiene and environmental cleanliness

A tree plantation drive was carried held in the school premises by the Executive Director and the faculty / staff members of THSTI, the Principal and the Headmistress of the School.



In addition to the above, the following activities were held at school premises:

- A nukkad natak was performed by some of the institute's employees to educate the students on the importance of maintaining cleanliness in their homes and surroundings
 - Dustbins were placed in all the requisite locations
- Masks were distributed to the students
- Uniforms were distributed to the students. These uniforms were purchased from the contributions made by the faculty members and other staff of THSTI

All the above activities conducted by the Institute, enabled us to take the mission of Cleanliness to the community, thereby creating mass awareness. The local leaders and members of the political parties and various other groups attended the drive and appreciated the efforts taken by THSTI.

Human Resources Section

The Human Resource Section of the Institute deals with all the employees' matters, such as recruitment, promotion, training, probation, travel, employee benefits, discipline, employee welfare, exit, and other related matters. HR section deals with service matters of more than 700 employees. HR section also deals with the legal cases pertaining to the establishment and other matters. During the FY 2022-23, the section dealt with two court cases, one each in the High court and District court.

Recruitment

Project Positions: 443 positions were filled up through 50 recruitment notices and many rolling recruitment notices. Rolling recruitment notices are issued to fill JRF/PA-I/SRF/PA-II//RA and clinical positions twice every month to cater for the urgent requirements that arise regularly.

Core Positions: The recruitment notices for core positions are published in national dailies and Employment News. The recruitment tests / interviews are conducted in-house by the recruitment committees which has external experts. During the year 2022-23, 11 regular positions were filled, and the following persons were appointed to the posts mentioned as on 31.03.2023 against their names:

S. No.	Name	Designation
1.	Dr. Jayanta Bhattacharya	Dean
2.	Dr. Amit Awasthi	Senior Professor
3.	Dr. Nitya Wadhwa	Senior Professor (Clinical)
4.	D. Dinesh Mahajan	Associate Professor
5.	Mr, Sunny Raj	Administrative Officer
6.	Dr. Mahendra Devidas Jamdhade	Technical Officer I
7.	Mr. Anuj Kamboj	Technical Officer I
8.	Mr Akhilesh Thakur	Management Assistant
9.	Mr. Manoj Kumar	Lab Technician
10.	Mr. Atul Kumar Sharma	Data Entry Operator
11.	Mr. Raj Kumar Tanwar	Data Entry Operator

Promotion/Upgradation:

During the year 2022-23, the under-mentioned technical employee was promoted under the THSTI Normal Assessment scheme for the promotion of Technical Cadre, which is based on the provisions of the CSIR Merit and Normal Assessment Scheme (MANAS) in accordance with the provisions contained in the approved recruitment rules:

S. No.	Name	Promoted From	Promoted To
1	Mr. Sandeep Goswami	Lab Technician	Lab Technician (NFSG)

Employees' benefits: THSTI provides its employees with the benefits like LTC, Medical reimbursement, telephone charges reimbursement, office briefcase and newspaper reimbursement, and children's education allowance by following the Government of India's directions. All these cases of reimbursement and other allowances were processed as per rules and in a time-bound manner.

Employee welfare: Various recreational facilities are available within the campus to motivate the employees and students. A family get-together and a sports meet are organized annually for the employees and their families. During the year 2022-23, HR section organized a family get-together for the employees and their families at Kaanya Damdama Retreats near Damdama Lake, Gurgaon, where various sports and recreational activities were organized.

To recognize exceptional research work and contribution to the overall development of the institute, THSTI has instituted the following awards by creating an endowment deposit supported through non-governmental funds. These awards are distributed every year during the Foundation Day celebrations. During the year 2022-23, the following personnel/teams were awarded:

S. No.	Name of the award	Cash award (in Rs)	Name of the employee / team
1	Dr. MK Bhan Group Award for the most impactful collaboration	Rs. 70000/-	Dr. Shinjini Bhatnagar Dr. Gaurav Batra Dr. Sweety Samal Dr. Jayanta Bhattacharya Dr. Shailendra Mani Dr. Tripti Shrivastava Dr. Pallavi Kshetrapal
2	Award for a faculty for the best-published paper	Rs. 15000/-	Dr. Amit Awasthi
3	Award for a PhD student for the best-published paper	Rs. 15000/-	Dr. Ramachandran T.
4	Award for a PhD student for the five years all-round performance	Rs. 15000/-	Mr. Rajdeep Dalal
5	Award for a faculty for overall contribution to the institutional development during the previous financial year	Rs.10000/-	Dr. Nitya Wadhwa
6	Award for an administrative staff for overall contribution to the institutional development during the previous financial year	Rs.10000/-	Mr. Deepak Badoni, Management Assistant and Mr. Manjeet Kumar, Technical Officer -I
7	Award for technical staff for overall contribution to the institutional development during the previous financial year	Rs.10000/-	Mr. Pradipta Jana, Senior Technical Officer and Mr. Saqib Kidwai, Technical Officer II

The HR Section from time to time carries out various training programs for the benefit and welfare of the employees. On 19th October 2022, a Cardiopulmonary Resuscitation (CPR) and Automated External Defibrillator (AED) training was held in collaboration with the Max Institute of Medical Excellence, New Delhi. Max Healthcare Institute is certified as International Training Centre for CPR and AED by American Heart Association (AHA). THSTI conducts such trainings regularly for its staff and students to educate them on improving survival rates during emergency medical conditions.

The HR Section conducts counselling sessions on mental health thrice a month for its employees and students.

Finance & Accounts

The F&A section advises on financial matters, receipt of funds from various funding agencies, and attends the day-to-day payments to contractors/ suppliers, payment of salaries to staff duly taking into account all tax matters etc. The section is also responsible for preparing the annual statement of accounts provided in the latter part of this report. The Final Accounts along with the Audit Report are placed on the tables of both Houses of Parliament through the Department of Biotechnology. For the FY 2022-23, the brief financial highlights are mentioned hereunder:

Details of the sanctioned funds and expenditure in respect of Core grant: -

As on 31.03.2023

(Rs in Lakhs)

Sources of Funds:

Head of Account	Opening Balance 01.04.2022	Net Grant Receipt During 2022-2023	Total Receipt	Expenditure up to 31.03.23	Amount lapsed	Balance available as on 31.03.23
1	2	3	4=2+3	5	6	7=4-6
GIA Capital	0.00	3500.00	3500.00	3500.00	0.00	0.00
GIA Salary	52.08	1085.00	1137.08	1011.17	285.00	-159.09
GIA General	0.00	2700.00	2700.00	2700.00	0.00	0.00
Total	52.08	7285.00	7337.08	7211.17	285.00	-159.09

The financial resources of the Institute are the core grant provided by the Government of India, through the Department of Biotechnology, against annual budgetary projections made by the Institute, and other resources in the form of research grants provided by the various National and International agencies. The components of the core grant are under Recurring head for meeting the expenditure on salaries and operating expenses, and under Non-Recurring head for meeting expenses on account of equipment, infrastructure, and building costs connected with institutional activities.

The total receipt of funds from various sources during the FY 2022-23:

S. No	Particulars	Amount (in Lakhs)	% of Total Receipt
1	THSTI-Core Grant #	7000.00	44.53%
2	DBT Funding towards Projects	2534.23	16.12%
3	Other Government Funding (BIRAC, DST, ICMR etc.)	3168.66	20.16%
4	Non-Government Grants	2010.71	12.79%
5	Internal Revenue	1005.09	6.39%
	Total	15718.70	

Out of the total sanctioned grant of Rs. 7285.00 lakhs under THSTI core, an amount of Rs. 285.00 lakhs (w.r.t. GIA Salaries) lapsed technical glitches in RBI server, hence total received Rs. 7000 lakhs.

The section has adopted various digital methods for disbursements/collections to avoid cash transactions. The section has implemented the PFMS EAT, TSA, ZBSA modules and also implemented the ERP system in the majority areas of working.

Stores and Purchase Section

The responsibilities of the Stores and Purchase Section (S&P Section) include the procurement of scientific equipment, consumables, sub sequential services, and common goods. The day-to-day operations of the section are overseen by the Standing Purchase Committee, consisting of faculty members and officers of the administration.

The procurement processes adopted by the S&P Section are in accordance with the comprehensive Rules and Regulations outlined in the General Financial Rules (GFR) of 2017. The Section complies with government orders pertaining to product reservations, purchase preferences, and other facilities granted to sellers in Micro and Small Enterprises, Domestically Manufactured Electronic Products, and similar entities. Further, THSTI follows the Central Vigilance Commission guidelines to enhance transparency and objectivity in public procurement.

The prime objective of the S&P Section is to ensure transparency, cost-effectiveness, and equal opportunities for suppliers throughout the purchase process. The ultimate aim is to procure high-quality goods at reasonable prices through fair competition. By doing so, the Section ensures the best value for money for the public exchequer and plays a crucial role in providing efficient services to researchers and other officials within the Institute.

