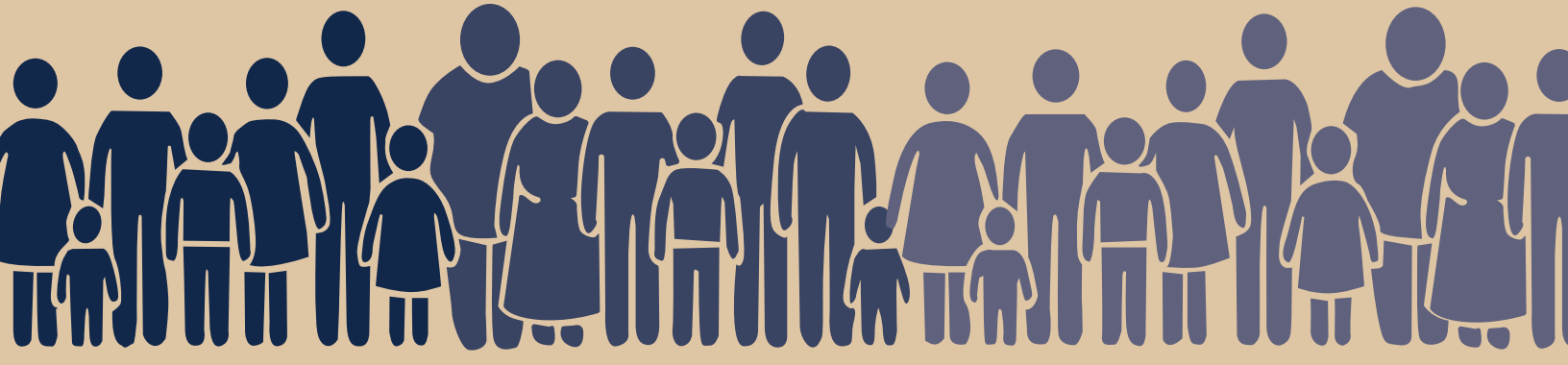
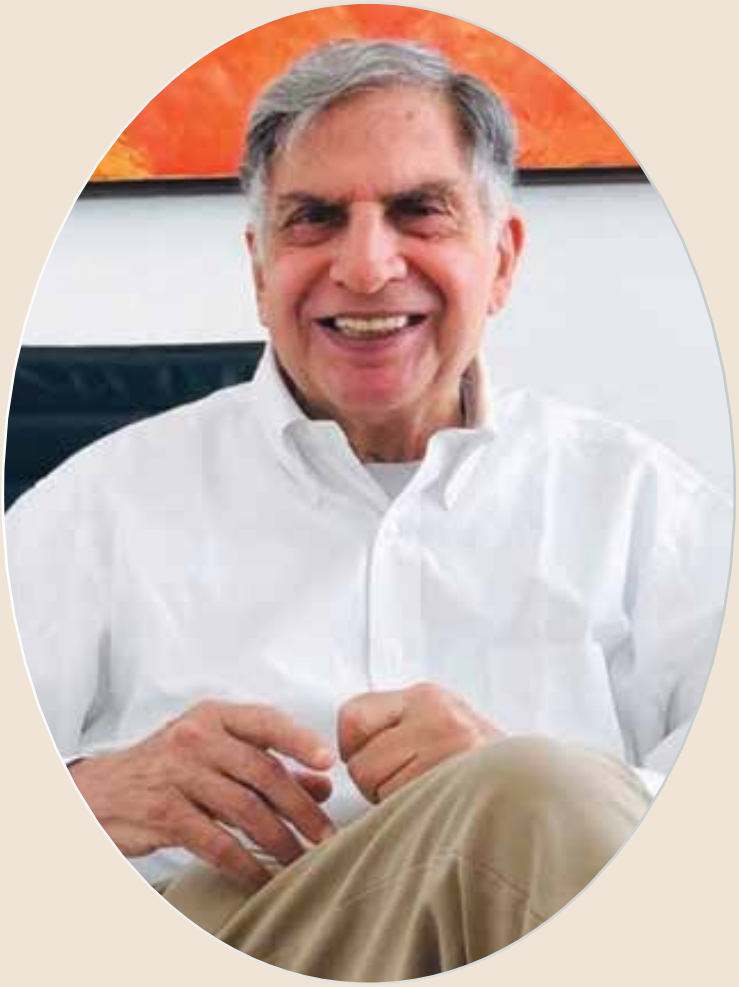
TIGS
Tata Institute for Genetics and Society

Annual Report 2023





"Recent advancements in genetics and genomics have the potential to solve some of the most complex challenges in agriculture and healthcare and create significant societal value. The Tata Institute for Genetics and Society was established with this vision, and I am pleased to note that the institute continues to focus on research in the areas of crop improvement, food security, point-of-care diagnostics and modern therapeutics"

Ratan N Tata

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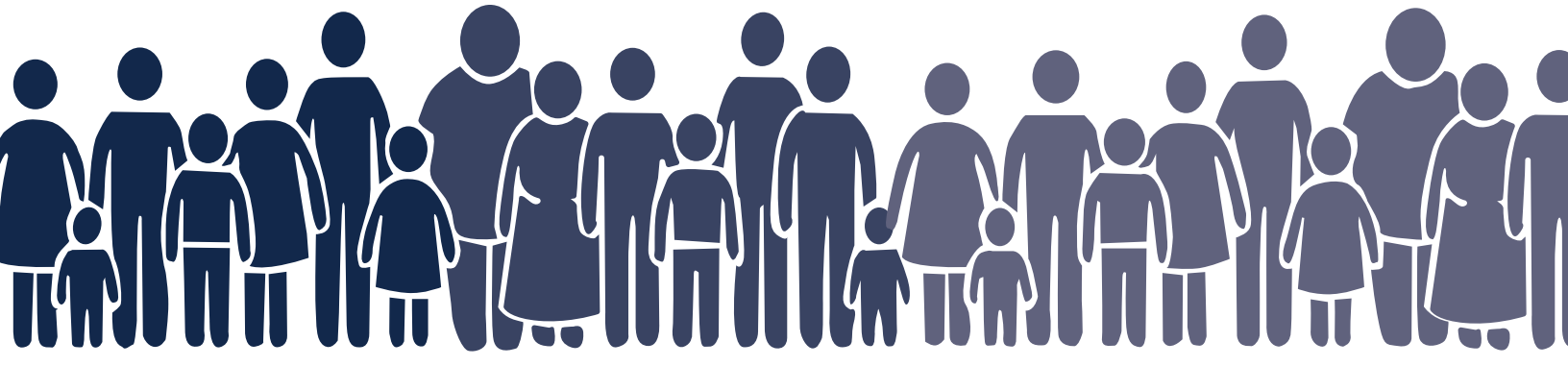

Published by:	**Rakesh K Mishra, Director, TIGS**
Editorial team:	**Harvinder Kour Khera** **Saveetha Meganathan** **Sham Bharadwaj** **Surabhi Srivastava**
Illustrations:	**Sampath Kumar** **Samruddhi Walaskar**

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Director's Message

In the recent past, we have witnessed remarkable strides in the field of genetics and genomics, characterized by breakthroughs in genome editing and a spectrum of DNA/RNA technologies. These advancements hold the potential to bring about transformative changes in healthcare, food security, and nutrition. At TIGS, we are excited by the prospect of leveraging these opportunities to actualize our vision.

While the challenges posed by infectious diseases, genetic disorders, soil health, and the environmental impact of food production are formidable, the pledges of scientific and technological progress are equally compelling. They are swiftly converging to tackle these challenges, aligning with Sustainable Development Goals (SDGs) and fostering sustainability.

TIGS is committed to harnessing scientific progress for the betterment of society. We have strategically positioned ourselves to channel state-of-the-art scientific developments, expediting the development of effective treatments for debilitating genetic diseases, formulating mitigation strategies for infectious diseases, and ensuring food and nutritional security. The Tata Trusts, renowned for their pioneering support in social and economic development in India, recognize the significance of our mission and generously fund TIGS as a conduit between groundbreaking scientific research and societal challenges in India.

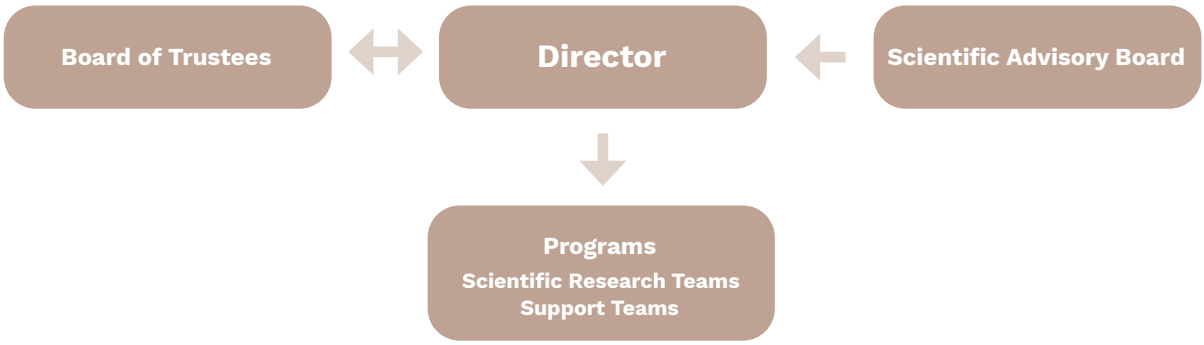
I am delighted to present this report, which highlights TIGS' rapid progress in making substantial contributions in these vital areas. Some notable achievements include our impactful contributions to environmental surveillance, monitoring real-time dynamics of infectious diseases, the development of numerous diagnostic options, measurable progress in mRNA therapeutic platforms for various rare genetic disorders, the advancement of genome-edited climate-resilient crops to the field trial stage, and a visible impact on outreach activities, effectively communicating scientific messages that resonate with society.

As we enter this exciting phase, there is every reason to be enthused about achieving our objective of utilizing cutting-edge science to address societal challenges.

Rakesh K Mishra
Director

TIGS as an Organization

The Tata Institute for Genetics and Society was founded in 2017 by Mr. Ratan N Tata as a charitable trust. Its primary mission is to foster scientific and technological research to solve some of India's most pressing issues in healthcare, agriculture, and related fields.



Manoj Kumar
Managing Trustee

Aparna Uppaluri
Trustee

With generous financial support from Tata Trusts, TIGS has developed state-of-the-art facilities and infrastructure dedicated to scientific research and development, including its integration with public policy and ethical considerations. Tackling the significant hurdles hindering health equity and nutrition security necessitates a systematic and evidence-based approach coupled with technological innovations. TIGS is committed to sharing its scientific findings widely and creating solutions that benefit society.

- **Manoj Kumar,** ***Managing Trustee***

Mr. Manoj Kumar is the founding trustee of TIGS. As a Senior Advisor to Tata Trusts, Manoj has spearheaded Tata Trusts' initiatives for institution building and engagements with universities globally. Manoj is also the founder of Social Alpha, a platform designed to curate and nurture science and technology start-ups addressing critical social, economic, and environmental challenges.

Scientific Advisory Board

TIGS has a biannual review with some of the leading experts in the field, academic as well as from industry. The board meets up with the scientists and staff over a couple of days of interactions held every six months. The scientists and team leaders present their findings and discuss their work and the SAB provides feedback and directions for the road ahead.

Prof. Ramesh Sonti
Director,
International Centre for Genetic Engineering and Biotechnology, New Delhi, India

Prof. Anil Gupta
Visiting Faculty
Indian Institute of Management, Ahmedabad, India

Dr. K. Thangaraj
J C Bose Fellow
CSIR - Centre for Cellular and Molecular Biology, Hyderabad, India

Dr. Sanjay Singh
Chief Executive Officer
Gennova Biopharmaceuticals, Pune, India

Dr. Shahid Jameel
Fellow
Green Templeton College, University of Oxford, UK

Prof. Gagandeep Kang
Director
Enterics, Diagnostics, Genomics and Epidemiology, Global Health,
Bill and Melinda Gates Foundation

Dr. Krishna Reddy
CEO
ACCESS Health International, Hyderabad, India

Prof. Suresh Subramani
Senior Advisor, TIGS
Distinguished Professor
University of California, San Diego, USA

Dr. Rakesh Mishra
Director
Tata Institute for Genetics and Society, Bengaluru, India

Overview

The Tata Institute for Genetics and Society (TIGS) is a non-profit research institute for developing solutions to challenges in human health and agriculture. A program-driven research institution, TIGS is a unique initiative of the Tata Trusts to support applications of cutting-edge science and technology in genetics and genomics and solve societal problems of the country. We are committed to contributing towards India's accelerated path in emerging as a global power through concerted efforts that use science-based solutions to prevent infectious diseases, improve access to affordable and quality diagnostics and therapeutics for rare genetic disorders, foster health equity, and achieve nutrition security through sustainable models for agriculture. Research programs at TIGS are focused on the following broad areas:

Infectious Diseases: The Infectious Diseases program studies vectors, pathogens, and their relationship to humans and the environment. The program includes development of new diagnostics, devising strategies to control vectors such as mosquitoes, employing environmental surveillance to understand the prevalence of disease-causing pathogens and developing approaches to reverse the threat of antibiotic resistance.

Rare Genetic Disorders: The Rare Genetic Disorders program focuses on genetic disorders that affect a small percentage of people but translates to a large number of patients given India's huge population. They mostly affect children yet do not have sufficient therapeutic or management options, causing significant social, economic and financial burden for affected families. Our efforts are directed towards developing accessible diagnostic assays that can be applicable for screening carriers of particular genetic disease traits as well as cost-effective therapeutic strategies.