Electrical Engineering Section

The electrical engineering section is responsible for the maintenance of scientific and other electrical equipments, electrical sub-station activities including operation of various diesel generator sets, fire alarm system, grid connectivity from the Pali sub-station of DHBVN, electrical installation in the campus, solar panels, fire extinguishing equipment, and statutory requirements to prevent the risk of fire, lift maintenance, BSNL/Airtel telephone connectivity, maintenance of Split & window AC etc..

Developments of facility:- During this financial year, electrical engineering section efficiently executed development of few new facilities viz. sequencing facility, SIB facility, M.Sc. Classrooms, Vaccine Design Development Centre (VDDC), SAF Interim Facility in the PRRC, BSL3 facility and the Ferret facility which are successfully running.

Procurement of High Speed Diesel:- Electrical Engineering procured the High Speed Diesel from the local authorized dealer/ petrol pump of IOCL & HP against the cost of diesel claim by IOCL (Direct procurement) and saved Rs. 20 Lakhs during this financial year.

Solar System in cluster: - Electrical Engineering section successfully executed the Solar System capacity 250 Kw and is regularly saving an amount of Rs. 2 Lakhs per month (approx.). An agreement has been executed with M/s REIL for another solar system capacity 250 Kw under RESCO Model to ensure saving more money.

Energy Audit: Energy audit was successfully executed through M/s National Productivity Council under Ministry of Commerce & Industry and the council has appreciated the efforts taken by THSTI for energy saving initiatives such as installation of the solar panel, LED lights and transformers.

Information Technology

The IT section of the institute is responsible for the ERP operations, maintenance of inhouse developed ethsti portal (for leave, LTC, tour programme, NOC, equipment booking etc), complete IT network infrastructure, hardware maintenance, website maintenance, operation and maintenance of CCTVs, purchase of IT equipment, and any other matter dealing with IT.

Backup storage facility:

During the year 2022-23, 25TB of BSNL cloud space was procured to provide a backup storage facility for the THSTI faculties and other employees and students such that their important data are accessible across multiple devices. This also ensures that a copy of the desired files and folder is available on the cloud in case the working computer gets corrupted.

Network Security Enhancement:

Next-generation firewall was implemented to bolster network security. Regular security audits and penetration was conducted to identify and address vulnerabilities proactively.

Website Development

A new application form was designed with the payment gateway for the new M.Sc. course in Clinical Trials and successfully implemented in its first year 2022-23.

The IBSC online exam platform was developed and used for wet lab personnel to get a valid biosafety training certificate

The IT section also designed 4 new websites for the international conferences viz. HMCW 2023, TB Conference 2023 and CEPI conference 2022 held in THSTI. The website developed included web page and registration form with online payment gateway. A new module was created for the sequencing of the samples under the indent module of eTHSTI.

Internet Setup

High Speed internet and computers have been set up in the newly established Knowledge Research Centre (Library) in the campus.

Civil Engineering Section

The FY 2022-23 saw an exceptional growth in the infrastructure with new buildings, labs and office space coming up. The civil engineering section successfully completed the upgradation of the Vaccine Design Development Laboratory, development of Knowledge Research Centre and setting up of Genomics Sequencing Facility (NGS Facility). The section coordinated with many urban local bodies and successfully obtained the approvals/NOC such as zoning plan, environmental clearance (EIA), mining approval, clearance from NCZ for the development of 85 Acres of land. Consequently, the construction of the Medical Research Centre, 2nd Hostel Building and the Translational Research Lab Building have been started and progressing as per the project's milestone. The civil engineering section is also looking after the estate management functions for the Institute.

Besides the developmental and construction activities, the estate management division of the institute has been leading the ecological works in the bio-cluster to ensure sustainable development with minimum environmental impact. They have created water recharge pits and developed a storm water collection reservoir in the campus to avoid depletion of ground water table.

Civil section aims to build the campus eco-friendly and helps to preserve the flora & fauna of the native place. Coordinated with the Forest department for the plantation of many native species in the campus, extension of the rain garden in such a way to provide pathway with nature walking experience. The section has ensured 100% recycling of used water, and the production of compost from the waste generated from the cluster.

CDSA- THSTI Administration

The functioning of the Clinical Development Services Agency (CDSA) as an independent legal society has ceased, and the society was dissolved by the Department of Biotechnology vide its letter no.RAD-30/7/2020-MED-DBT- Part (1) dated 18 November 2021. Accordingly, the administrative setup of CDSA will also come under the purview of the THSTI administration.

HUMAN RESOURCE

A new organogram has been sanctioned for the CDSA-THSTI Centre in the 25th GB meeting of THSTI. A total of eighteen positions have been sanctioned. Out of the sanctioned positions, 16 have been filled, and the hiring for the balance vacant positions is in progress. The centre is hiring project staff sanctioned for various extramural projects implemented by the centre. All the employee & human resource-related matters are handled in the centre with approvals from the competent authority.

FINANCE

The Books of accounts of the erstwhile CDSA Society were closed on 31 December 2021, and the balances were transferred to THSTI. The centre maintains the accounts with effect from 1 January 2022 as a sub-Centre of the Institute. The status of CDSA core funds received and spent for the period from 01 April 2022 to 31 March 2023 is as shown below:

Amount in Rs Lakhs

HEAD OF ACCOUNT	Opening Balance 01.04.2022	Grant Receipt During 2022- 2023	Total Receipt	Expenditure up to 31.03.23	Balance available as on 31.03.23
1	2	3	(4=2+3)	5	(6=4-5)
Grant-in-Aid (Contingency)	0.00	3.00	3.00	3.00	0.00
Grant-in-Aid (Manpower)	0.00	45.37	45.37	45.37	0.00
Grant-in-Aid (Meeting & Travel)	0.00	2.00	2.00	2.00	0.00
Grant-in-Aid (Training)	0.00	10.00	10.00	10.00	0.00
Grand Total	0.00	60.37	60.37	60.37	0.00



SINGHAL GUPTA & CO. LLP

CHARTERED ACCOUNTANTS

Branch Office: K-1/124, L.G.F., Chittaranjan Park, New Delhi – 110019

H.O.: S M Kuteer, Mandir Marg, 92 Civil Lines, Near Meerut College, Meerut – 250001, U.P.

Email: dkmunjal@hotmail.com, Ph. 9891624096

INDEPENDENT AUDITOR'S REPORT

To The Trustees,
Translational Health Science and Technology Institute, Faridabad.

Report on the Audit of the Financial Statements

Opinion

We have audited the financial statements of **Translational Health Science and Technology Institute, Faridabad ("the Society")** which comprises the Balance Sheet as at 31st March, 2023, and the Income and Expenditure Account, the Receipts and Payments Account for the year then ended and notes to the financial statements, including a summary of significant accounting policies.

In our opinion, the accompanying financial statements give a true and fair view of the financial position of the Society as at 31st March, 2023 and its financial performance and its Cash Flows for the year then ended in accordance with the Accounting Standards Issued by the Institute of Chartered Accountants of India (ICAI), to the extent Applicable.

Basis for Opinion

We conducted our audit in accordance with the Standards on Auditing (SAs) issued by the ICAI. Our responsibilities under those Standards are further described in the Auditor's Responsibilities for the Audit of the Financial Statements section of our report. We are independent of the Society in accordance with the ethical requirements that are relevant to our audit of the financial statements and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Responsibilities of Management for the Financial Statements

Management is responsible for the preparation and fair presentation of the financial statements in accordance with the aforesaid accounting standards, and for such internal control as management determines is necessary to enable the preparation of the financial statements that are free from material misstatement, whether due to fraud and error.

In preparing the financial statements, management is responsible for assessing the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless management either intends to liquidate the Society or to cease operations, or has no realistic alternative but to do so.

Those charged with the governance are responsible for the overseeing the entity's financial reporting process.



Auditor's Responsibility for the Audit of the Financial Statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance but is not a guarantee that an audit conducted in accordance with SAs will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

As part of an audit in accordance with SAs, we exercise professional judgment and maintain professional skepticism throughout the audit. We also:

- Identify and assess the risks of material misstatement of the financial statements, whether due to fraud or error, design and perform audit procedures responsive to those risks, and obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- Obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances. Under Section 143(3)(i) of the Act, we are also responsible for expressing our opinion on whether the company has adequate internal financial controls with reference to financial statements in place and the operating effectiveness of such controls.
- Evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management.
- Conclude on the appropriateness of management's use of the going concern basis of accounting and, based on the audit evidence obtained, whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Company's ability to continue as a going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the standalone financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause the Company to cease to continue as a going concern.
- Evaluate the overall presentation, structure and content of the financial statements, including the disclosures, and whether the standalone financial statements represent the underlying transactions and events in a manner that achieves fair presentation.



We communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that we identify during our audit.

For Singhal Gupta & Co. LLP
Chartered Accountants
Firm Reg. No. 004933C/C400028



(D. K. Munjal)
Partner
M. No. 510229
UDIN: 23510229BGUZNC5283

Place: New Delhi
Date: 26/09/2023

TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY INSTITUTE, FARIDABAD

BALANCE SHEET AS AT 31ST MARCH, 2023

Amount (In Rs.)

CORPUS/CAPITAL FUND AND LIABILITIES	Schedule	31.03.2023	31.03.2022
Corpus / Capital Fund	1	2,584,823,164	2,306,339,370
Reserves and Surplus	2	302,239,869	241,222,521
Earmarked/Endowment Funds	3	-	-
Secured Loans and Borrowings	4	-	-
Unsecured Loans and Borrowings	5	-	-
Deferred Credit Liabilities	6	-	-
Current Liabilities and Provisions	7	910,251,057	951,300,850
TOTAL		3,797,314,090	3,498,862,741
ASSETS			
Fixed Assets	8	1,877,905,872	1,709,946,191
Investment From Earmarked/Endowment Funds	9	-	-
Investment-Others	10	8,700	2,700
Current Assets, Loans, Advances etc.	11	1,919,399,518	1,788,913,850
Miscellaneous Expenditure (to the extent not written off or adjusted)		-	-
TOTAL		3,797,314,090	3,498,862,741
SIGNIFICANT ACCOUNTING POLICIES AND NOTES ON ACCOUNTS	24		
CONTINGENT LIABILITIES	-		

Schedules 1 to 24 form an integral parts of Accounts.

As per our separate Report
of even date attached
For Singhal Gupta & Co.LLP
Chartered Accountants

(SUNNY RAJ) (M.V.SANTO)
ADMIN OFFICER (F & A) HEAD ADMINISTRATION
TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY INSTITUTE
FARIDABAD
Place: Faridabad
Date: 26/09/2023

(Dr.JAYANTA BHATTACHARYA)
EXECUTIVE DIRECTOR (ADDL.CHG.)

(D.K.MUNJALI)
PARTNER
M. No. 510229
SINGHAL GUPTA & CO.
NEW DELHI

FRN: 004933C/C400028

TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY INSTITUTE

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31ST MARCH, 2023

Amount (in Rs.)

INCOME	Schedule	31.03.2023	31.03.2022
Income from Sales/ Services	12	83,040,373	146,913,970
Grants/Subsidies (recurring)	13	350,000,000	318,500,000
Fees/Subscriptions	14	893,547	90,000
Income from Investments (Income on Invest. from earmarked/endow.Funds transferred to Funds)	15	-	-
Income from Royalty, Publication etc.	16	94,746	-
Interest Earned on Govt Grants	17	28,204,104	28,822,777
Other Income	18	16,480,513	35,722,478
Increase/decrease in stock of Finished goods and works- in- progress	19	-	-
Deferred Income-Fixed Assets		190,109,432	167,442,517
TOTAL (A)		668,822,715	697,491,741
EXPENDITURE			
Establishment Expenses	20	107,617,265	92,250,382
Other Administrative Expenses etc.	21	277,328,992	240,160,815
Expenditure on Grants , Subsidies etc.	22	-	-
Interest refundable on Govt Grants	23	28,204,104	28,822,777
Depreciation (Net Total at the year-end-corresponding to Schedule-8)		190,109,432	167,442,517
Prior period Adjustment A/c (ANN-A)		-	-
TOTAL(B)		603,259,793	528,676,490
Balance being excess of Income Over Expenditure (A-B)		65,562,922	168,815,251
Transfer to special Reserve(Specify each)		-	-
Transfer to /from General Reserve		65,562,922	168,815,251
BALANCE BEING SURPLUS /(DEFICIT) CARRIED TO CORPUS/CAPITAL FUND		-	-
SIGNIFICANT ACCOUNTING POLICIES AND NOTES ON ACCOUNTS	24		
CONTINGENT LIABILITIES	-		

Schedules 1 to 24 form an integral parts of Accounts

(SUNNY RAJ)
ADMIN OFFICER (F&A)

Place: Faridabad
Date: 26/09/2023



(Dr. JAYANTA BHATTACHARYA)
EXECUTIVE DIRECTOR (ADDL.CHG.)

As per our separate Report
of even date attached
For Singhal Gupta & Co.LLP
Chartered Accountants

(D.K.MUNJAL)
PARTNER

M. No. 510228

FRN: 004933C/C400028



TRANSLATIONAL HEALTH SCIENCE & TECHNOLOGY INSTITUTE (THSTI)
Faridabad

CONSOLIDATED RECEIPTS AND PAYMENTS ACCOUNT FOR THSTI, PROJECTS & FELLOWSHIP FOR THE YEAR ENDED 31ST MARCH, 2023

AMOUNT-IN-RUPEES

RECEIPTS	31.03.2023		31.03.2022	
OPENING BALANCE:-				
Fellowship	(9,396,458)		(9,236,690)	
Projects	943,373,230		546,010,129	
THSTI	390,586,646		212,654,707	
Grant-In Aid Received:-				
Fellowship	21,824,148		14,509,959	
Projects	798,354,152		1,024,406,713	
THSTI	700,000,000		428,500,000	
Other Receipts -THSTI				
Guest House Receipt	3,581,529		2,058,600	
Income from Sales and Services	75,258,302		139,166,346	
Interest Received from Banks	28,204,104		6,625,033	
Miscellaneous Receipts	3,040,878		145,557	
Penalty Receipt	-		107,906	
Receipt from STTP	142,797		90,000	
Recruitment Fee	805,480		1,422,508	
RTI Receipt	50		30	
Sales of Scrap	676,983		46,366	
Tender Fee	37,000		42,542	
Vendor Registration Fee	68,932		57,881	
Donation	6,001		3	
Receipt from CDSA	12,522,173			
Fee and Subscription	750,750			
Sponsorship - Income	2,620,000			
Seminar & Conference Fee Receipt	998,305			
Accrued Interest Received	1,752,353		545,390	
Advance Receipt From Debtors	240,885		-	
Building Contribution From Constituents	86,526,970		87,500,000	
Decrease in advances	3,183,960		52,713,923	
Earnest Money Deposit	1,333,042		486,510	
Govt. Dues Payable	4,793,380		5,098,700	
Other Liabilities/Payable	213,970,856		118,724,747	
Security / Hostel Deposit Received	3,936,669		4,323,367	
TOTAL		3,289,193,116		2,636,000,218

As per our separate Report
of even date attached
For Singhal Gupta & Co. LLP
Chartered Accountants

(SUNNY RAJ)
ADMIN OFFICER (R & A)

PLACE: Faridabad
DATE: 26/09/2023



(M.V. SANTO)
HEAD ADMINISTRATION

(DR. JAYANTA BHATTACHARYA)
EXECUTIVE DIRECTOR (ADDL. CHG.)



(D.K. MUNJAL)
PARTNER

M. No. 510229

FRN: 004933C/C400028

Contd....

**TRANSLATIONAL HEALTH SCIENCE & TECHNOLOGY INSTITUTE
(THSTI)**

RECEIPTS & PAYMENTS ACCOUNT OF THSTI FOR THE YEAR ENDED 31ST MARCH, 2023

PAYMENTS Particulars	31.03.2023		31.03.2022	
Fellowship Paid	16,298,633		14,669,718	
Projects Expenditure	1,067,579,312		627,043,612	
THSTI Expenditure:-				
Fixed Assets	176,774,744		113,481,026	
Patent WIP	-		1,564,086	
Work-in-Process- Building	13,225,257		-	
Escrow Account	246,526,970		87,500,000	
Consumables	71,496,739		84,955,691	
Manpower	101,130,029		92,250,382	
Administrative Expenses	193,357,632		154,814,737	
Advances, Receivables & Liabilities	412,544,963		135,157,548	
Closing Cash & Bank Balance				
Fellowship	(3,870,943)		(9,396,458)	
Projects	674,148,070		943,373,230	
THSTI	319,981,710		390,586,646	
TOTAL		3,289,193,116		2,636,000,218

As per our separate Report
of even date attached
For Singhal Gupta & Co. LLP
Chartered Accountants


(SUNNY RAJ)
ADMIN OFFICER (F & A)


(M.V. SANTO)
HEAD ADMINISTRATION


(DR. JAYANTA BHATTACHARYA)
EXECUTIVE DIRECTOR (ADDL. CHG.)