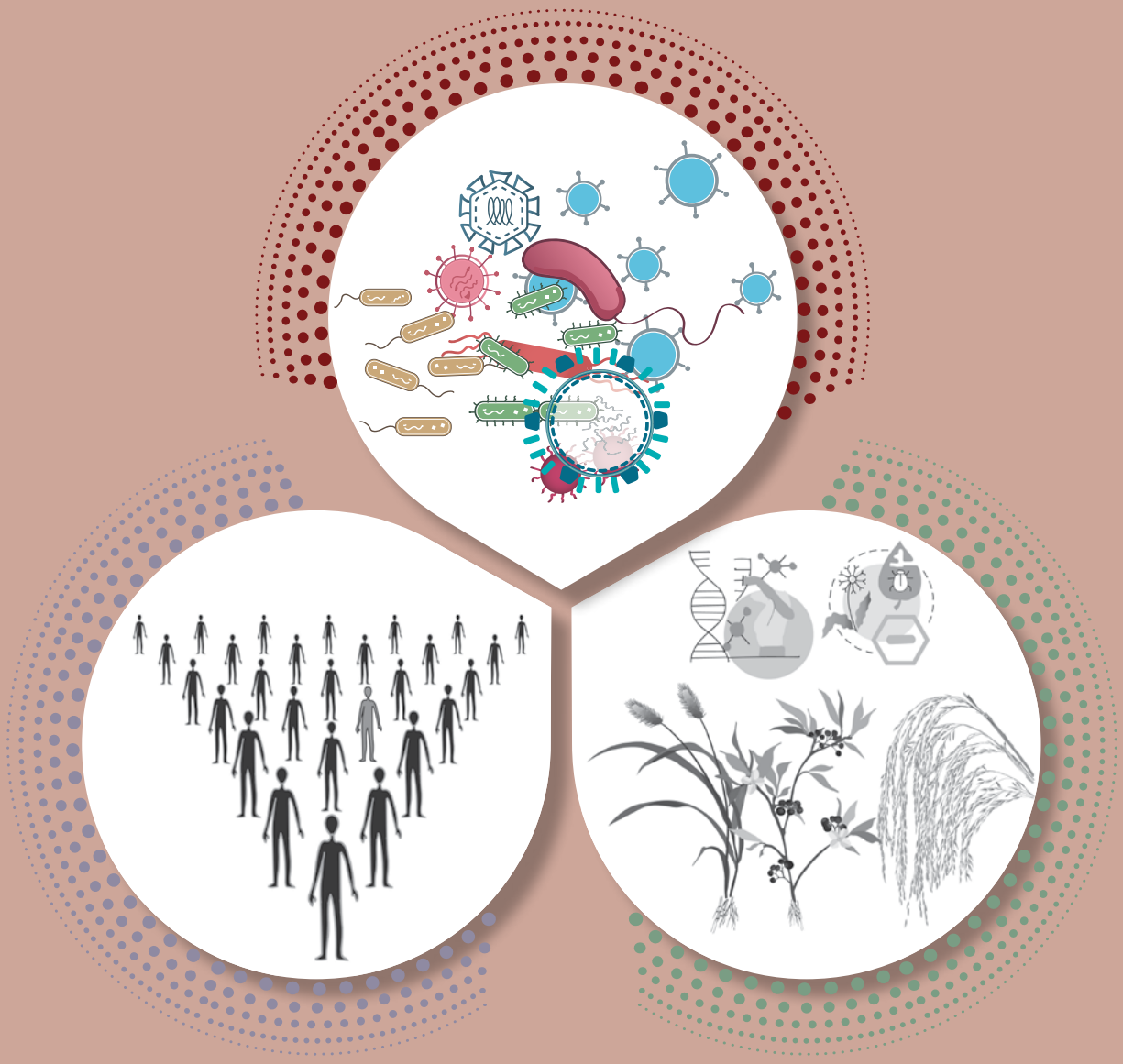
Crop Improvement: The Crop Improvement program is aimed at developing food crop varieties that are nutrient-rich, more resilient to diseases and pests, and drought tolerant. With growing challenges in food production, land availability and climate change, as well as diseases and pests, the agricultural sector needs major technological innovations and interventions to meet the needs of the current and future generations.

TIGS has also been working towards establishing technology platforms that facilitate cutting-edge research and training in the country. The institute houses a state-of-the-art, world-class insectary that supports research on mosquito biology, disease transmission, parasite interactions and population dynamics. We are also building platforms for mRNA and cell-based therapeutics, and diagnostics development.

TIGS' research efforts are synergized by valuable scientific associations that it has established with institutes and researchers across the country. These associations bring together exceptional talent and know-how, thus accelerating and amplifying our resolve in tackling some of the biggest challenges in human health and agriculture. The institute is also deeply invested in engaging with society and disseminating scientific knowledge among communities through socially conscious community engagement programs and science communication. It is equally important to create platforms for regulatory and policy aspects to ensure that the benefits of advanced and safe technologies are not ignored. Through these efforts, TIGS endeavours to fulfil its vision of synergising visionary philanthropy and outstanding science to serve humanity.

Research Programs

Infectious Diseases



Infectious Diseases

Arati Ramesh

Farah Ishtiaq

Jay Prakash Shukla

Mansi Malik

Sampath Kumar

Sanjay Lamba

Shivranjani C Moharir

Sonia Sen

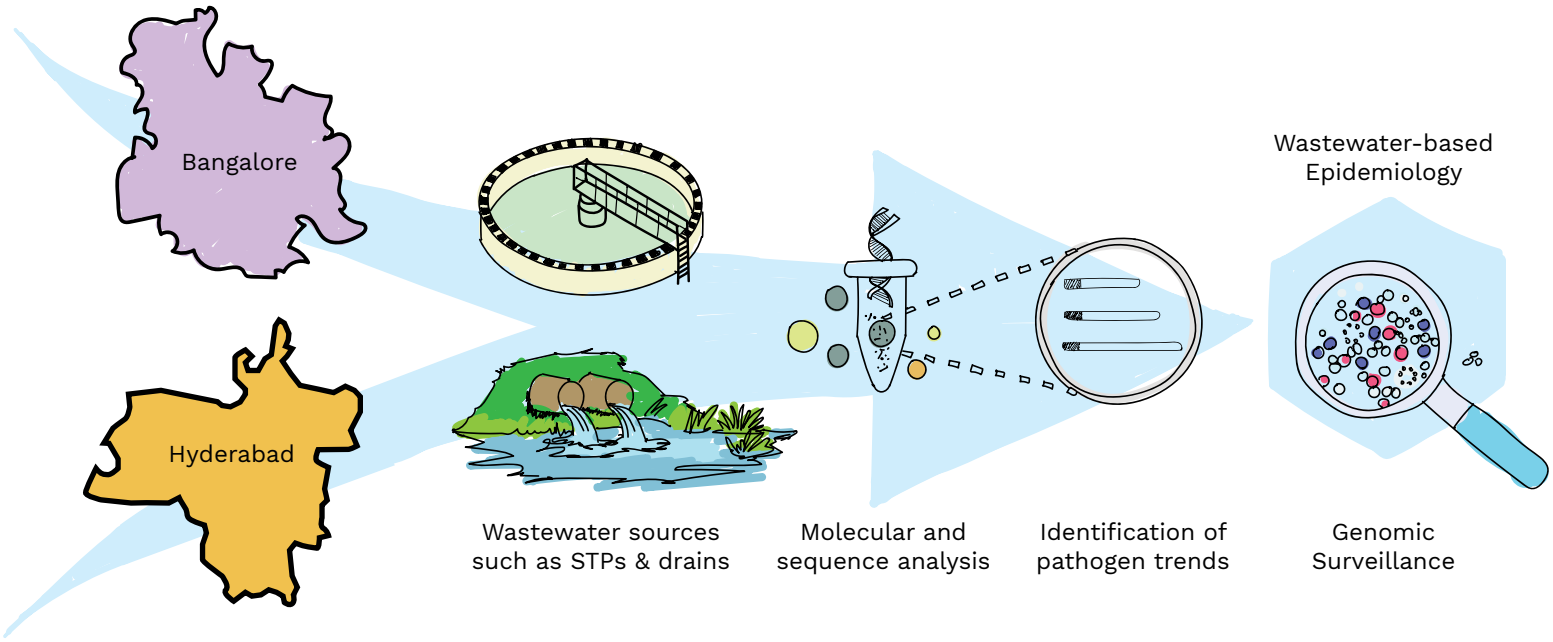
Sunita Swain

The emergence of virulent infectious pathogens (viral, parasitic, or bacterial), antimicrobial resistance, and lack of adequate surveillance are serious evolving threats to human and animal health. We integrate human health with disease ecology using a transdisciplinary strategy - a One Health approach - which recognizes that the health of people is closely connected to the health of animals and our shared environment.

Environmental Surveillance & Disease Ecology

Environmental surveillance has emerged as a smart surveillance tool to detect, quantify, and track pathogens of interest. It serves as an early warning system to take appropriate measures and build infrastructure to contain or circumvent public health crises. Monitoring public health by sample collection at individual patient level can be extremely costly. Environmental samples, such as wastewater samples, are composite samples that represent the contribution from many individuals in the community and are thus unbiased and cost-efficient for routine surveillance of infectious diseases. Globally, wastewater-based epidemiology (WBE) has been used for over 40 years to track measles, cholera, polio, and HIV outbreaks. More recently, with the ongoing pandemic, WBE has emerged as a cost-effective and efficient tool to predict rise in COVID-19 infections.

Environmental surveillance helps identify disease hotspots and needs to be combined with ecological drivers of diseases in both space and time. We strive to underpin this by studying the field of disease ecology which encompasses the ecological study of host-parasite interactions within the context of their environment and evolution. Many arboviruses, such as those that cause Chikungunya and Dengue, have zoonotic origins, and their interactions with mosquito vectors have evolved in parallel with the urbanisation of their key mosquito hosts (***Aedes*** species), and this understanding is fundamental to the One Health approach. Vector-pathogen interactions are critical to the transmission and epidemiology of vector-borne diseases. Our work focusses on the mechanisms and scale of pathogen interactions at individual, population, and community levels. We take an interdisciplinary approach drawing on genetics, molecular ecology, epidemiology, and modelling to understand how biological, social, and physical aspects of our environment can influence disease transmission, intensity, and distribution.



Wastewater-based epidemiology in Bengaluru city: Beyond SARS-CoV-2

Farah Ishtiaq

[In collaboration with NCBS, Bangalore Water Supply and Sewerage Board (BWSSB), Bruhat Bengaluru Mahanagara Palike (BBMP) and Biome Environmental Trust, Bengaluru]

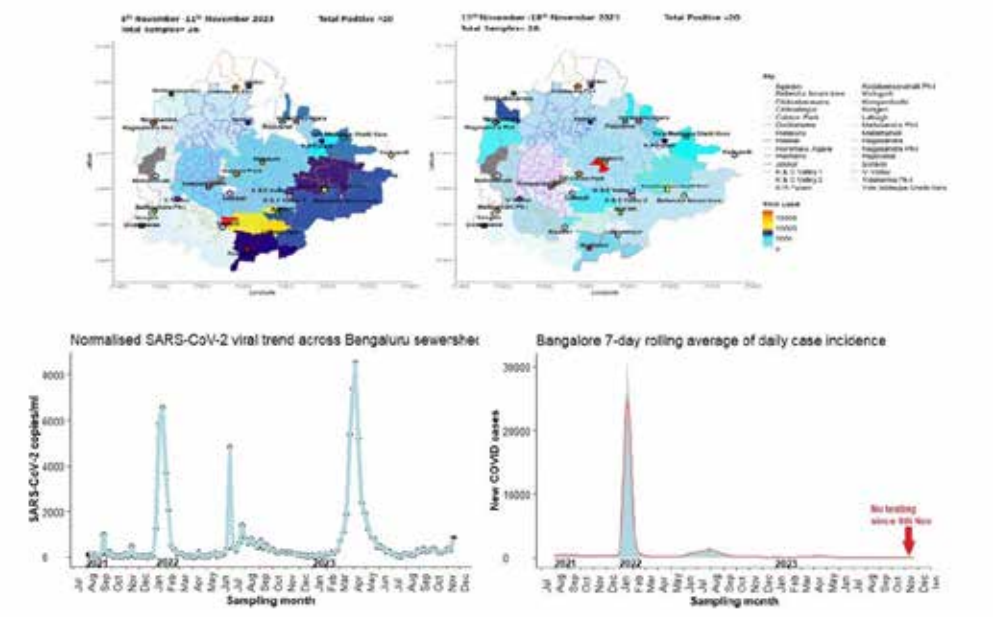
In India, tracking of the COVID-19 pandemic relies heavily on testing symptomatic individuals for the presence of SARS-CoV-2 RNA and counting the positive tests over time. Many SARS-CoV-2 infected persons are asymptomatic or oligosymptomatic (few symptoms) and are generally not tested by RT-qPCR, leading to underestimation of COVID-19 cases. Furthermore, infected and even asymptomatic individuals start to shed the virus via faecal route 4-7 days in advance of symptoms and clinical testing, which means the increase in viral load in sewage water ahead of reported cases works as an early warning system. Wastewater-based epidemiology (WBE) thus complements the routine diagnostic surveillance by capturing near real-time virus circulation at a community level.

TIGS, in collaboration with Biome Environmental Trust and National Centre for Biological Sciences (NCBS), has led a longitudinal study (ongoing since August 2021) across 28 Bengaluru sewershed sites capturing data from more than 11 million people. The wastewater infrastructure of Bengaluru (under BWSSB jurisdiction) offers an effective resource to access and estimate the spread of the SARS-CoV-2 across the city. The Bangalore One Health Consortium (under the Bengaluru Science and Technology Cluster) initiated the city-wide WBE of SARS-CoV-2 and is now expanding it to other pathogens in Bangalore and nearby areas. The SARS-COV-2 viral trend in wastewater is shared on a regular basis with the municipal authorities (BBMP and BWSSB) which is helpful in making policy and taking decisions as early as by ~one-week of the emerging infection trend. In collaboration with the NCBS, and support from the Rockefeller Foundation, Tata Trusts, and Indian Council of Medical Research, our WBE approach also includes genomic analysis of emerging viral variants driving the spike in viral load.

Two years of Wastewater Surveillance of SARS-CoV-2

28 Sewage Treatment Plants are being monitored

- Early warning system developed
- Real-time Genomic Surveillance
- Comparison with Clinical data
- Work with BBMP on prioritization of pathogens using Wastewater surveillance



Plots showing the SARS-CoV-2 RNA load in wastewater from 28 STPs in Bengaluru

From data to policy

One of the most important aspects of this study is reporting viral load and citywide positivity rates and a regular discussion with BBMP and BWSSB so that the information can be used for making policy decisions. We have been sharing weekly reports on viral trend and genomic surveillance with BBMP and how this relates to COVID-19 data in the city.

TIGS initiative for Environmental Surveillance of SARS-CoV-2

An initiative by Tata Institute for Genetics Society (TIGS) in collaboration with Biome Environmental Trust, National Centre for Biological Sciences (NCBS), and Bangalore Water Supply and Sewerage Board (BWSSB).

Weekly Report

Snapshot of the weekly report sent to Bruhat Bengaluru Mahanagara Palike (BBMP), Bengaluru the local municipality.

Wastewater surveillance played a crucial role in the eradication of poliovirus in India in 2012. What we now need is to scale up the Environmental Surveillance beyond poliovirus and SARS-CoV-2 virus to pan-pathogen surveillance and integrate with the main healthcare system. Such surveillance has the power to predict neglected and emerging diseases. Our approach and protocols developed lend support to establishing surveillance for monitoring and an early-warning system for detecting multi-pathogens (e.g., dengue, avian influenza, influenza, hepatitis, cholera). As an evidence-based approach, it is very useful for predicting risks to human as well as animal health. We are therefore working on a One Health approach to recognize the connection between the health of humans, animals, and the environment.