(D.K. MUKIAL)
PARTNER
M. No. 510229

PLACE: Faridabad
DATE: 26/09/2023



FRN: 004933C/C400028

TRANSLATIONAL HEALTH SCIENCE & TECHNOLOGY INSTITUTE (THSTI)
Faridabad

CONSOLIDATED RECEIPTS AND PAYMENTS ACCOUNT FOR THSTI CORE, PROJECTS & FELLOWSHIP FOR THE YEAR ENDED 31ST MARCH, 2023

RECEIPTS	CURRENT YEAR	PREVIOUS YEAR	PAYMENTS	AMOUNT IN (₹)	
				CURRENT YEAR	PREVIOUS YEAR
OPENING BALANCE:-					
Fellowship	(9,396,458)	(9,236,699)	Fellowship Paid	16,298,633	14,669,718
Projects	943,373,230	546,010,129	Projects Expenditure	1,067,579,312	627,943,612
THSTI	390,586,646	212,654,707	THSTI Expenditure:-		
Grant-in Aid Received:-			Fixed Assets	176,774,744	113,481,024
Fellowship	21,824,148	14,309,959	Patent WIP	-	1,564,086
Projects	798,354,152	1,624,406,713	Work-in-Process- Building	13,225,257	-
THSTI	700,030,000	428,500,000	Escrow Account	246,526,970	87,500,000
Interest Received			Consumables	71,496,739	84,955,691
Interest Received from Banks	28,204,104	6,825,033	Manpower	101,130,029	92,250,382
Other Income			Administrative Expenses	193,357,632	154,814,737
Guest House Receipt	3,581,529	2,058,660	Advances, Receivables & Liabilities	412,544,963	135,157,548
Income from Sales and Services	75,258,302	139,166,346			
Miscellaneous Receipts	3,040,878	145,557			
Penalty Receipt	-	107,966			
Receipt from STTP	142,797	90,000			
Recruitment Fee	805,489	1,422,508			
RTI Receipt	50	30			
Sales of Scrap	676,981	46,366			
Tender Fee	37,000	42,542			
Vendor Registration Fee	68,932	57,881			
Donation	6,601	3			
Receipt from CDISA	12,522,173	-			
Fee and Subscription	750,750	-			
Sponsorship - Income	2,620,000	-			
Seminar & Conference Fee Receipt	998,305	-			
Other Liabilities/Payable			Closing Cash & Bank Balance		
Accrued Interest Received	1,752,353	545,399	Fellowship	(3,870,943)	(9,396,458)
Advance Receipt From Debtors	240,885	-	Projects	674,148,070	943,373,230
Building Contribution From Constituents	86,526,970	97,300,900	THSTI	319,981,710	390,586,646
Decrease in advances	3,163,960	52,713,923			
Earnout Money Deposit	1,233,042	486,510			
Govt. Dues Payable	4,793,380	5,098,700			
Other Liabilities/Payable	213,970,856	118,724,747			
Security / Hostel Deposit Received	3,936,669	4,323,367			
TOTAL	3,289,193,116	2,636,000,218	TOTAL	3,289,193,116	2,636,000,218

(SUNNY RAJ)
ADMIN OFFICER (F&A)
PLACE: Faridabad
DATE: 26/09/2023

(M.V. KANTO)
HEAD ADMINISTRATION

TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY INSTITUTE
FARIDABAD

As per our separate Report
of even date attached
For Singhal Gupta & Co. LLP
Chartered Accountants

(DR. JAYANTA BHATTACHARYA)
EXECUTIVE DIRECTOR (ADDL. CHG.)

(D.K. MUNIAL)
PARTNER
M.No. 510229

FRN: 004933C/C40002F

Invited talks for the year 2022-2023

Name of the Faculty member/Scientist	Title of the talk	Title of the event	Date
Dr. Jayanta Bhattacharya	Neutralizing antibodies in preventing infectious diseases	National Symposium on Biological Therapeutics, NIPER, Hajipur, Bihar	11th Mar 2023
Dr. Jayanta Bhattacharya	Diversity in the neutralizing antibody responses developed in an unvaccinated SARS-CoV-2 infected individual	IUBMB meeting on RNA viruses, RCB, Faridabad	15th -18th Nov 2022
Dr. Jayanta Bhattacharya	Antibody specificities elicited through SARS-CoV-2 hybrid immunity- by Dr. Jayanta Bhattacharya	Grand Challenges Annual Meeting, Brussels, Belgium	24th Oct 2022
Dr. Jayanta Bhattacharya	Discovery of potentially neutralizing and protective monoclonal antibody cocktails from an Indian donor against SARS-CoV-2	Medical Science and Engineering Research Center (MEDSER), IISER, Bhopal	30th Jun- 1st Jul 2022
Dr. Jayanta Bhattacharya	Panel Discussion	India vaccines leaders conclave, Mumbai	26th Aug 2022
Dr. Jayanta Bhattacharya	Discovery of potentially neutralizing novel monoclonal antibodies against SARS-CoV-2 from an unvaccinated Indian donor	Invited Talk, NIV, Pune	17th Jun 2022
Dr. Jayanta Bhattacharya	Discovery of novel and protective human monoclonal antibodies against SARS-CoV-2 variants of concern	Invited talk, ICMR-NIRRH	13th Jun 2022
Dr. Amit Awasthi	Infection and Immunity	Immunocon 2022, PGIMER Chandigarh	24th -26th Nov 2022
Dr. Amit Awasthi	SARS-CoV2 Infection and T-Cell response	Foundation Day, Nirma University, Ahmedabad	6th Sep 2022
Dr. Amit Awasthi	Vaccines and T cell response	CEPI Meet, THSTI	5th-6th Dec 2022
Dr. Amit Awasthi	Infection and Immunity	National Conference on Biotechnology, Madurai Kamraj University, Chennai	22nd -23rd Mar 2023
Dr. Amit Awasthi	Infection and Immunity	IOSICON 2023, Jaipur	20th-22nd Jan 2023
Dr. Amit Awasthi	Infection and Immunity	Interactive Session at GLA university, Mathura	16th Dec 2022
Dr. Amit Awasthi	Lessons Learnt From Covid-19	Preparedness and Technological Solutions for Management of Future Pandemics, DRDE Gwalior	26-30th Sep 2022

Name of the Faculty member/Scientist	Title of the talk	Title of the event	Date
Dr Guruprasad R Medigeshi	Supporting the global efforts on SARS-CoV-2 Vaccines, Variants and Diagnostics	UTSAV 2022-23, THSTI	22nd Feb 2023
Dr Guruprasad R Medigeshi	Evolving strains of SARS-CoV-2	Division of Epidemiology & Communicable diseases, ICMR (Online)	5th Jan 2023
Dr Guruprasad R Medigeshi	Influence of pre-existing neutralizing antibodies on dengue viremia and serotype dominance	International Conference on Virus Evolution, Infection and Disease Control, Hyderabad Central university	15-17th Dec 2022
Dr Guruprasad R Medigeshi	Panel Discussion: Starting as Principal Investigator and Setting up a Lab	Ramalingaswami Re-Entry Fellowship & MK Bhan Young Researcher Fellowship Joint Conclave 2022-23, Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram	30th Nov-3rd Dec 2022
Dr Guruprasad R Medigeshi	Dengue Bioassay laboratory	Indo-U.S. Vaccine Action Programme 5th Meeting of the Candidate Vaccine Advisory Committee Meeting (CVAC) September 23-24, 2022, NII, Delhi	23-24th Sep 2022
Dr Guruprasad R Medigeshi	Divergent role of micronutrient zinc in dengue infection – A target for adjunct therapy	Science2Solutions, Merck (Online)	11th May 2022
Dr. Nisheeth Agarwal	Post-antibiotic effect in Mycobacterium tuberculosis: Deciphering the role of a novel transcriptional regulator	Towards End TB: Achievement, Challenges and Future Directions, THSTI	23-25th Mar 2023
Dr. Nisheeth Agarwal	Protein homeostasis in Mycobacterium tuberculosis: Identification of novel drug targets	Exploring New Horizons In Biotechnology (ENB-2023)" & mini-symposium on "Recent Advances In Biotechnological Innovations (RABI-2023), Banaras Hindu University, Varanasi	10-12th Feb 2023
Dr. Nisheeth Agarwal	Application of CRISPR/Cas9-based gene silencing approach in characterization of unknown genes in Mycobacterium tuberculosis'	Advanced training in Immunology of Tuberculosis, ICGEB, New Delhi	16th- 22nd May 2022

Name of the Faculty member/Scientist	Title of the talk	Title of the event	Date
Dr. Nisheeth Agarwal	Science & Society	Celebration of Vigyan Utsav as a part of Azadi ka Amrit Mahotsav, Haryana State Council for Science, Innovation & Technology	18th Apr 2022
Dr. Milan Surjit	MIV, MAHE: Webinar on World Hepatitis Day 2022	Online, Manipal institute of virology, MAHE	26th Jul 2022
Dr. Milan Surjit	Exploring the cross-talk between human endogenous retroviruses (HERVs) and SARS-CoV-2	IUBMB focused meeting on Biochemistry & Molecular Biology of RNA viruses, RCB, Faridabad	15-17th Nov 2022
Dr. Milan Surjit	Exploring the cross-talk between human endogenous retroviruses (HERVs) and SARS-CoV-2	International conference on virus evolution, infection and disease control, University of Hyderabad	15-17th Dec 2022
Dr. Bhabatosh Das	WGS based analysis of different MDR bacterial isolates (2016-2022) from five different hospitals located across India	National meeting on Antimicrobial Resistance: Genomic surveillance, ICMR, New Delhi	24th Feb 2023
Dr. Bhabatosh Das	NGS: Advances and Applications	Hands-on workshop on "Next Generation Sequencing and Data Analysis, THSTI, Faridabad	15th Feb 2023
Dr. Bhabatosh Das	Genome plasticity and antimicrobial resistance in bacterial pathogens	International meeting on An Interdisciplinary Approach to Biological Sciences, IACS, Kolkata	3rd Feb 2023
Dr. Bhabatosh Das	NGS: Recent advances in chemistry and technology	Nucleic Acids Sequencing and Analysis, NIPER, Guwahati	31st Mar 2023
Dr. Bhabatosh Das	Overview of Bioinformatics for the analysis of Next Generation Sequencing data	DNA sequencing workshop, JIPMER, Pondicherry	9th Mar 2023
Dr. Bhabatosh Das	Rapid Detection of Antimicrobial Resistance Genes in Clinical Isolates by Dipstick Methods	Winter school lecture, NDRI, Karnal	4th Mar 2023
Dr. Bhabatosh Das	Antibiotic Resistance in Gram-negative Human Pathogens: Genetic Heterogeneity and Dynamics	91st Annual Meeting of the Society of Biological Chemists, SBC, Kolkata	10th Dec 2022
Dr. Bhabatosh Das	Genome Editing for Next-Gen Probiotics	6th Biennial PAi Conference and Int'l Symposium on Psychobiotics and Gut: Potential in Neurological Disorders, NDRI, Karnal	6th Dec 2022
Dr. Bhabatosh Das	Next generation sequencing technologies: Advances and applications in research and diagnostics	16th Asian Conference on Diarrhoeal Disease and Nutrition, NICED, Kolkata	11th Nov 2022

Name of the Faculty member/Scientist	Title of the talk	Title of the event	Date
Dr. Bhabatosh Das	Human microbiome in health and disease	Annual meeting of the International Life Sciences Institute, ILSI New Delhi	12th Oct 2022
Dr. Bhabatosh Das	Basic of Human microbiome	International conference on A Gateway to Understand Complex Pancreatic Disorders, Indian Pancreatic Club	8th Oct 2022
Dr. Amit Kumar Pandey	Animal models in Tuberculosis Research: Disease Biology and Pre-clinical Studies	Animal Models for One Health Program: Challenges and Future Perspectives	3rd-4th Jun 2022
Dr. Amit Kumar Pandey	Targeting "adaptability": Exploring novel therapeutic opportunities and strategies against tuberculosis	MCARS Lecture Series-2023: Bacterial Pathogenesis: The role of stress	10th Feb 2023
Dr. Amit Kumar Pandey	Transgenics and Genome Editing Technology: Mechanism, Applications and future prospects	Certification Course on Laboratory Animal Science (CCLAS)	6th-17th Feb 2023
Dr. Samrat Chatterjee	Mathematical modeling and big data analysis	Mathematical Modelling of Biosystems with special focus on epidemiology	22nd-26th Aug 2022
Dr. Samrat Chatterjee	Identification of possible drug target through big data analysis	8th Indo-US workshop on mathematical chemistry (IWMC) 2022	13th-17th Sep 2022
Dr. Samrat Chatterjee	Studying diabetes through data analysis and mathematical model	National Conference on Mathematics: Various Aspects in Society (NCMVAS-2023)	13th-14th Mar 2023
Dr. Sweetly Samal	A Novel Platform for Development of Universal Betacoronavirus Vaccine	i-Connect 2022, THSTI	13th Jun 2022
Dr. Sweetly Samal	Indigenous vaccine platform for emerging infectious viral diseases of zoonotic and pandemic potential	Biotechnology-Trends and future prospects, GKVK, University of Agricultural Sciences, Bangalore	15th Sep 2022
Dr. Sweetly Samal	Leveraging Pseudovirus Or Reverse Genetics Tool To Probe New And Emerging Viruses	CEP course on 'Preparedness and technological solutions for management of future pandemics: lessons learnt from COVID-19', DRDO, Gwalior	29th Sep 2022
Dr. Sweetly Samal	Mapping of SARS-CoV-2 mutations to understand the mechanisms of SARS-CoV-2 entry and fusion into cells	RCB-IUBMB focused meeting on Biochemistry and Molecular Biology of RNA Viruses, RCB, Faridabad	18th Nov 2022

Name of the Faculty member/Scientist	Title of the talk	Title of the event	Date
Dr. Sweety Samal	A novel vaccine platform for the development of pan beta corona vaccine	International Meet on "Preparedness for Future Epidemics: Is India ready to meet the CEPI 100 days vaccine challenge?", THSTI	5th Dec 2022
Dr. Sweety Samal	Next generation COVID vaccine development (Multivalent self assembled nanocage based vaccine platform)	Indo-U.S. Vaccine Action Programme (5th Meeting of the Candidate Vaccine Advisory Committee (CVAC)), NII, New Delhi	23rd Sep 2022
Dr. Shailendra Asthana	Role of computation in drug discovery	Workshop on drug discovery Schrodinger, BITS, Goa	5th Jan 2023
Dr. Shailendra Asthana	Advanced computing for structural modeling	Accelerating Biology 2023: Discovery to Delivery, C-DAC, Pune	27th Feb 2023
Dr. Shailendra Asthana	Antibody-based drug discovery	International Biophysical events (Online)	12th Mar 2023
Dr. Shailendra Asthana	Protein-protein interaction to map the transition from unstructured-to-structured protein states	Biomolecular drug discovery, IIT-BHU	2nd Dec 2022
Dr. Amit Kumar Yadav	Quantitative proteomics & PTM analysis	Workshop on Proteomics and Data Analysis, Translational Health Science and Technology Institute	10th Feb 2023
Dr. Amit Kumar Yadav	Mining tandem mass spectra for identifying peptides, proteins and modifications.	PSI meeting education day talk, 14th Annual Meeting of the Proteomics Society of India and International Conference on Proteins & Proteomics (PSI-ICPP 2022)", CSIR-Indian Institute of Chemical Biology (IICB), Kolkata	2nd Nov 2022
Dr. Amit Kumar Yadav	Large-scale analysis of protein post-translational modifications (PTMs) from the human proteome and mass spectrometry data	Virtual Podium Asia Pacific (VPAP) 2022 in Proteomics, Metabolomics and Lipidomics	26th Oct 2022
Dr. Amit Kumar Yadav	From proteins to peptides and back - analysis of tandem mass spectra for inferring peptides, proteins and modifications	Computational Workshop on Genomics, Proteomics and Metagenomics 2022 (CWG-PM-2022)	22nd July 2022
Dr Ruchi Tandon	3D Spheroids and Organoid cultures in drug discovery research on NAFLD	One Day symposium on metabolic associated fatty liver disease(MAFLD), THSTI	25th Jun 2022
Dr Ruchi Tandon	Seahorse XFp Technology and its applications	Two-day workshop on the Seahorse XFp Technology and its applications	13-14th Sep 2022
Dr. Soma Patnaik	Intellectual Property Rights: In Focus-THSTI	Celebration of Vigyan Utsav as a part of Azadi ka Amrit Mahotsav, DST Haryana	17th Aug 2022

SCIENTIFIC EVENTS AND OUTREACH

Over the years, THSTI has been involved in scientific events that help disseminate the research outcomes and share the knowledge with policy-makers, researchers and young minds. During the year 2022-23, THSTI carried out various scientific and outreach events.

On 22nd February 2023, Honourable Minister, Dr. Jitendra Singh ji, Union Minister of State (Independent Charge) Science & Technology; Minister of State (Independent Charge) Earth Sciences; MoS PMO, Personnel, Public Grievances, Pensions, Atomic Energy and Space, visited Translational Health Science and Technology Institute (THSTI) and laid the foundation stone for a 'Medical Research Centre' and 'Translational Research Laboratories' in its campus. The THSTI fraternity welcomed the minister and celebrated the occasion as UTSAV 2023 (Unveiling THSTI's Scientific Achievements and Vision). Dr. Singh appreciated the scientific achievements of THSTI and lauded the commitment of the organization to work towards biomedical innovations to improve the health of people in India and the world. During the celebrations, a video highlighting the THSTI's research activities and major achievements was released by the Hon'ble Minister.

CONFERENCES/SYMPOSIUM/MEET

On 11th May 2022, Translational Health Science and Technology Institute (THSTI) celebrated **National Technology Day** by conducting a Science Setu seminar on the theme "An Integrated Approach to Science and Technology for a Sustainable Future." The seminar was attended by students and teachers of J.C. Bose University of Science and Technology, YMCA, Faridabad. Addressing the participants, Prof. Pramod Garg, ED, THSTI stressed the need to be Atmanirbhar. He highlighted the work done by THSTI in the field of drug discovery and vaccines, especially during the COVID-19 pandemic.