Wastewater-based epidemiology in Hyderabad and public health surveillance using molecular biology, genomics and data analytics

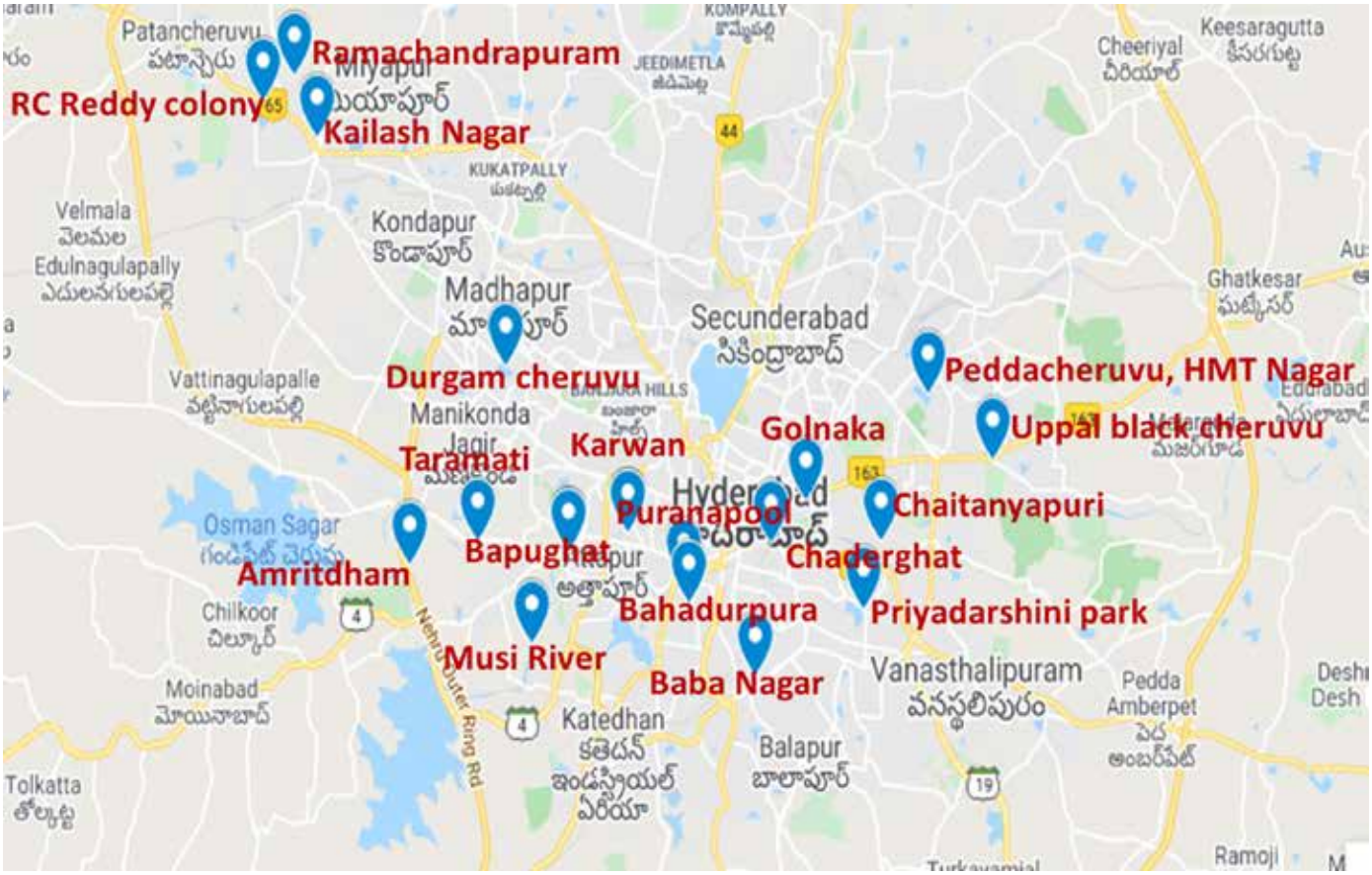
Shivranjani Moharir

[In collaboration with CSIR-CCMB, Hyderabad]

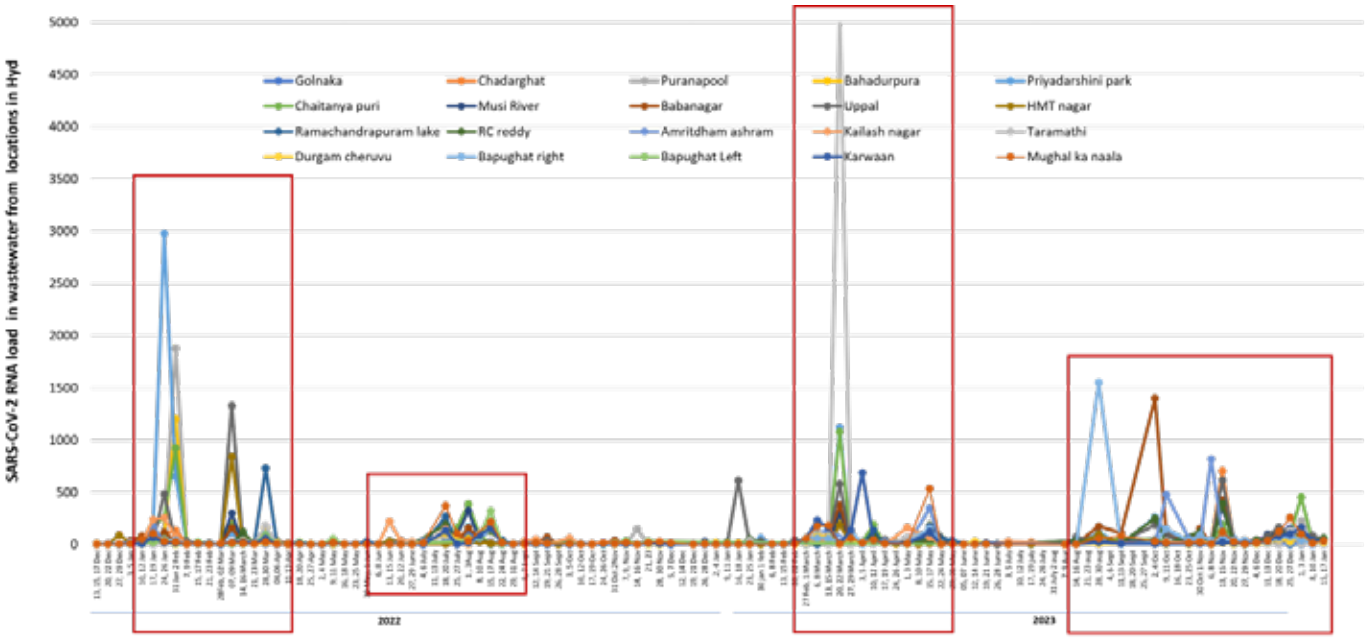
Routine monitoring of public health can help in the early detection of emerging or upcoming infectious disease waves in the community and can help in preventing future pandemics. Wastewater is the warehouse of thousands of parasitic, non-parasitic, infectious, non-infectious, and saprophytic microorganisms. These microorganisms find their way in the wastewater mainly through human or animal excreta or through soil. The qualitative and quantitative analysis of the microbiome of sewage water in a particular geographical location can be a read out of the general health of the people inhabiting that area.

We analyse environmental samples using molecular biology and genomics approaches for surveillance of pathogenic microbial diversity, including SARS-CoV-2, in wastewater. Since SARS-CoV-2 is shed by infected individuals in their faeces irrespective of their symptomatic status, wastewater-based epidemiology serves as a tool to monitor even dormant and unreported COVID-19 infections.

Over the two years, routine WBE-based surveillance of SARS-CoV-2 in Hyderabad has been set up at 18 sampling locations, including open drains, across the city. Sampling protocols including collection, processing, and analysis have been standardized. SARS-CoV-2 RNA load at all the sampling locations is routinely monitored to map the trend of viral infectivity in different parts of the city and the viral RNA is sequenced for identifying emerging variants.



Plot showing the SARS-CoV-2 RNA load in wastewater from 18 locations in Hyderabad

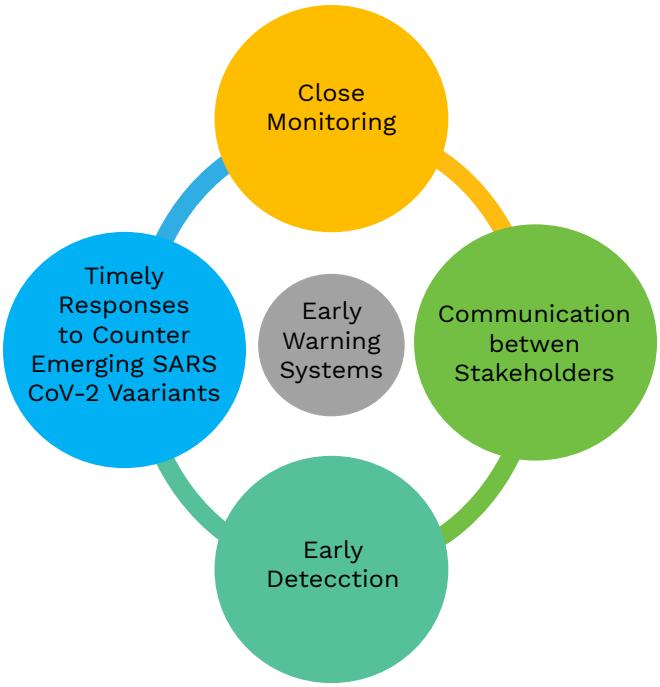


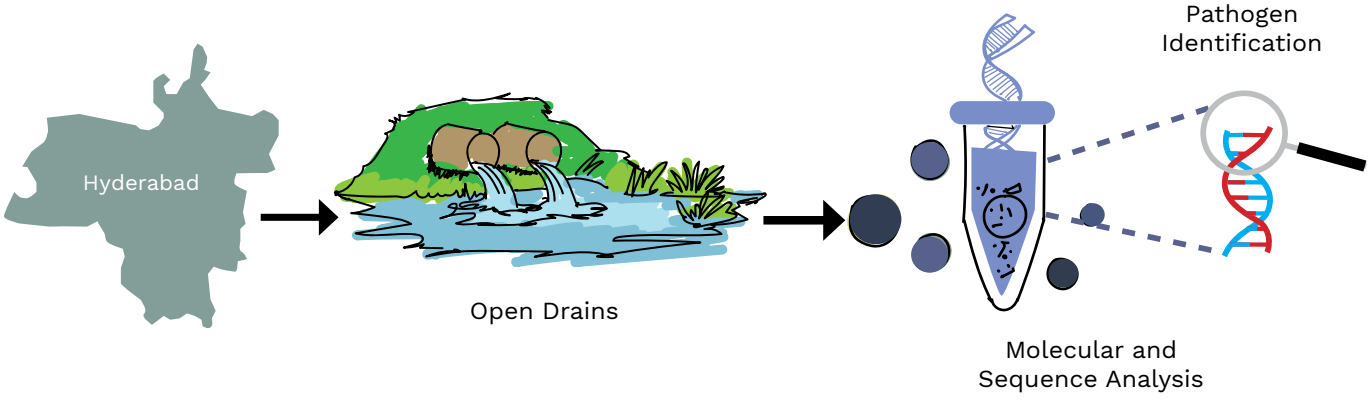
Modelling the longitudinal data obtained from wastewater-based surveillance of SARS-CoV-2 in Hyderabad

Shivranjani Moharir, Sanjay Lamba

[In collaboration with CSIR-CCMB, Hyderabad]

The longitudinal data generated from wastewater-based surveillance of SARS-CoV-2 was modelling. Using statistical modelling and different machine learning approaches, we developed an early warning system and demonstrated how wastewater monitoring could be used for community-level detection and tracking of the SARS-CoV-2 virus, thereby informing public health policy decisions. In conclusion, monitoring temporal variation in viral loads in wastewater combined with other analyses can detect a virus outbreak at least one week in advance.





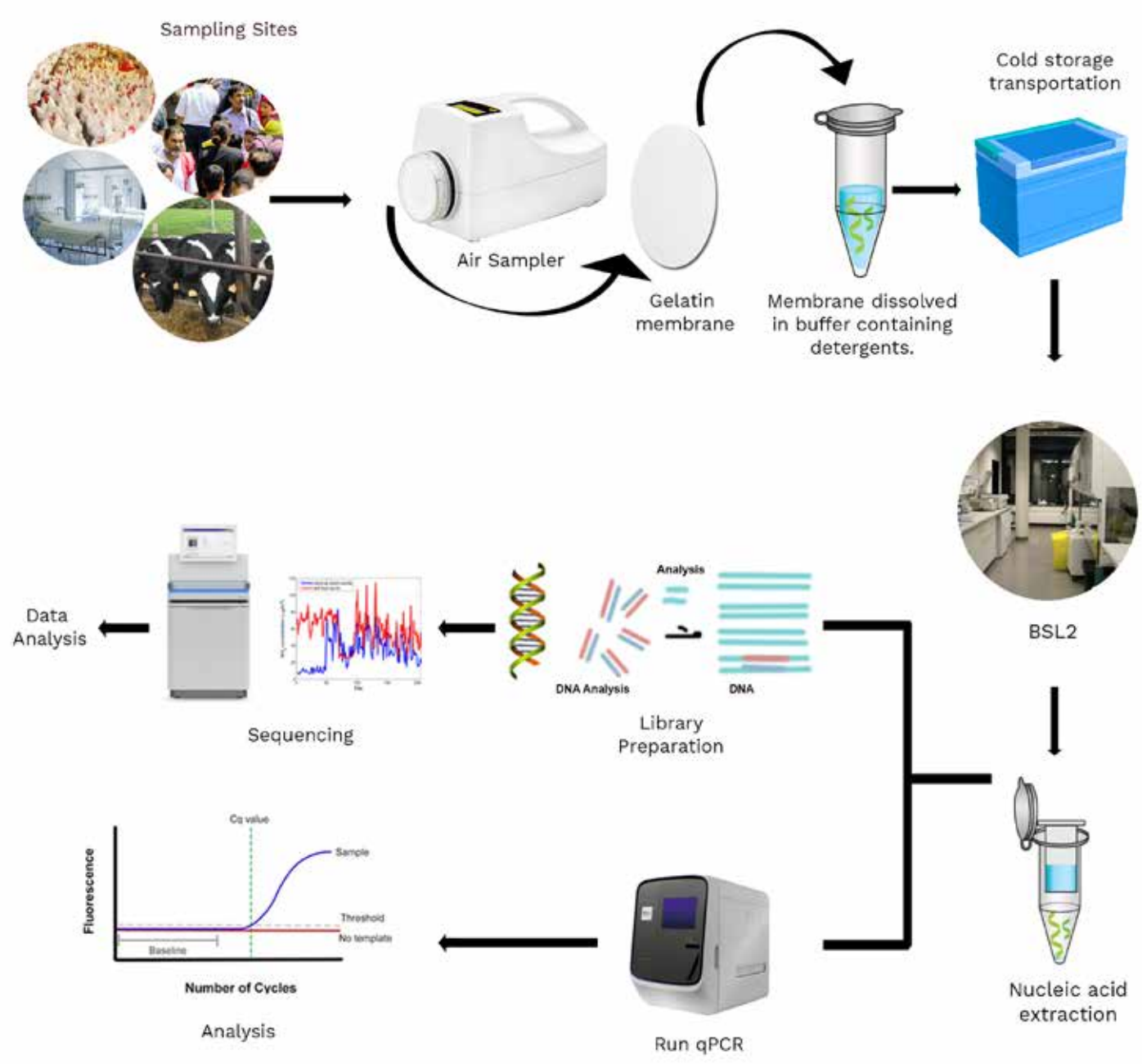
Pictorial representation of developing an early warning system from waste water surveillance

Air surveillance study to identify pathogens in different environmental niches

Shivranjani Moharir

Air surveillance of pathogens is a critical aspect of public health and epidemiological monitoring. It involves the systematic monitoring of the air to detect the presence of microorganisms, such as viruses, bacteria, and fungi. This surveillance is essential to understanding infectious disease transmission patterns and implementing timely preventive measures.

This project involves collecting and analyzing air samples from diverse environmental settings, including hospitals, zoos, densely populated areas, and sparsely populated regions.



A pictorial representation of the protocol for air surveillance

Molecular detection and screening of pathogens and associated biomarkers in clinical samples

Mansi Malik and Farah Ishtiaq

[In collaboration with Bruhat Bengaluru Mahanagara Palike (BBMP)]

Communicable diseases need continuous surveillance activities to track, predict, and control emerging, re-emerging, and novel infections that are potential threats to human health and wellbeing. Dengue and chikungunya are the two common vector-borne diseases in India transmitted by the Aedes spp. mosquitoes Aedes aegypti and Aedes albopictus, respectively. The epidemiology of chikungunya and dengue infections is thus likely to be temporally and spatially linked. Similarly, bacterial infections such as scrub typhus (caused by Orientia tsutsugamushi) and Leptospirosis (caused by Leptospira) account for 35 - 50% and 52% cases, respectively, of acute undifferentiated febrile illness. Currently, there are no molecular markers that can be used in clinical settings for a speedy diagnosis.

Bengaluru, located in the state of Karnataka in Southern India, is the third most populous city in India. It has an area of 709 km^2 with a projected population of 1.3 crores (UN Population Prospects). The above-mentioned diseases are highly prevalent in Bangalore and are a threat to public health. The Bruhat Bengaluru Mahanagara Palike (BBMP), the municipal body of Bangalore has already established a network of public health centres in the proximity of slums and slum-like settlements to address this lacuna in urban healthcare. A laboratory providing free diagnostic services was also established in the year 2018 in BBMP under National Urban Health Mission (NUHM) programme to cater to the urban poor. Currently, there are 6 Referral hospitals (RH), 13 Maternity homes (MH), and 141 Urban Primary Health Centres (UPHC) under the ambit of BBMP. ELISA-based diagnostic services are provided to the beneficiaries free of cost under various national health programmes.

We have collaborated with the BBMP to work on molecular surveillance of various communicable diseases, with the following objectives:

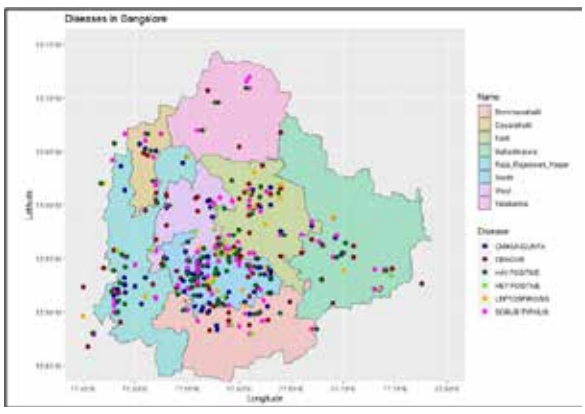
- To estimate the seroprevalence of Malaria, Dengue, Chikungunya, Leptospirosis, Scrub typhus, and Hepatitis using a combination of screening methods – ELISA in BBMP nodal laboratory and advanced molecular diagnostics at TIGS.
- To perform sequencing of samples for serotyping and strain identification of Malaria, Dengue, Chikungunya, Leptospirosis, Scrub typhus and Hepatitis to help in determining the prevalent strains/serotypes in Bengaluru city.

We have been working with the BBMP for developing a pipeline for disease surveillance in Bengaluru and have already established a molecular diagnostic setup for ELISA and nucleic acid extraction at the H.Siddaiah Referral hospital, BBMP. We have also standardized RT-PCR based molecular screening of Dengue, Dengue serotypes, Leptospirosis, and Scrub typhus, and initiated molecular surveillance of Hepatitis B & C from antenatal care samples by ELISA as well as via RT-PCR.

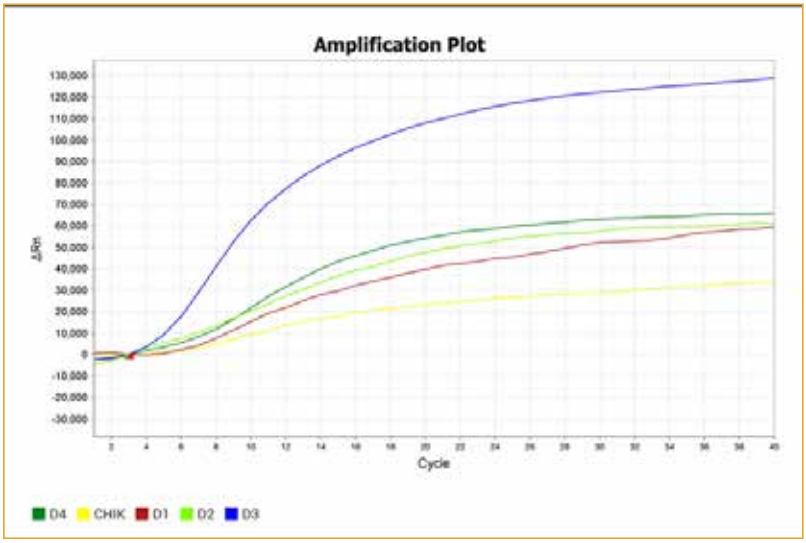
Approximately 1563 clinical samples have been screened until November 2023 and molecular screening has been performed for infections such as Dengue, Chikungunya, Leptospirosis, Scrub typhus, Hepatitis A, E, B, and C for early and accurate detection and to determine the disease prevalence, respectively.

We have developed multiplex molecular assays based on qRT-PCR to facilitate rapid, accurate and low-cost detection of these infections from patient samples, with clinical validation currently ongoing.

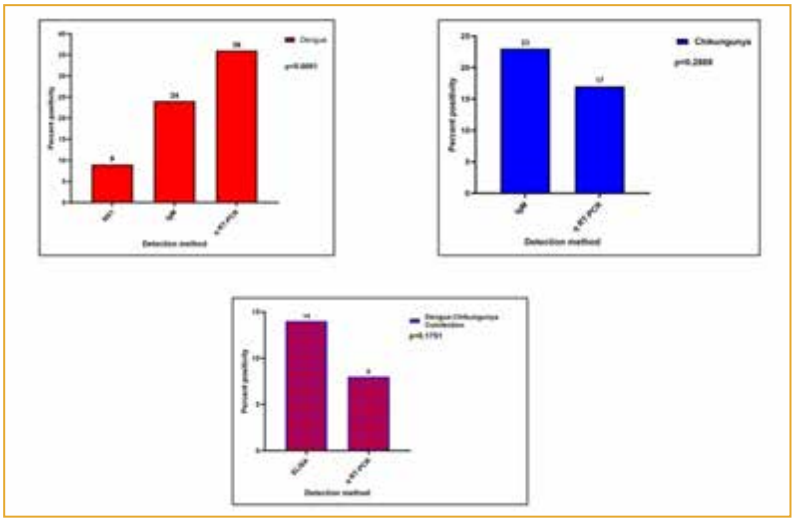
1. Prevalence of various infectious diseases in urban Bengaluru



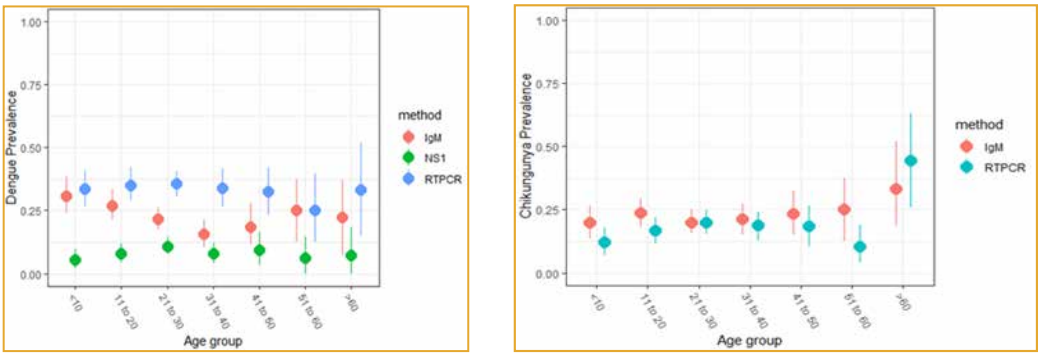
2. Dengue and chikungunya surveillance from clinical samples



A)" DENCHIK' a multiplex qRT-PCR based assay to simultaneously detect dengue serotypes and chikungunya.



B) Detection of dengue, chikungunya and co-infections across NS1 ELISA, IgM ELISA and DENCHIK



C) Age wise prevalence of dengue and chikungunya detected by ELISA and PCR

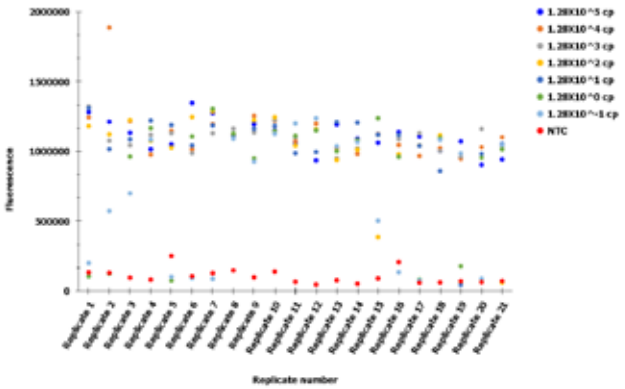
Developing indigenous point-of-care CRISPR/ CAS based diagnostics for infectious diseases for field application in India

Harvinder Kour Khera

Accurate diagnosis is the key to the right treatment, and early diagnosis of a disease is critical for saving lives. Taking a molecular approach, we are developing CRISPR/ Cas based diagnostic assays for various infectious diseases that are a major source of concern in India. These technologies are planned for implementation as point-of-care diagnostic solutions for field application, including in primary health care centers and rural settings.

Malaria

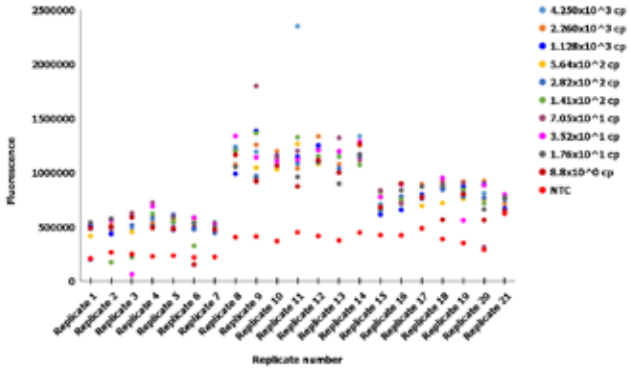
Malaria poses a significant global health threat, particularly in countries like India, resulting in substantial mortality and morbidity. The disease is primarily caused by four Plasmodium species. Timely and precise diagnosis is crucial for administering appropriate treatment and saving lives. Inaccurate diagnoses contribute to antimalarial overuse, fostering rapid resistance. Current diagnostic methods, such as microscopy and Rapid Diagnostic Tests (RDT), have limitations. Microscopy requires skilled personnel, and RDTs lack the ability to distinguish all Plasmodium species, exhibiting low sensitivity. The employment of two antigen targets, Histidine-rich protein 2 (HRP-2) and lactate dehydrogenase (pLDH), in RDTs raises concerns due to reported gene deletion in PfHRP 2. Addressing this diagnostic gap, we at TIGS are developing a CRISPR-based malaria detection solution characterized by robustness, accuracy, and sensitivity.



Dot plot shows the fluorescence values for various dilutions over 21 replicates conducted over a period of 3 days (7 replicates per day)

Tuberculosis

Ensuring timely and precise disease diagnosis is imperative to administer appropriate treatments and save lives. Inaccurate diagnoses contribute to antibiotic overuse, fostering rapid resistance. Significant challenges in this domain include high costs and limited availability in rural areas due to technology and skilled labor-intensive diagnostic assays. India constitutes 27% of global tuberculosis cases, with one-fourth being drug-resistant TB cases. Current diagnostic methods, such as culture-based and Nucleic Acid Amplification Test (NAAT), have limitations, including the accessibility and complexity of phenotypic drug susceptibility testing (DST) and the selective use of GeneXpert (NAAT) for Rifampicin resistance testing. Addressing these challenges, CRISPR Cas emerges as a next-generation diagnostic tool, offering high specificity and sensitivity for developing more impactful, sensitive, rapid, and cost-effective tuberculosis diagnostics in low and middle-income countries where TB is most prevalent.



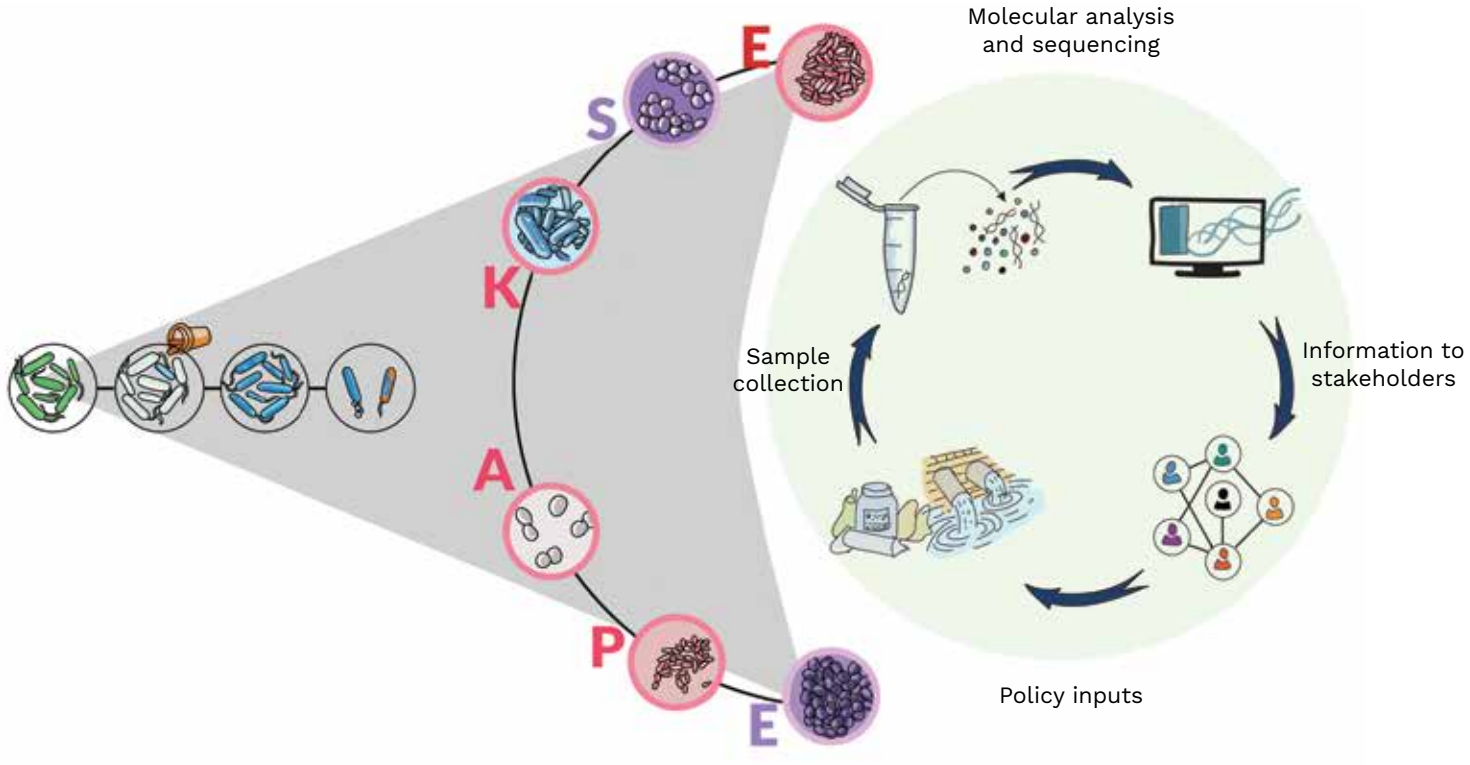
Dot plot shows the fluorescence values for various dilutions over 21 replicates conducted over a period of 3 days (7 replicates per day)

Antimicrobial Resistance

Antimicrobial Resistance (AMR) among bacterial pathogens is reaching an all-time high and this has been characterised as a 'silent tsunami' by the World Health Organization (WHO). India specifically has been identified as a hotspot of emerging antibiotic resistance owing to excessive use of antibiotics in both domestic animals and humans. A careful examination of approaches for countering the multifaceted complex problem of multidrug-resistant pathogens is needed, as the rise of antibiotic failure poses a severe threat to global health. There is growing concern that this failure is not solely driven by stable antibiotic resistance but also by a subpopulation of transiently non-growing, antibiotic tolerant bacteria, that are thought to seed relapsing infections. Bacterial pathogens such as ***Pseudomonas aeruginosa***, ***Salmonella, Shigella***, and pathogenic ***Escherichia coli*** (Enteropathogenic ***E. coli*** and Enterohemorrhagic ***E. coli***) cause life-threatening diseases, particularly in young children and immuno-compromised individuals.