THSTI organized a one-day symposium on 25th June 2022 to highlight the importance of understanding **Metabolic Associated Fatty Liver Disease (MAFLD)** and discuss the outcomes and ways to address the issue of MAFLD. The symposium saw a confluence of clinicians, academicians, researchers and young students working in the area of MAFLD.

On the eve of Foundation Day, THSTI organized a one-day symposium in a hybrid mode on **"INFLAMMATION"** at M. K. Bhan Auditorium at THSTI on 14th July 2022. Eminent clinicians, scientists & researchers across the country came together to deliberate on INFLAMMATION, a key driver of human health & disease. Prof. N. K. Mehra, Hon. Emeritus scientist, ICMR and former Dean & National Chair, AIIMS was the chief guest. The symposium saw an overwhelming participation of more than 600 attendees both in physical and online mode.

THSTI attended the National Conference on **"Akash Tatva - Akash for Life"** at Uttaranchal University Campus in Dehradun from 5th-6th November 2022. As a part of the conference, THSTI displayed posters on the research work being done at THSTI and showcased some of the products developed in-house.

Every year, THSTI commemorates Dr M K Bhan's anniversary on 9th November by conducting the **"Dr M K Bhan Memorial Oration."** This year, Dr Rajiv Bahl, Secretary Department of Health Research (DHR) and Director General of the Indian Council of Medical Research (ICMR) delivered the "Dr M K Bhan Memorial Oration." Dr. Bahl highlighted the excellent work done in India on Rotavirus Vaccine, Childhood Diarrhea and Kangaroo Mother Care which has significantly reduced neonatal mortality. Dr. Bahl also interacted with the faculty and scientists of THSTI.

THSTI organized an International Meet on **"Preparedness for Future Epidemics: Is India ready to meet the CEPI 100 days vaccine challenge?"** from 5th-6th December 2022. This meeting brought together leaders and experts from academia, industry and regulators to discuss important aspects of vaccine development for emerging infectious diseases. Experts from the academia, industry and regulators viz., Leiden University Medical Center, The Netherlands, Emory University USA, IISc Bangalore, CMC Vellore, THSTI, ICMR, CDSCO, WHO, CEPI, Serum Institute of India Pvt. Ltd., Zydus Life Sciences, Bharat Biotech International Ltd., Premas

Biotech Pvt. Ltd., Biological E Pvt Ltd., Panacea Biotech Ltd., & Gennova Biopharmaceuticals Ltd. participated in the meet. Capacity building, strong supply chains, academia-industry partnerships, and ideation banks in universities were some of the key takeaways of the International Meet to achieve faster vaccine development for emerging infectious diseases.

Translational Health Science and Technology Institute (THSTI) participated in the 8th edition of the India **International Science Festival (IISF) 2022** and put up a stall showcasing its research achievements. The stall attracted many visitors from different walks of life, including young children, students from schools and colleges, researchers and the common man. THSTI also set up free COVID-19 antibody testing for visitors in its mobile lab, and more than 120 visitors availed of the service.

Every year India celebrates National Science Day on 28th February. This year THSTI celebrated this Day with the theme **"Global Vaccines for Global Well-Being"**. Undergraduate and postgraduate students from Sri Venkateswara College, DU, Maitreyi College, DU, Shaheed Rajguru College of Applied Sciences for Women, DU, Manav Rachna International Institute of Research and Studies, Faridabad and MVN University, Palwal were invited to THSTI. There were expert talks from THSTI and industry, a quiz competition and a visit to THSTI's research facilities for these students.

THSTI organized a conference on the **Human Microbiome in Health and Disease** on 15th February 2023 at its campus. The conference brought together researchers, policymakers and experts from various fields to discuss the latest advancements and research findings in the human microbiome and its role in health and diseases. Dr. Rajesh S. Gokhale, Secretary, Department of Biotechnology (DBT), India was the chief guest for the conference. Dr Gokhale launched the BiomLife™, a universal buffer for the transport and long-term storage of various biological specimens, developed by THSTI. presentations and discussions at the conference provided insights into the latest research trends and potential therapeutic approaches for microbiome-related diseases.

To mark World Tuberculosis Day on 24th March, THSTI organized a three-day symposium on **"Towards End TB: Achievements, Challenges and Future Directions"** from 23rd-25th March 2023 at its campus. The symposium saw leading clinicians, physician-scientists, academicians and researchers from academia and industries deliberating on the way forward to *"Mukt Bharat"* of Tuberculosis (TB), an important mission of the Government of India. The symposium had 400+ participants that included undergraduate, postgraduate and research students coming from various parts of India.

WORKSHOPS

As a part of capacity building, THSTI conducted workshops during the year 2022-23. A workshop on **"Roadmap for Patent Creation"** was conducted by THSTI in collaboration with Cell for IPR Promotion and Management (CIPAM), Ministry of Commerce and Industry, Govt. of India on 22nd August 2022. Researchers & students from Acharya Narendra Dev College, Ram Lal Anand College, Maitreyi College and Manav Rachna International Institute of Research and Studies and THSTI attended the workshop. The workshop consisted of sessions on what can be patented in India, the importance of patent filing and types of patent applications for filing in India and abroad and pre-grant and post-grant opposition in India.

THSTI conducted a workshop on **Proteomics and Data Analysis** in association with the Proteomics Society of India (PSI) on 9-10th February 2023. The workshop was attended by researchers from various organizations. The workshop had sessions that covered the basics of proteomics and mass spectrometry, integration of genomics & proteomics i.e. proteogenomics, for novel gene discovery, application of various quantitative proteomics techniques in cancer biology & cellular signalling, multiplexing techniques for quantitation, PTM analysis, sample preparation and data acquisition. The participants were given training for sample preparation, and data acquisition followed by various types of high-throughput data analysis. They were also trained to use various databases and tools for data interpretation.

As a part of a conference on Human Microbiome in Health and Disease, THSTI conducted a two days workshop (16-17th Feb 2023) on **Next-generation (Next-gen) sequencing and analysis for the microbiome**. Thirty participants included scientists, research scholars and postgraduate students who were given hands-on training on sample preparation for library preparation for Next-gen sequencing followed by data analysis using different bioinformatics tools.

THSTI hosted the first in-person Dengue Alliance Meeting in India on February 6-7, 2023, with experts and scientists from India, Malaysia, Thailand, Brazil and Switzerland present to kick off plans to develop treatments for Dengue which causes substantial morbidity and mortality globally at its premises.

On 17th March 2023, eleven PG trainees, along with a faculty from Armed Forces Medical College (AFMC), Pune, visited THSTI to know and understand the research work done at THSTI. During the visit, it was proposed to have a research collaboration between THSTI and AFMC in the future. The trainees were also taken on a lab tour to some of the research facilities of THSTI

In the year 2022-23, THSTI invited many eminent scientists to share their research achievements and experiences to motivate and foster future collaborations. Prof. Vijay Kuchroo, Samuel Wasserstrom chair of Neurology, and Director of Evergrande Center for Immunological Disease at Harvard Medical School and Brigham and Women's Hospital, Boston (USA) visited Translational Health Science and Technology Institute (THSTI) on 22nd July 2022. Prof. Kuchroo is credited with the discovery of the TIM family of molecules, Th17, and other helper T cell subsets. During his visit, he delivered a distinguished lecture on the "Role of checkpoint molecular TIM-3 in anti-tumour immunity." He gave insights into the research that led to the discovery of TIM-3. He briefly described the role of TIM-3 in immunology and more specifically its role as a checkpoint molecule in anti-tumor immunity.

Prof. Vijay Pancholi from Ohio State University visited THSTI on 12th December 2022. During his visit, he delivered a talk on "Targeting Ser/Thr/Tyr (STY) phosphorylation-related post-translational modifications to abate antimicrobial resistance." Prof. Pancholi in collaboration with Dr. Shailendra Asthana, THSTI has been working towards developing small molecules for Antimicrobial resistance (AMR).

Prof. Prashant Jha, School of Biomedical Engineering & Imaging Sciences, King's College, London, visited THSTI on 22nd December 2022. Prof Jha is an editor, inventor and serial entrepreneur who heads the affordable medical technologies division at the School of Biomedical Engineering and Life Sciences at King's College London. During his visit to THSTI, Prof. Jha delivered a talk on "Medical Technologies for Women's and Children's Health." He spoke about various innovations that his team is working on in the field of maternal and child health care which can be used by health care workers at the village level/patient's home. Prof Jha expressed his desire to collaborate with THSTI towards developing inventions that can help poor/underprivileged people.

Prof. Kjell Arne Johansson from Bergen Centre for Ethics and Priority Setting, Bergen University, Norway, visited THSTI on 4th January 2023. Prof Johansson has been engaged in developing innovative methods for fair priority setting in global health and applying them to low and high-income country settings. During his visit, Prof Johansson delivered a talk on "Priority Setting in Health." During his talk, Prof Johansson spoke about ways for universal health coverage by prioritizing financial protection and giving priority to the worst-off segments of the population.