Given this predicament, we are investigating health linkages between humans, animals, and their shared environments to embrace the concept of an integrated One Health approach.

Along with infectious disease surveillance, there is a need to study and understand the scale of the crisis raised by AMR. Due to the non-availability of information on the magnitude of resistance, the overall resistome, and against which drugs, there is a dire need for surveillance of AMR genes in the environment. We are working towards developing the capacity to detect AMR at a city-wide level, which is crucial for taking measures to mitigate the problem and avoid the future loss of lives, as well as economic losses.



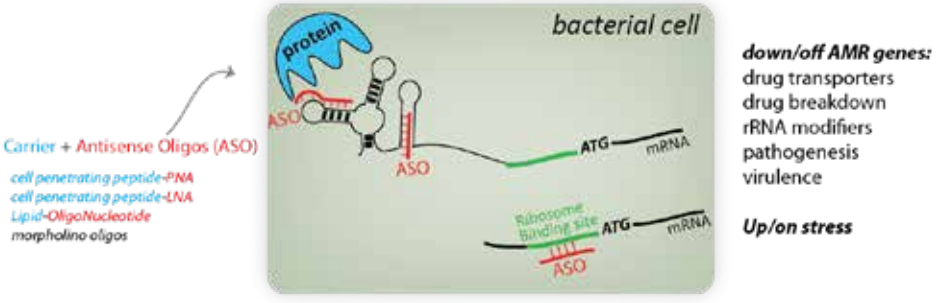
Developing novel therapeutics and early diagnostics to target infectious diseases, with a focus on AMR

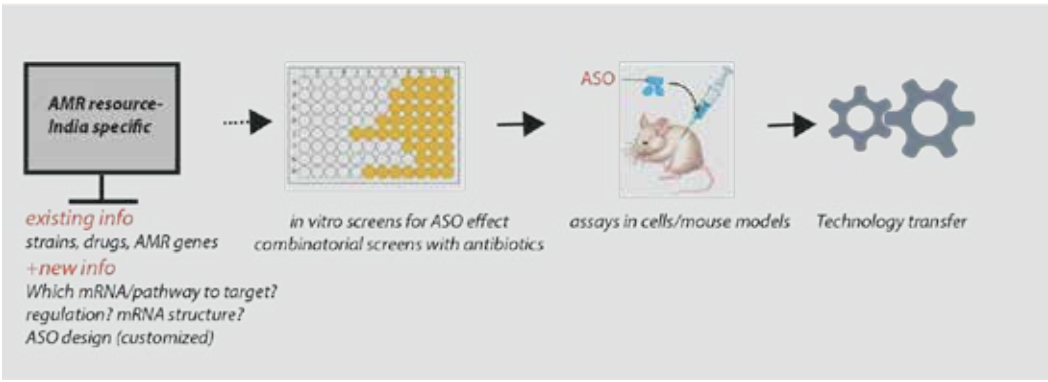
Arati Ramesh and Mansi Malik

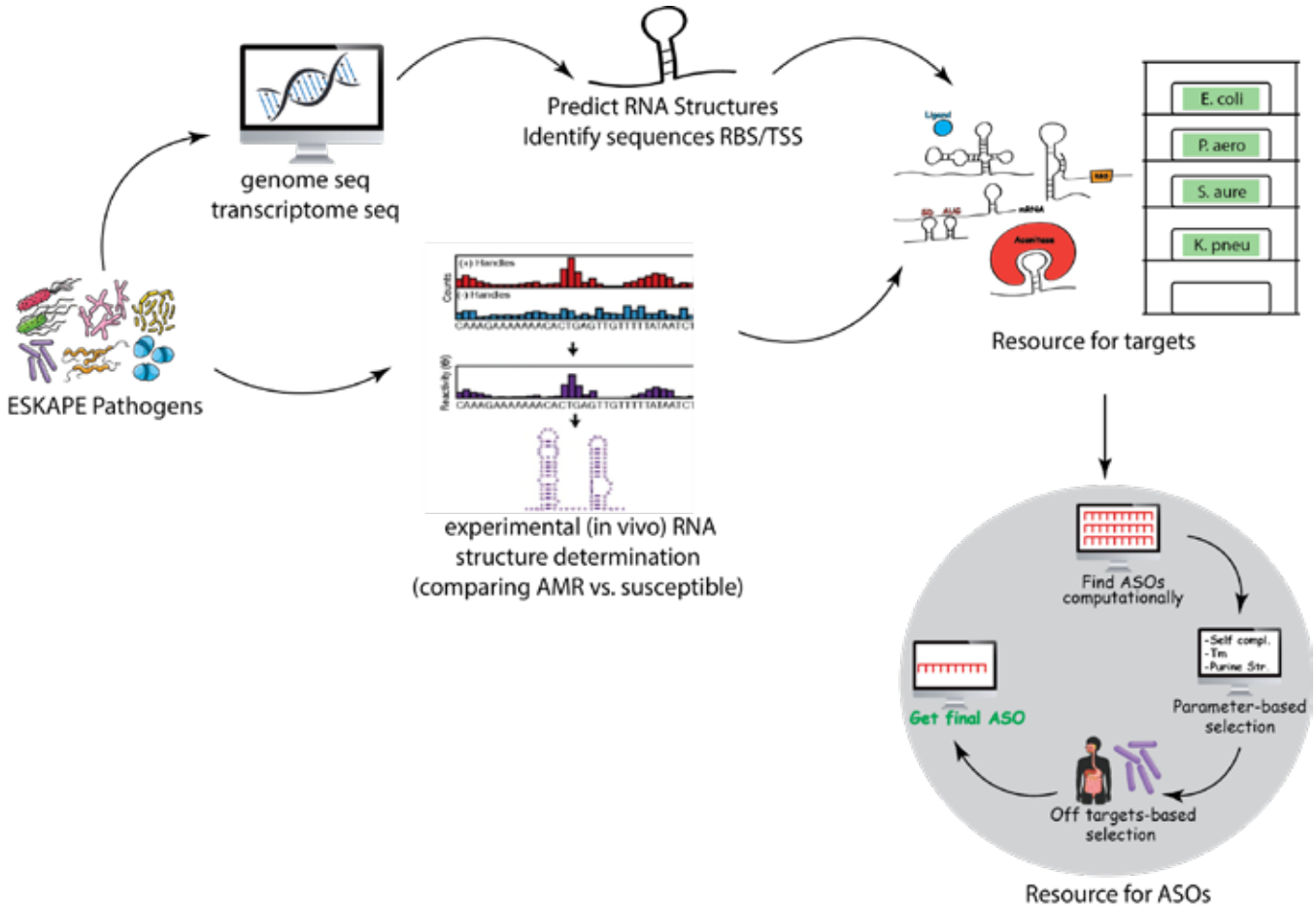
The AMR problem is where disease-causing microbes (bacteria, fungi, and viruses) are becoming less and less susceptible to existing antibiotics. This has resulted in the increased use of some of the most potent antibiotics ever known. One of the approaches needed to address the AMR problem would be to develop novel therapeutics that microbes have not been exposed to thus far. Along these lines, our team seeks to develop novel therapeutic oligonucleotide molecules, designed to target select aspects of microbial physiology. Such Antisense Oligonucleotide (ASO) therapy is designed to either directly kill the microbe (acting as a new antibiotic) or increase it's susceptibility towards existing antibiotics (repurposing obsolete antibiotics).

Carrier groups (such as cell-penetrating peptides or lipids) conjugated to oligonucleotide derivatives (such as peptide nucleic acid, locked nucleic acid, morpholino oligos, etc) are used to block the synthesis of essential proteins in the microbe. We are further evaluating the effects of these therapeutic oligos on microbial growth, organization into biofilms, pathogenicity, virulence and resistance to conventional antibiotics. To enable this approach we have set up a BSL-2 level laboratory with three of the six ESKAPE pathogens that are of utmost priority in the Indian AMR context. Initial testing of therapeutic oligos against UTI-causing bacteria and Staphylococcus aureus, a common cause of respiratory infections, skin infections, and abscesses show promising results, both for developing novel antibiotics and for repurposing existing antibiotics (see Figure).

AMR is a problem of such magnitude, that it will require the collective efforts of all stakeholders. To nucleate such a collective effort, we are in the process of developing an open-resource database which would serve as a knowledge base of the particular strains and variants of infectious organisms most encountered in the Indian population, their genome sequences, available transcriptome profiles, and most importantly, identify targets within the microbial transcriptome that may be most amenable to ASO therapy. We hope that an open-resource such as this would be valuable towards finding collective solutions for AMR.







Enabling early diagnosis of AMR in patients suffering from infectious disease

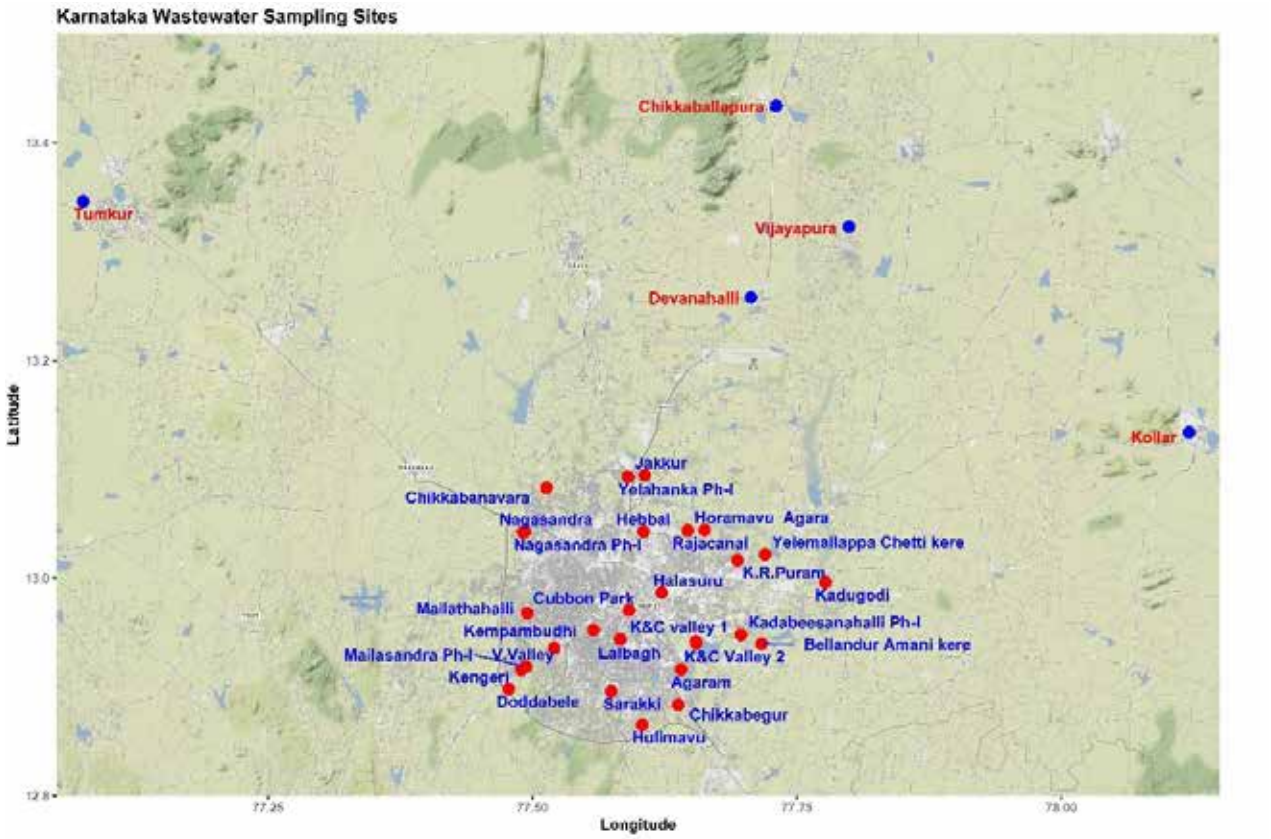
One of the biggest challenges faced by the medical community is the early detection of the antimicrobial resistance profile of the disease-causing organism. Conventional methods to identify germs and their antibiotic susceptibility take several days, in which time patients can only be treated with broad-spectrum antibiotics, which may not have any effect on the specific infection. This is not only dangerous for the patient but also contributes heavily to increased antibiotic usage and the resultant AMR problem. All efforts must be made to diagnose infectious agents early, along with the ability to predict which antibiotics would be best for treatment.

We have initiated work towards understanding the prevalence of AMR by detecting the pathogens, crucial biomarkers and antimicrobial resistant genes (ARGs) from clinical samples. We are developing q RT-PCR based assays for rapid, accurate, and low-cost detection. Next-generation sequencing (NGS) approaches shall also be employed to understand the changing AMR landscape of the city.

Surveillance for Antimicrobial Resistance Genes in wastewater

Farah Ishtiaq

Climate change and health are inextricably linked with urban wastewater. Water security is an imminent issue in India. Water scarcity and the reduced availability of agricultural water have spurred increased interest in the use of recycled irrigation water. There is concern that antibiotic resistance genes (ARGs) persisting in recycled irrigation water could potentially contribute to the growing overall public health challenge of increasing rates of antibiotic-resistant bacterial infections. Bengaluru (12.9716° N, 77.5946° E, Karnataka, India) is the third largest city (~11 million inhabitants) in India with an efficient sewage network of 28 STPs that processes ~1142.5 million litres per day (MLD) of wastewater (Fig.1). Each STP follows a water treatment technology depending on the quality of raw sewage to make the treated water reusable.

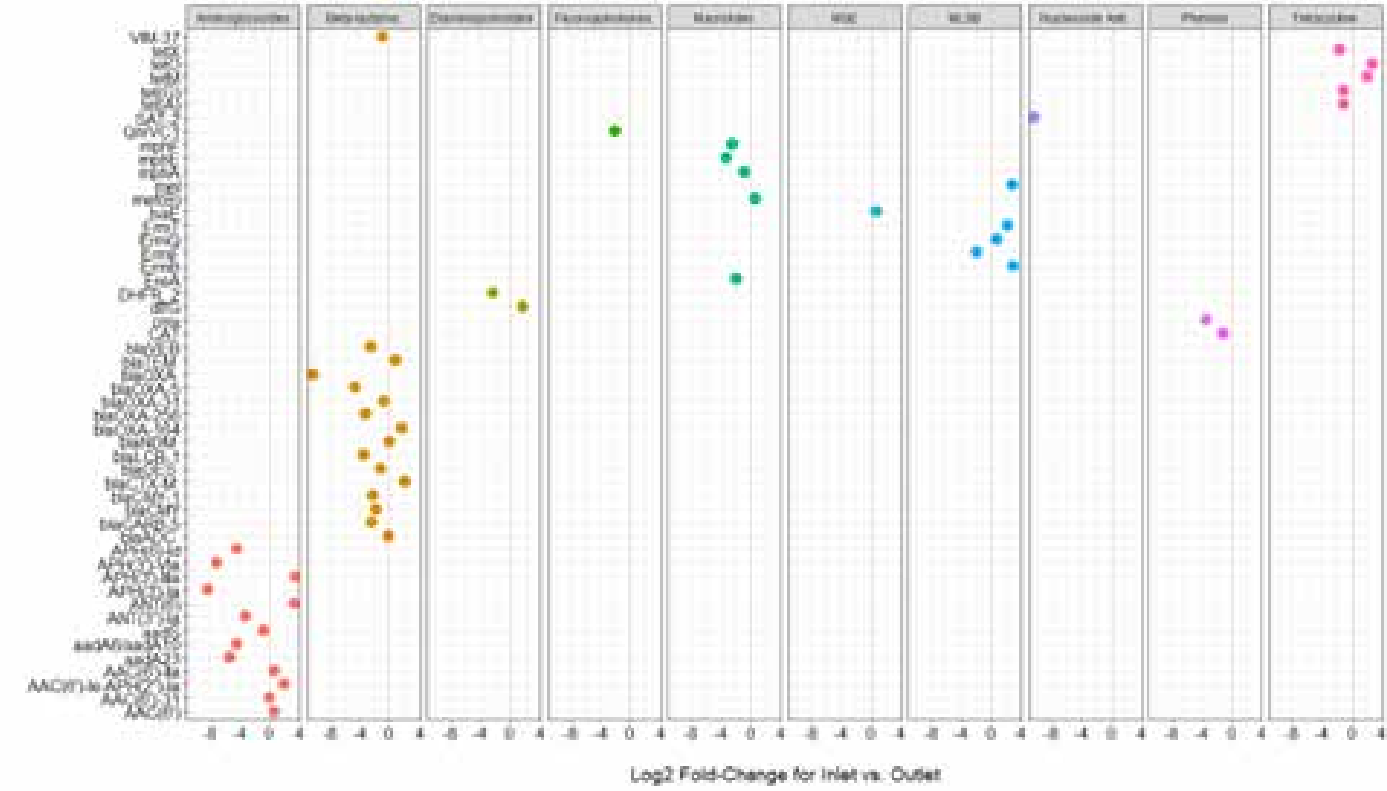


Location of Karnataka wastewater surveillance sites for SARS-CoV-2 and antimicrobial resistance genes.

Bengaluru has the largest water footprint compared to any Indian city where treated wastewater is used not only for agriculture but for recharging groundwater of drought-prone regions outside the city. For example, Kolar district of Karnataka, one of the worst affected districts in terms of drought and climate change, with treated wastewater pumped from Bengaluru, has helped improve groundwater quality and perennial availability of water irrespective of weather and climate patterns. While it is essential to minimise the public health risks before using treated wastewater, it is important to understand the effectiveness of treatment plants in removing harmful parasites and if there is a spatial and temporal segregation in AMR and related bacterial and fungal diversity. To explore this, treated and non-treated urban sewage samples were collected from 28 STPs in Bengaluru. Our goal is to quantify the effect of water treatment mechanism on ARG diversity and abundance in the outlet of four STPs in Bengaluru where treated water is used for agriculture. Using a combination of

metagenomic approaches, our preliminary finding based on 273 ARG screened in wastewater show 54 dominant genes and a downward shift in drug class from inlet to outlet samples except for aminoglycosides, beta-lactams, MLSB, and Tetracycline (Fig.2)

We will be working with the Bengaluru Water Supply and Sewerage Board (BWSSB) to improve on water treatment mechanisms of four key STPs which supply treated water for agriculture and groundwater recharging in peri-urban areas. By extending this study to Bengaluru peri-urban areas (e.g., Kolar, Chikkaballapura, Tumkuru and Kolar: Fig. 1), we are profiling ARGs, bacterial, fungal diversity to evaluate the health impact of treated water in the areas while working with BWSSB in developing a policy and strategy for water quality issues associated with the use of recycled water e.g., possible persistence of bacterial, viral, protozoan pathogens is identified and remediated.



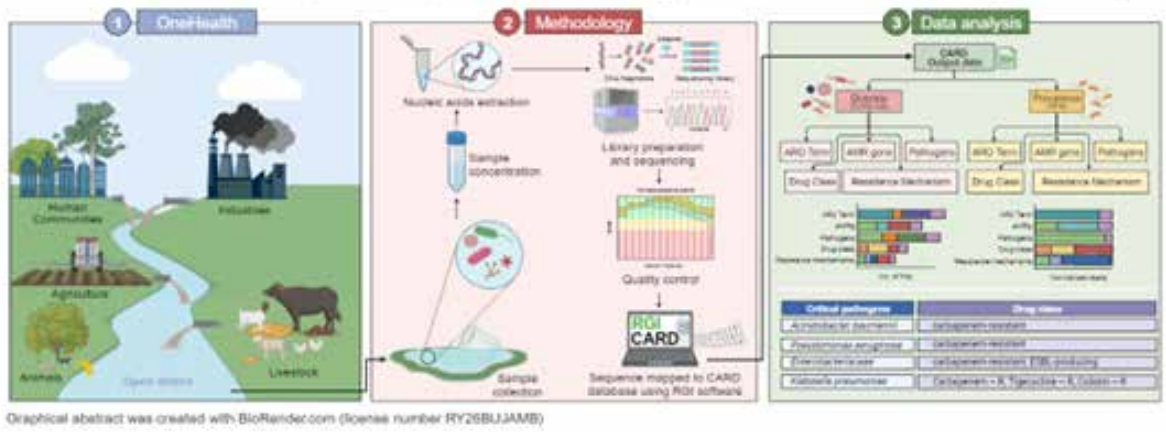
Log2 Fold-Change from Inlet to Outlet of 28 STPs analysed in samples collected from 2021-2022.

Understanding the antimicrobial resistance landscape through wastewater-based epidemiology from open drainage systems

Shivranjani Moharir

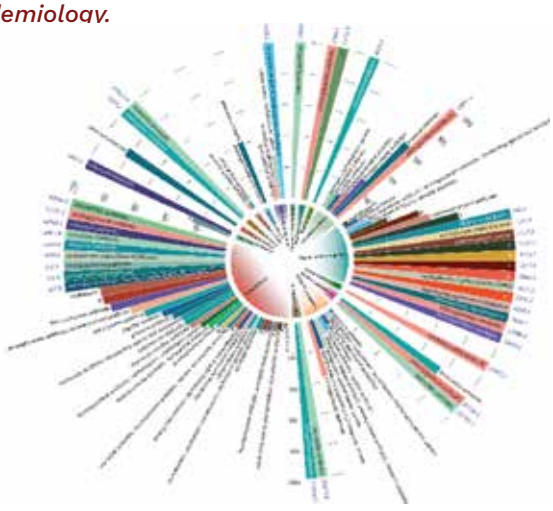
The One Health concept recognizes the inextricable interactions of the diverse ecosystems and their subsequent effect on human, animal and plant health. Antimicrobial resistance (AMR) is a major One Health concern and is predicted to cause catastrophes if appropriate measures are not implemented. In this study, to understand the AMR landscape in a metropolitan city context, we performed metagenomic analysis of open drain wastewater samples.

We analysed 17 samples from open drains that receive influx from human, animal, agricultural and industrial wastes. Our data suggests that macrolide antibiotics have developed the highest resistance in the city through mutations in the 23S rRNA gene, which is present in multiple pathogens including Escherichia coli, Campylobacter jejuni, Acinetobacter baumannii, Streptococcus pneumoniae, Pseudomonas aeruginosa, Neisseria gonorrhoeae, Klebsiella pneumoniae and Helicobacter pylori. Except for a few geographical locations, most other locations show similar landscape for AMR. Considering human mobility and other similar anthropogenic activities, we suggest that such an AMR landscape may be common across other regions.



Graphical abstract depicting the workflow for antimicrobial resistance surveillance through wastewater based epidemiology.

Our data indicates that many major pathogens are evolving and acquiring antibiotic resistance genes to evade antibiotics of multiple major classes in diverse hosts. The outcomes of the study are relevant not only in understanding the resistance landscape at a broader level but are also important for understanding the resistant drug classes, the mechanisms of gaining resistance and for developing new drugs that target specific pathways. This kind of surveillance protocol can be extended to regions in other developing countries to assess and combat the problem of antimicrobial resistance.

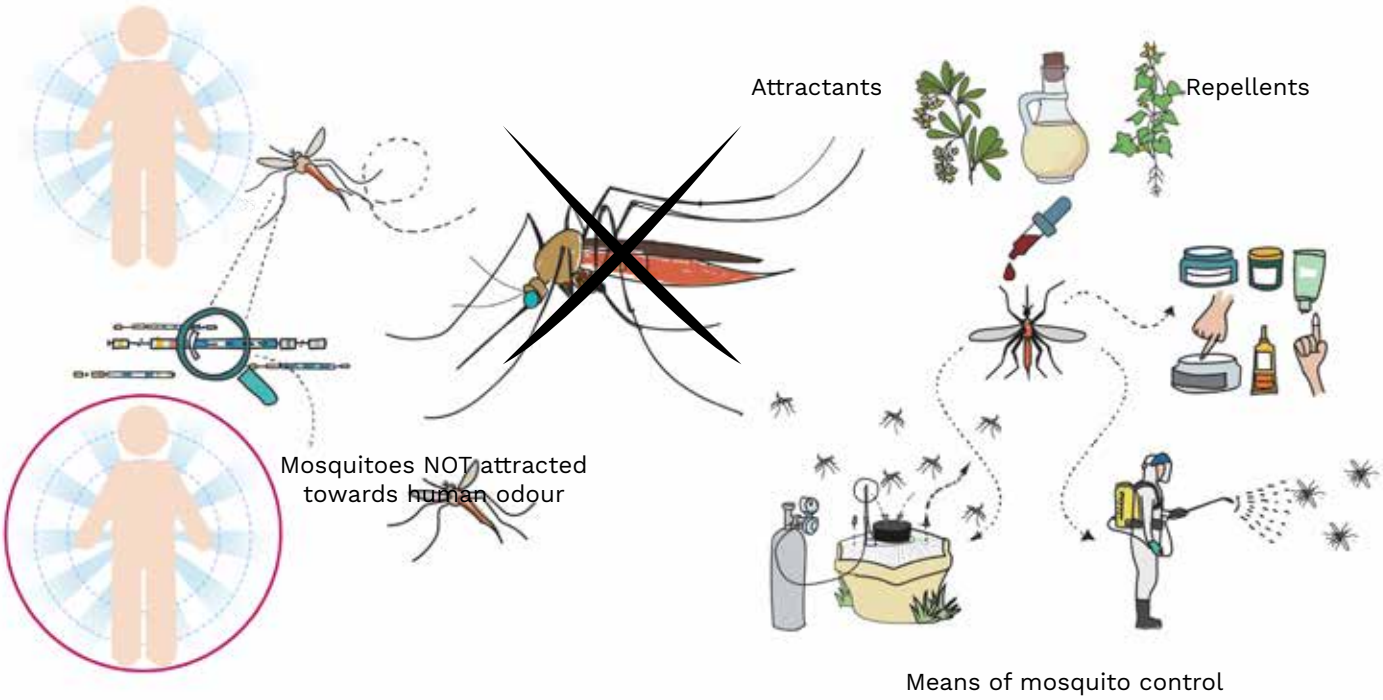


Plot showing the abundance of the WHO Global and Indian Priority Pathogens and the respective resistant drug classes seen in the samples.

Vector Control

Many infectious diseases are transmitted via an obligatory insect vector host for the successful completion of the pathogen's life cycle. Managing vector-borne diseases thus involves dealing with a triad of players – the human host, the pathogen, and the vector. Mosquitoes are one such critical vector, involved in the transmission of a large number of diseases. We use evidence-based understanding of the behaviour, biology, and ecology of mosquitoes to develop better, more specific, and ecologically responsible means of controlling them.

We have designed a multi-tiered approach to this challenging problem. The first tier is environmental engineering; what environmental features support and sustain or deter mosquito populations at the larval and adult stages. In the second approach, we seek to improve methods that reduce mosquito-human encounters. For this, we use knowledge of the chemical ecology of mosquitoes and tap into traditional deterrents to identify novel compounds. Finally, we seek to use specific molecular knowledge of mosquito species to intervene in their behaviour, particularly the host seeking and mating behaviours. We apply both modern and traditional knowledge in this context to develop specific and ecologically responsible interventions.



Fine-scale population ecology and genomics of *Aedes* sp. and its association with dengue cases in Bengaluru city

Farah Ishtiaq

[In collaboration with Bruhat Bengaluru Mahanagara Palike (BBMP)]

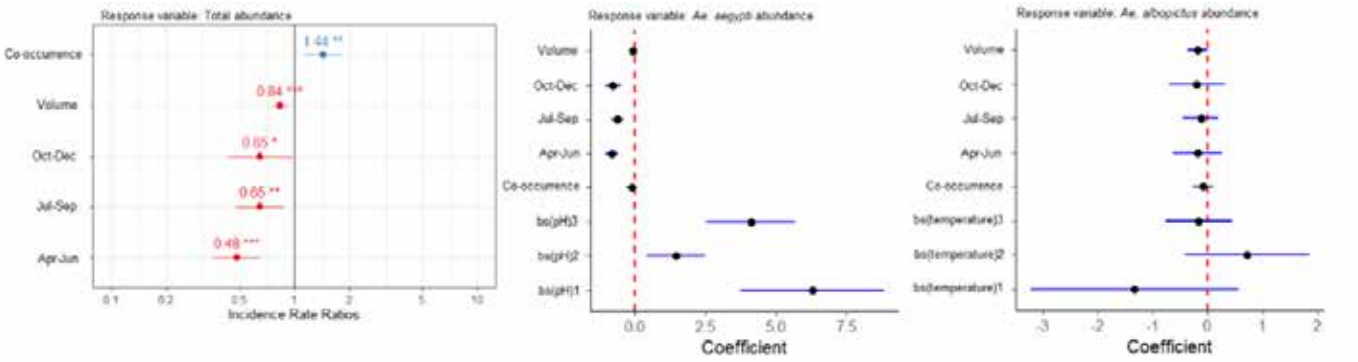
Dengue is an annual epidemic in India. In 2019, the dengue burden in India peaked at about 1,57,315 cases and Karnataka recorded 16,986 cases. Of these, Bengaluru contributed ~50% (9,029) of dengue cases (National Centre for Vector Borne Diseases Control; NCVBDC). Like many cities, in Bengaluru, ***Aedes*** population surveillance primarily involves indoor larval surveillance as per WHO protocols to measure house index, container index and Breteau index to quantify the disease risk in a specific residential area. Source reduction (emptying water holding containers), anti-larval spraying, and providing health education/awareness are the main intervention strategies for ***Aedes*** control. The areas with highest house indices and larval counts are considered as productive. These indices record relative larval abundance in a locality for a specific period with no correlation with adult abundance and without regard for seasonal fluctuation in larval abundance. Furthermore, entomological surveys are often biased towards locations or houses with high mosquito densities or disease outbreaks.