THSTI has been regularly conducting DBT's outreach program "SCIENCE SETU" to create awareness, promote students' interests and motivate them to build a career in science. In the year, 2022-23, undergraduate and postgraduate students from various colleges across Delhi-NCR and Jabalpur were part of ten such events conducted as a part of Science Setu.

THSTI Committees

1.	THSTI Management Committee	Executive Director and Heads of all the Centres Chairperson - Executive Director
2	Maintenance Committee	• Dr. Ramandeep Singh • Dr. Krishnamohan Atmakuri • Dr. Nisheeth Agarwal • Dr. Niraj Kumar • Dr. Shailendra Asthana • Dr. Shailaja Sopory • Mr. G.R. Agarwal • Mr. Virendra Singh Rao • Mr. Vishal Gupta • Mr. Gopal Kishan Chauhan • Chairperson - Dr. Ramandeep Singh • Co-chairperson - Dr. Krishnamohan Atmakuri
3	Purchase Committee	• Dr. Amit Awasthi • Dr. Bhabatosh Das • Dr. Gaurav Batra • Dr. Santosh S. Mathapati • Dr. Dinesh Mahajan • Mr. Virendra Singh Rao • Mr. Manoj Kumar • Mr. Satish Kumar • Chairperson- Dr. Amit Awsathi • Co-chairperson – Dr. Bhabatosh Das
4	Specification sub committee	• Dr. Milan Surjit • Dr. Amit Kumar Pandey • Dr. Sankar Bhattacharyya • Dr. Sweety Samal • Mr. Mohd. Arif Saifi • Chairperson - Dr. Milan Surjit • Co-chairperson - Dr. Amit Kumar Pandey
5	IT & Communication Committee	• Dr. Samrat Chatterjee • Dr. Susmita Chaudhuri • Dr. Shailendra Asthana • Mr. M.V. Santo • Mr. G. R. Agarwal • Mr. V. S. Rao • IT section representative • Chairperson - Dr. Samrat Chatterjee • Co-chairperson - Dr. Susmita Chaudhuri
6	Institutional Ethics Committee (Biomedical and Health Research) (Reg No. EC/NEW/INST/2021/HR/0033)	• Prof. Satinder Aneja • Prof. Subir Kumar Maulik • Dr. Arti Kapil • Dr. Suvasini Sharma • Dr. Ujjayini Ray • Dr. Bhabatosh Das • Dr. Shailaja Sopory • Mr. Munawwar Naseem • Ms. Jasmine Singh • Ms. Vidhya Krishnamoorthy • Chairperson - Prof. Satinder Aneja • Member Secretary - Ms. Vidhya Krishnamoorthy

7	Institutional Animal ethics committee	• Dr. Amit Awasthi • Dr. Milan Surjit • Dr. Amit Pandey • Dr. Susmita Chaudhuri • Chairperson - Dr. Amit Awasthi
8	Institutional Committee for Stem Cell Research (IC-SCR)	• Prof. Narinder Mehra • Prof. Sujata Mohanty • Dr. Sam Mathew • Dr. Prasad Abnave • Prof. Prasenjit Guchhait • Dr. Sivaram Mylavarapu • Dr. Thribuvan Pal Yadav • Dr. Ujjayini Ray • Ms. Jasmine Singh • Mr. Munawwar Naseem • Ms. Vidhya Krishnamoorthy • Chairman - Prof. Narinder Mehra • Coordinator/Member Secretary - Ms. Vidhya Krishnamoorthy
9	Institutional Biosafety Committee	• Dr. Vinay Kumar Nandicoori • Dr. Prasenjit Guchhait • Dr. Milan Surjit • Dr. Krishnamohan Atmakuri • Dr. Bhabatosh Das • Dr. Nitya Wadhwa • Dr. Susmita Chaudhuri • Dr. Shailaja Sopory • Chairperson - Dr. Krishnamohan Atmakuri • Member Secretary - Dr. Milan Surjit
10	Academic Committee	• Dr. Ramandeep Singh • Dr. Milan Surjit • Dr. Nitya Wadhwa • Dr. Susmita Chaudhuri • Dr. Niraj Kumar • Chairperson - Dr. Ramandeep Singh • Co-Chairperson - Dr. Nitya Wadhwa
11	RTI Act	• Dr. Amit Kumar Pandey – Appellate Authority • Dr. Susmita Chaudhuri– PIO • Mr. M.V. Santo – Nodal Officer • Executive Director – Public Authority
12	Complaints Committee (to enquire into complaints of sexual harassment)	• Dr. Shinjini Bhatnagar • Dr. Nita Bhandari • Dr. Krishnamohan Atmakuri • Dr. Nitya Wadhwa • Dr. Pallavi Kshetrapal • Ms. Gagandeep Kaur (external member) • Dr. Shobha Broor (external member) • Mr. M. V. Santo • Chairperson – Dr. Shinjini Bhatnagar

13	Student & Employee Welfare, Sports and Hostel Committee	• Dr. Bhabatosh Das • Dr. Amit Kumar Pandey • Dr. Niraj Kumar • Dr. Santosh S. Mathapati • Dr. Sweety Samal • Dr. Tripti Srivastava • Mr. Raj Kumar • Chairperson - Dr. Bhabatosh Das • Co-Chairperson - Dr. Amit Kumar Pandey
14	Tender Opening Committee	• Mr. Manoj Kumar • Mr. Satish Kumar • Mr. Gopal Kishan Chauhan • Ms. Rajni Verma • Chairperson – Mr. Manoj Kumar / Mr. Satish Kumar
15	Vigilance Officer	• Dr. Nisheeth Agarwal
16	Building Committee for Campus-II, Faridabad	• Dr. V.S. Chauhan, Ex-Director, ICGB • Executive Director, THSTI • Executive Director, RCB • Director, NII • Director, NIPGR • Director, NBRC • Dr. Feroz Suri, RCB • Mr. Narender Kumar • Controller of Administration, RCB • Head-Administration, THSTI • Chairman - Dr. V.S. Chauhan • Member-Secretary- Head-Administration, THSTI
17	SC/ST Grievance Redressal Committee	• Dr. Niraj Kumar • Dr. Pallavi Kshetrapal • Dr. Santosh S. Mathapati • Mr. Raj Kumar • Chairperson - Dr. Niraj Kumar • Co-Chairperson - Dr. Pallavi Kshetrapal
18	Official language Implementation Committee	• Dr. Amit Kumar Pandey • Dr. Pallavi Kshetrapal • Dr. Amit Kumar Yadav • Chairperson - Dr. Amit Kumar Pandey • Co-Chairperson - Dr. Pallavi Kshetrapal
19	Scientific misconduct and plagiarism investigation committee	• Dr. Shinjini Bhatnagar • Dr. Krishnamohan Atmakuri • Dr. Susmita Chaudhuri • Chairperson – Dr. Shinjini Bhatnagar
20	Civil Works committee	• Dr. Bhabatosh Das • Dr. Pallavi Kshetrapal • Dr. Santosh S. Mathapati • Mr. Narender Kumar • Mr. Virendra Singh Rao • Chairperson - Dr. Bhabatosh Das • Co-Chairperson– Dr. Pallavi Kshetrapal

21	Pandemic Response Team	• Dr. Guruprasad R. Medigeschi • Dr. Ramandeep Singh • Dr. Amit Awasthi • Dr. Nitya Wadhwa • Mr. M. V. Santo • Chairperson– Dr. Guruprasad R. Medigeschi • Co-Chairperson - Dr. Ramandeep Singh
22	Staff Welfare Fund Committee	• Dr. Pramod Kumar Garg, Executive Director – Chairperson (ex-officio) • Dr. Nitya Wadhwa • Mr. M.V. Santo, Head-Admin – Secretary (ex-officio) • Mr. Sunny Raj • Mr. Narender Sharma • Ms. Rajni Verma • Chairperson– Dr. Pramod Kumar Garg, Executive Director • Secretary - Mr. M.V. Santo, Head-Administration
23	Electromechanical Committee	• Dr. Guruprasad Medigeschi • Dr. Saikat Bhattacharjee • Dr. Feroz Kumar Suri • Mr. G. R. Agarwal • Mr. R. K. Rathore • Mr. Narender Kumar • Chairperson - Dr. Guruprasad Medigeschi
24	Housekeeping Committee	• Dr. Krishnamohan Atmakuri • Dr. Nidhi Adlakha • Dr. Ruchi Tandon • Dr. Supratik Das • Mr. R. K. Rathore • Mr. Narender Kumar • Mr. V. M. S. Gandhi • Mr. Rakesh Yadav • Mr. Rajkumar • Chairperson - Dr. Krishnamohan Atmakuri
25	Cafeteria Committee	• Dr. Amit Kumar Pandey • Dr. Manjula Kalia • Dr. Prem S. Kaushal • Dr. Deepak Rathore • Mr. V. M. S. Gandhi • Mr. Rajkumar • Chairperson - Dr. Amit Kumar Pandey
26	THSTI-RCB Day-Care committee	• Dr. Sivaram V. S. Mylavarapu • Dr. Divya Chandran • Dr. Deepti Jain • Dr. Pallavi Kshetrapal • Dr. Susmita Chaudhuri
27	Standing Disposal Committee	• Mr. Manoj Kumar • Mr. Satish Kumar • Mr. Gopal Kishan Chauhan • Mr. Manjeet Kumar