Aedes-borne disease risk is associated with contemporary urbanization practices where city developing structures function as a catalyst for creating mosquito breeding habitats. We lack better understanding on how the links between landscape ecology and urban geography contribute to the prevalence and abundance of mosquito and pathogen spread. In this longitudinal study conducted during the COVID-19 pandemic period, we quantify the mosquito larval habitat across a gradient of urban landscape.

Map of Bengaluru showing grid locations by macrohabitat types and larval sites by mosquito species.

- The majority (>90%) larval habitats were man-made artificial containers.
- Our neighbourhood larval survey showed that ***Ae. aegypti*** and ***Ae. albopictus*** were the highly abundant mosquito species which was reflected in the Aedes (***Stegomyia***) mosquito infestation indices estimated above the WHO thresholds.
- The increase in Aedes mosquito infestation indices corresponds to seasonal rise in larval prevalence which mirrored the increase in dengue cases in the city.
- Both ***Aedes*** species showed high prevalence in discarded grinding stones and negative association with stagnant water.

- The larval prevalence of ***Ae. aegypti*** was particularly positively associated with discarded tires. ***Ae. albopictus*** showed negative association with storage containers whereas ***Aedes aegypti*** was marginally positively associated. Storage containers are actively in use but provide high disturbance ephemeral habitats for ***Aedes*** species.
- The prevalence of ***Ae. aegypti*** larval habitat was positively associated with coconut shells, whereas ***Ae. albopictus*** was recorded in plant axils and tree holes albeit at low frequency and negatively associated with coconut shells.
- In general, mosquito species richness and diversity were significantly high in plantations and declined in urbanized areas. Similar patterns have been observed in forest communities where presence of diverse habitat types and less disturbance supports a diversity of mosquito species.
- Larger mosquito size is positively associated with survival, blood feeding frequency, which is likely to increase disease transmission. Co-existence with other species seems to affect only ***Ae. albopictus*** with reduction in wing length (proxy for body size).
- We show that landscape ecology drives mosquito diversity and abundance even at a small spatial scale which could be affecting the localized outbreaks.
- Our study relies on outdoor surveillance which highlights the importance of 'neighbourhood surveillance' in public places which can help in real-time forecasting of dengue cases in urban areas.
- Our findings showed that sampling strategies for mosquito surveillance must include urban environments with non-residential locations and dengue transmission reduction programmes should focus on 'neighbourhood surveillance' as well to prevent and control the rising threat of ***Aedes***-borne diseases.



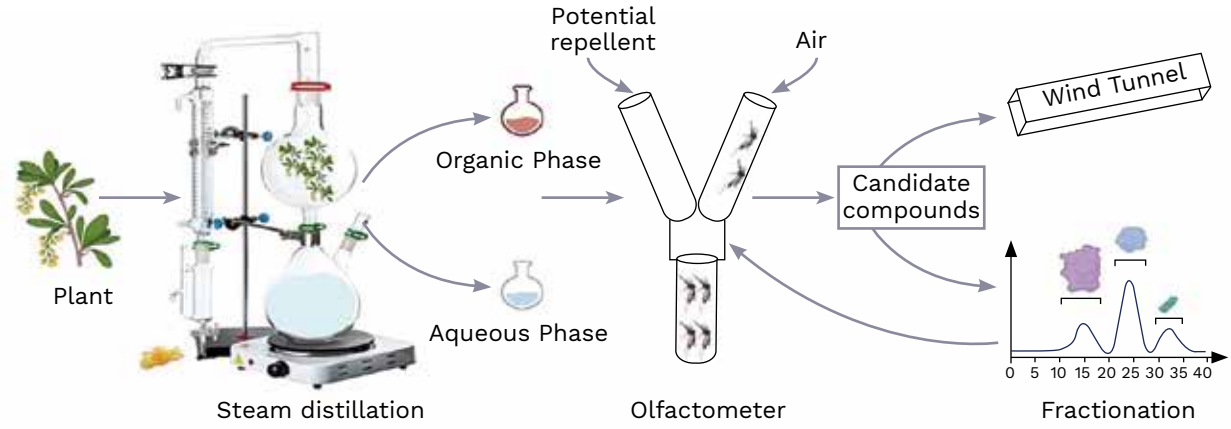
Model summary of parameter estimates from the best-fit generalized linear mixed-effects model predicting larval abundance, based on a candidate set model combinations of the variables: macrohabitat, microhabitat, pH, temperature, volume, season, and sympatric species. The models also include the random effects of grid.

Screening for novel mosquito attractants and repellents

Jay Prakash Shukla

Mosquitoes act as vectors for the spread of deadly diseases such as malaria, dengue, Zika, and chikungunya. Current methods of controlling mosquito populations for the control of diseases include the use of insecticide spraying, insecticide-impregnated nets, and use of chemical mosquito repellents. Escalating resistance to available insecticides demands novel approaches for vector control. Most of the effective repellents available in the market are costly and have side effects like asthma, cough, headache, eye irritation, etc.

We aim to identify novel mosquito attractants and repellents from plants and animals. Our priority will be to screen plants mentioned as potential mosquito repellents in traditional knowledge of different cultures. Dual choice olfactometer, wind tunnel assays, and methods like chemical fractionation, and electrophysiology will be used to find better safer, and eco-friendly mosquito repellents.



Stepwise outline: Following plant identification, steam distillation will be performed to extract plant essential oil and test for mosquito behavior activity in the dual choice olfactometer and wind tunnel. Potential candidates will be subjected to chemical fractionation for separation at the molecular level and subjected to re-testing.

Designing and making of dual choice olfactometer (Y maze)

We are adopting our olfactometer design from a recently published olfactometer from Leal et al. 2017. Since its inception, dual choice olfactometer has evolved over time. This design offers controlled, clean laminar air flow and, decision making chamber advantage to avoid odour mixing before behavioural output. The prototype of the olfactometer has now been created and is available in the TIGS insectary and we have also developed a set-up for computer controlled air and odor delivery in a precise manner.

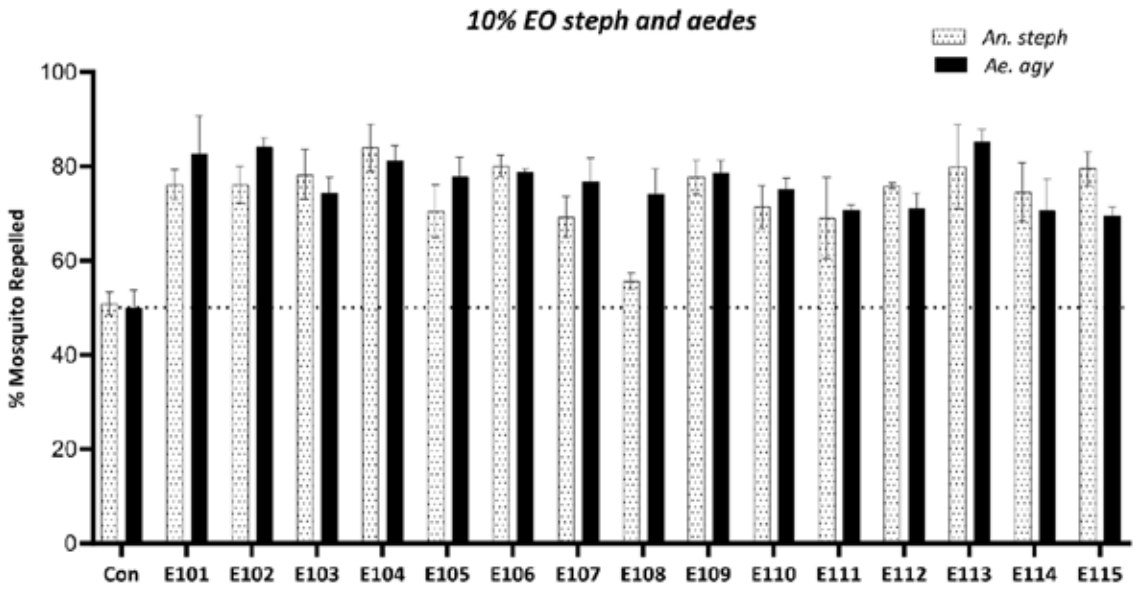
Mosquito behaviour has been linked to environmental conditions and we have developed methods to monitor parameters such as air velocity, temperature, and humidity as well as to understand chemical compound stability/degradation over time.

Screening plant essential oil for mosquito repellent property-

We have procured aromatic plant essential oils used in traditional medicine from the Central Institute of Medicinal and Aromatic Plants (CIMAP), Bengaluru Center. To understand the optimum dose threshold, we

have screened four dilutions (2.5%, 5%, 10%, and 20%) of each essential oil. We have used two truly diverse medically important mosquito species, Aedes aegypti, and Anopheles stephensi to know the repellent effect (depth) of these plant essential oils.

Although these aromatic plants have been explored for their mosquito-repellent property, we screened them with our setup to re-verify their repellent property in comparison to one another. These findings will pave the way ahead in finding the most effective essential oil and organic fraction and GC-MS (gas chromatography-mass spectrometry) to find the molecular identity of the same. Our results suggest that aromatic plants have varying degrees of mosquito-repellent properties, and these plant essential oils and active compounds derived from them could be better, safer, and eco-friendly deterrents for mosquitoes.



Graph showing mosquito response to various plant essential oils. Y-axis showing % of mosquitoes repelled in the presence of plant essential oils (10% plant essential oil diluted with 70% ethanol). The X-axis shows different plant essential oils from E101 to E115. 70% Ethanol was used as a control. The grey bar represents Anopheles stephensi, and the black bar represents Aedes aegypti response towards various plant essential oils.

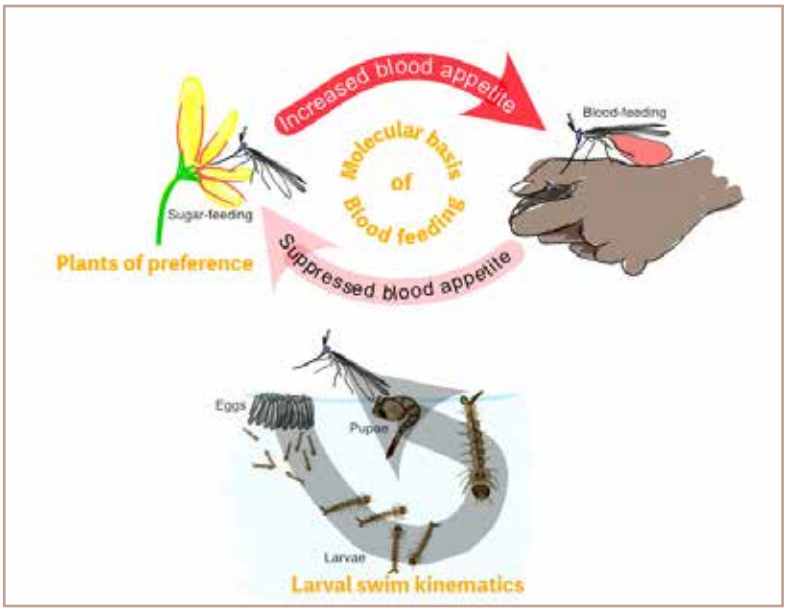
Behavioral studies in mosquitoes

Sonia Sen

Mosquitoes, both male and female, usually feed on carbohydrate-rich sources of nectar or sap. Occasionally, the female switches to taking a blood meal. This dramatic change in dietary preference is essential for the development of her eggs. Because of this, female mosquitoes of some species have become important vectors of infectious diseases. While Anopheles species can transmit malaria, *Aedes aegypti* can transmit dengue, and chikungunya, and Culex species can transmit filariasis. We take a multidisciplinary approach to understanding the behavioral patterns of these important vectors, by combining field studies, lab-based controlled behavioural assays, and molecular approaches.

Our studies on blood-feeding reveal many species-specific differences that will inform vector control strategies that rely on behavioural interventions. For example, we find that while *Aedes aegypti* females need to mate to develop an appetite for blood, Anopheles stephensi females don't. In fact, their appetite for blood is stronger and sustained for longer. This has implications for vector control strategies that seek to interfere with mating to curb vector-borne diseases. Taking a molecular approach, we have identified two neuropeptides that promote blood-feeding in Anopheles stephensi. These will be useful targets for developing small-molecule interventions for blood-feeding. We also study the sugar-feeding behaviours of mosquitoes to understand what cues attract or repel them. Finally, we also study the swim kinematics of mosquito larvae. Larva of the different genera have distinct swimming patterns that are easily recognizable by eye. We study these kinematics under various conditions to identify key diagnostic qualities for each genera under different conditions.

Overall our programme is rooted in the chemical ecology of the mosquito and we take every approach necessary to understand various aspects of mosquito behaviour so that these can form the bedrock of behavioural interventions to mitigate the human-mosquito conflict.