28	Inventory Verification Committee	• Mr. Vishal Gupta • Mr. Manoj Kumar • Mr. Gopal Kishan Chauhan • Mr. Saqib Kidwai • Mr. Mohd.Arif Saifi
29	Space Allocation Committee	• Dr. Ramandeep Singh • Dr. Bhabatosh Das • Dr. Gaurav Batra • Dr. Nitya Wadhwa • Dr. Pallavi Kshetrapal • Dr. Dinesh Mahajan • Mr. M. V. Santo • Mr. Narender Kumar • Chairperson - Dr. Ramandeep Singh • Co-Chairperson - Dr. Bhabatosh Das
30	Science Setu Committee	• Dr. Gaurav Batra • Dr. Niraj Kumar • Dr. Sankar Bhattacharya • Dr. Sweety Samal • Dr. Yogita Adlakha • Dr. Ajay Kumar • Chairperson - Dr. Gaurav Batra • Co-Chairperson - Dr. Niraj Kumar
31	EHS Committee	• Dr. Nisheeth Agarwal, Professor • Dr. Krishnamohan Atmakuri • Dr. Nitya Wadhwa • Dr. Susmita Chaudhuri • Dr. Dinesh Mahajan • Mr. Vishal Gupta • Mr. Narender Sharma • Dr. Meenakshi Sharma • Chairperson - Dr. Nisheeth Agarwal • Co-chairperson - Dr. Susmita Chaudhuri • Member Secretary - Mr. Vishal Gupta
32	Ecological Committee	• Dr. Amit Kumar Pandey • Dr. Krishnamohan Atmakuri • Dr. Tushar K. Maiti • Dr. Feroz Khan Suri • Mr. Narender Sharma • Mr. M. V. Santo • Mr. Ramesh Kumar Rathore • Chairperson - Dr. Amit Kumar Pandey
33	Sports Committee	• Dr. Amit Awasthi • Dr. Samrat Chatterjee • Dr. Pallavi Kshetrapal • Dr. Amit Kumar Yadav • Dr. Pramod Kumar R • Dr. Ramesh Chandra Rai • Chairperson - Dr. Amit Awasthi • Co-Chairperson - Dr. Samrat Chatterjee

34	Radiation Safety Committee	• Dr. Guruprasad R. Medigeshe • Dr. Bhabatosh Das • Dr. Krisnamohan Atmakuri • Dr. Susmita Chaudhuri • Dr. Dinesh Mahajan • Mr. Vishal Gupta • Chairperson - Dr. Guruprasad R. Medigeshe • Co-Chairperson - Dr. Bhabatosh Das
35	Liaison Officer for SC, ST and Persons with Disabilities	• Dr. Niraj Kumar
36	Liaison Officer for OBC and Ex-Servicemen	• Dr. Santosh S. Mathapati
37	BSL-3/IDRF Committee	• Dr. Ramandeep Singh • Dr. Prasenjit Guchhait • Dr. Guruprasad Medigeshe • Dr. Feroz Suri • Dr. Zaigham Abbas Rizvi • Mr. GR Agarwal • Mr. Ramesh Kumar Rathore • Mr. Saqib Kidwai • Dr. Priyanka Bhatnagar • Chairperson - Dr. Ramandeep Singh • Co-Chairperson - Dr. Prasenjit Guchhait

List of Seminars & Conferences attended:

Name of the participant	Meeting title	Venue	Date
Dr. Amit Awasthi	Immunocon 2022, PGIMER	Chandigarh	24th -26th Nov 2022
Dr. Amit Awasthi	Foundation Day, Nirma University	Ahmedabad	6th Sep 2022
Dr. Amit Awasthi	National Conference on Biotechnology, Madurai Kamraj University	Chennai	22nd -23rd Mar 2023
Dr. Amit Awasthi	IOSICON 2023	Jaipur	20th-22nd Jan 2023
Dr. Amit Awasthi	Interactive Session at GLA university	Mathura	16th Dec 2022
Dr. Amit Awasthi	Preparedness and Technological Solutions for Management of Future Pandemics	DRDE, Gwalior	26th-30th Sep 2022
Dr. Guruprasad R Medigeshe	1st Preclinical Workshop, Dengue Therapeutics Global Partnership	THSTI	10th May 2022
Dr. Guruprasad R Medigeshe	WHO Health Emergencies Programme, Meeting on Pathogen X	Virtual	29th-30th Aug 2022
Dr. Guruprasad R Medigeshe	Announcement of India's first indigenously developed quadrivalent Human Papilloma Virus (qHPV) Vaccine, CERVAVAC	India International Centre, New Delhi.	1st Sep 2022
Dr. Nisheeth Agarwal	International conference on "Exploring New Horizons In Biotechnology (ENB-2023)" & mini-symposium on "Recent Advances In Biotechnological Innovations (RABI-2023)"	BHU, Varanasi	10-12th Feb 2023
Dr. Nisheeth Agarwal	Advanced training in Immunology of Tuberculosis	ICGEB, New Delhi	16th- 22nd May 2022
Dr. Nisheeth Agarwal	Celebration of Vigyan Utsav as a part of Azadi ka Amrit Mahotsav	Haryana State Council for Science, Innovation & Technology	18th Apr 2022
Dr. Milan Surjit	IUBMB focused meeting on Biochemistry & Molecular Biology of RNA viruses	RCB, Faridabad	15th-17th Nov 2022
Dr. Milan Surjit	International conference on virus evolution, infection and disease control	University of Hyderabad	15th-17th Dec 2022
Dr. Amit Kumar Pandey	LASACON-2022: Animal Models for One Health Program: Challenges and Future Perspectives	NIAB-NARFBR, Hyderabad	3rd-4th June, 2022
Dr. Sweetly Samal	ISIRV Respiratory Virus School	Christian Medical College, Vellore, India	14th-18th Nov 2022

Name of the participant	Meeting title	Venue	Date
Dr. Tripti Shrivastava	Addressing the challenges of the RNA virus; genetic diversity, through structurally occluded conserved epitopes directed vaccine candidate	IUBMB focused meeting on Biochemistry & Molecular Biology of RNA viruses, RCB, Faridabad	15th-18th Nov 2022
Dr. Tripti Shrivastava	Role of antigens in Antibody Isolation	Monoclonal antibodies: Principles of production, applications in immunodiagnostics and therapeutics", IAV, Thiruvananthapuram	8th-9th Dec 2022
Dr. Amit Kumar Yadav	Computational Workshop on Genomics, Proteomics and Metagenomics CWGPM-2022),	IGIB	20th-23rd Jul 2022
Dr. Amit Kumar Yadav	Virtual Podium Asia Pacific (VPAP) 2022 in Proteomics, Metabolomics and Lipidomics	Online	25th-27th Oct 2022
Dr. Amit Kumar Yadav	14th Annual Meeting of the Proteomics Society of India and International Conference on Proteins & Proteomics (PSI-ICPP 2022)"	CSIR-Indian Institute of Chemical Biology (IICB), Kolkata, India	2nd-5th Nov 2022
Dr. Amit Kumar Yadav	One day symposium on NAFLD	THSTI (Co-organizer)	25th Jun 2022
Dr. Amit Kumar Yadav	Two-day Workshop on "Proteomics and Data Analysis"	THSTI (as the Organizer and Coordinator)	9th-10th Feb 2023
Dr. Deepjyoti Paul	International Conference on Infectious Diseases	Kuala Lumpur, Malaysia	Nov 2022
Dr. Soma Patnaik	Celebration of Vigyan Utsav as a part of Azadi ka Amrit Mahotsav, DST Haryana	Haryana State Council for Science, Innovation & Technology	17th Aug 2022

All the faculty, scientists, students, research fellows and scientific staff attended the following symposiums/conferences held at THSTI:

- Symposium on Metabolic Associated Fatty Liver Disease (MAFLD) on 25th June 2022
- Symposium on INFLAMMATION on 14th July 2022Conference
- Conference on Preparedness for Future Epidemics: Is India ready to meet the CEPI 100 days vaccine challenge
- Conference on Human Microbiome in Health and Disease on 15th Feb 2023
- UTSAV-2023 on 22nd Feb 2023
- Conference on TOWARDS END TB: ACHIEVEMENTS, CHALLENGES AND FUTURE DIRECTIONS on 23rd-25th March 2023



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एवं प्रौद्योगिकी संस्थान

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