Summary of feeding behaviour in Anopheles stephensi

Infectious Diseases Team

Geetha G T
Senior Research Associate

Mahadeva Swamy H S
Research Associate

Prashali Bansal
Research Associate

Akshay Sanjeev K
Research Assistant

Anamika Shukla
Research Assistant

Deepanraj S P
Research Assistant

Edrea Valora Mendonca
Research Assistant

Hemalatha Rao
Research Assistant

K Divya Kala
Research Assistant

Kevin Joseph Dilip
Research Assistant

Majji Ritika
Research Assistant

Manas Madhukar
Research Assistant

Manju T
Research Assistant

Manjunatha A T
Research Assistant

N Annamalai
Research Assistant

Namrta D
Phd Student

Nirupama Singh
Research Assistant

PM Satyanarayana
Research Assistant

Priyanka Chandran
Research Assistant

Infectious Diseases Team

Rebecca Fern Daniel
Research Assistant

Samruddhi Walaskar
Research Assistant

Sankarnarayanan Aravid
Research Assistant

Sanskruthi Wadi
Research Assistant

Soujanya Nagendra
PhD Student

Subash K K
Research Assistant

Sutharsan Ganesan
Research Assistant

Vikram Sen
Research Assistant

Yashwanth Bharathwaj A S
Research Assistant

Sreelekshmi RS
PhD Student

D Deepa
PhD Student

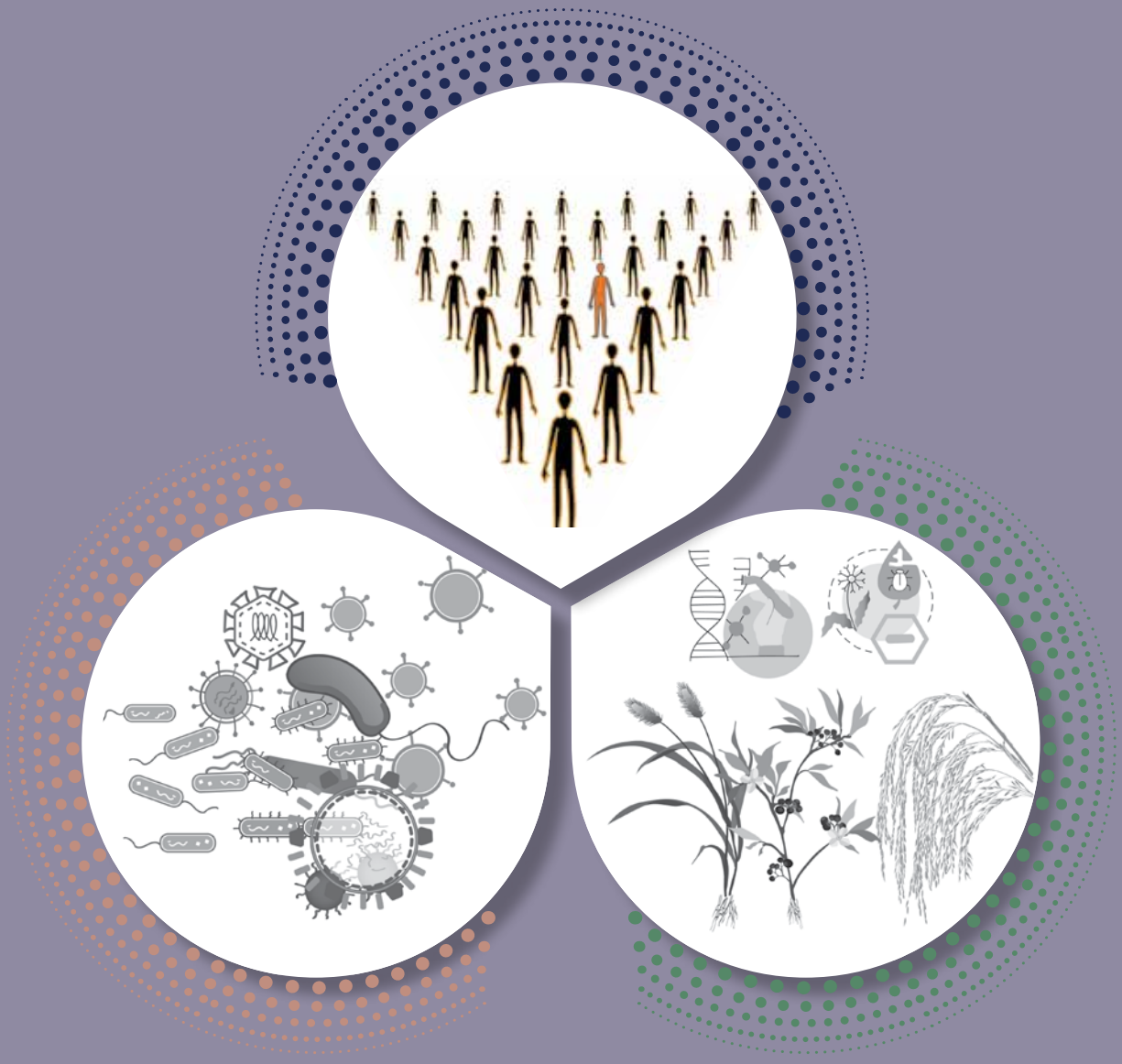
Leena B Chandra
Fly Technician

Manoj Kumar S
Laboratory Assistant

Pradeep
Field Assistant

Vikas V
Field Assistant

Rare Genetic Disorders



Rare Genetic Disorders

Gayatri Iyer

Harvinder Kour Khera

Iliyas Rashid

Runa Hamid

Shivranjani C Moharir

Vasanth Thamodaran

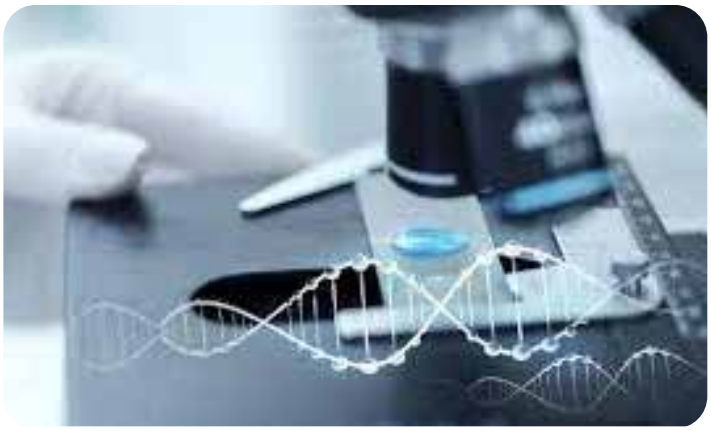
Genetic disorders are far from rare in India, owing to the high population, which translates to a very high disease burden. 5000-8000 rare genetic diseases have been identified globally, 450 of which have been reported in India. Mostly affecting children, they carry a huge socio-economic, emotional and physical burden on affected families. Difficulties involved in reaching out to widely dispersed carriers or patients and absence of point-of-care diagnostics adds to the complexity in tackling these disorders at an early stage.

We take multiple approaches to reduce the rare genetic disease burden in the country. One model is to develop diagnostics that can be used for screening at population scale to accurately identify carriers and/or patients. In parallel, we also aim for indigenization and development of low-cost and affordable therapeutic interventions.

Diagnostics and Screening

Rare Genetic Disorders (RGDs) are clinical conditions with underlying genetic origins. Though RGDs are of low prevalence and individually rare, collectively they affect a considerable number of people in a highly populous country like India. The diagnosis of RGDs is challenging due to the lack of awareness, the genetic heterogeneity and variety of overlapping symptoms they present with, as well as the unavailability of accurate genetic tests. Where available, the cost of associated diagnostic and medical tests is beyond the reach of most people in our country.

Palliative treatment (where available) relies on obtaining a correct diagnosis of the disorder as early as possible. We are working towards developing diagnostic kits for RGDs that are cost-effective, suitable for carrier and newborn screening, and specific for disease-associated genetic mutations common among the Indian population.

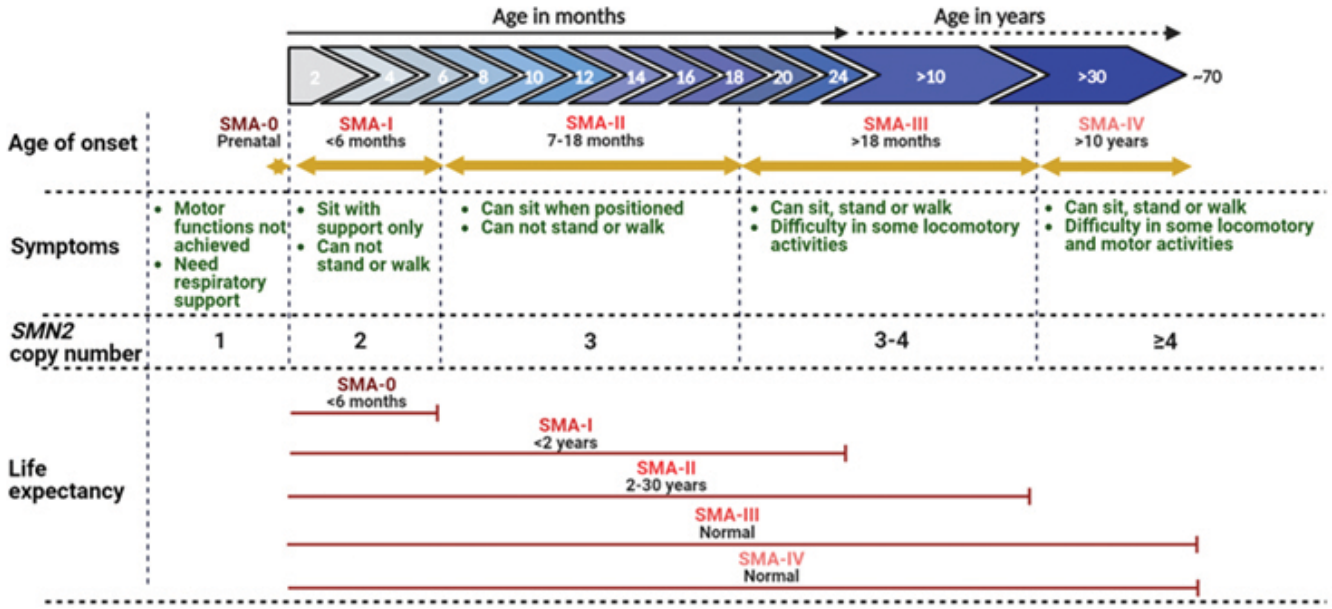


Development of diagnostic assays for rare genetic disorders

Shivranjani C Moharir and Harvinder Kour Khera

[In collaboration with CSIR-CCMB, Hyderabad]

The actual proportion of human genetic diseases caused due to copy number variations is unknown. With the advent of molecular techniques and whole genome sequencing-based approaches, the underlying cause of several genetic disorders can be unfolded. We are working towards identifying Indian population-specific mutations and developing indigenous diagnostic tools and kits for population-level screening. Initially, the target disorder is spinal muscular atrophy (SMA), with goals to later expand to other RGDs. The survival motor neuron genes (SMN1 and SMN2) are the causative genes for SMA with copy number variations and gene conversion events eventually leading to a degeneration of motor neurons.



Schematic depicting the different types of SMA, the age of onset, symptoms, SMN2 copy number, and the life expectancy. (Aasdev et. al., Spinal muscular atrophy: Molecular mechanism of pathogenesis, diagnosis, therapeutics and clinical trials in the light of Indian context)

Recent diagnostic advancements have shifted towards molecular testing, allowing for quick and accurate detection of homozygous SMN1 deletions. Alongside identifying SMN1 mutations, determining the copy number of SMN2 is essential, as SMN2 serves as a disease modifier. Quantitative assessment of SMN1 and SMN2 using multiplex ligation-dependent probe amplification (MLPA) is considered the gold standard for SMA genetic testing. However, other methods such as quantitative PCR and next-generation sequencing are also available. The number of SMN2 copies correlates inversely with the severity of the symptoms. Knowledge of SMN2 copy numbers is crucial for the diagnosis as well as clinical trials. Digital PCR (dPCR), with its high sensitivity and accuracy, is a reliable method for quantifying SMN1 and SMN2 copy numbers over a wide range, providing valuable clinical insights. Under this project, we aim to demonstrate the feasibility and clinical relevance of a cost-effective dPCR-based assay to determine the mutations in SMN1 as well as the copy number of the SMN2 gene.

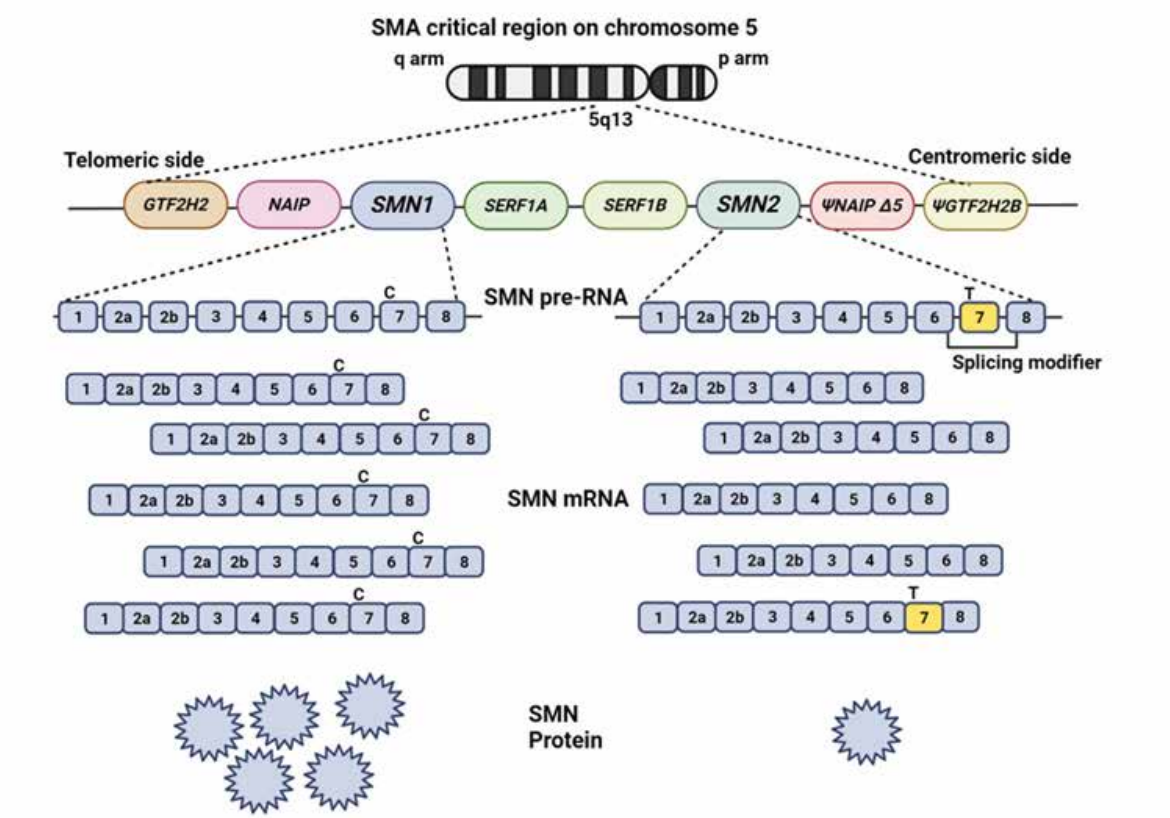


*Image showing the SMA critical region on chromosome 5. The SMA critical region on chromosome 5q13 consists of four genes SERF1A, SMN1, NAIP, GTF2H2 and their duplicated copies SERF1B, SMN2, **Ψ**NAIP Δ5 (pseudogene NAIP with exon 5 deletion), and **Ψ**GTF2H2B (GTF2H2 pseudogene). ~95% of SMA patients have a deletion of exon 7 of the SMN1 gene or conversion of SMN1 to SMN2. SMN1 and SMN2 differ by a single nucleotide in the coding region. The 'C' in exon 7 in SMN1 is replaced by 'T' in SMN2, leading to the skipping of exon 7 in most of SMN2 transcripts. Very few complete transcripts, without the skipping of exon 7, are also formed from SMN2, which results in the production of minute amounts of functional SMN protein from SMN2. (Aasdev et. al., Spinal muscular atrophy: Molecular mechanism of pathogenesis, diagnosis, therapeutics and clinical trials in the light of Indian context)*

Another approach that we are simultaneously developing involves MLPA. Multiplex ligation-dependent probe amplification (MLPA) is a multiplex, semi-quantitative method for diagnostic testing of genetic disorders. The method is suitable for the identification of deletions or duplications over a broad range, from SNPs to chromosomal aneuploidies, given a suitable set of probes covering the entire target region. By coupling MLPA-amplified probes with sequencing, one can include many hundreds of probes in a single reaction. The incorporation of a Next Generation Sequencing (NGS)-based detection approach would make the diagnostic strategy suitable for population level and carrier screening as multiplexing a large number of samples for many disorders in a single assay would cut down the cost.

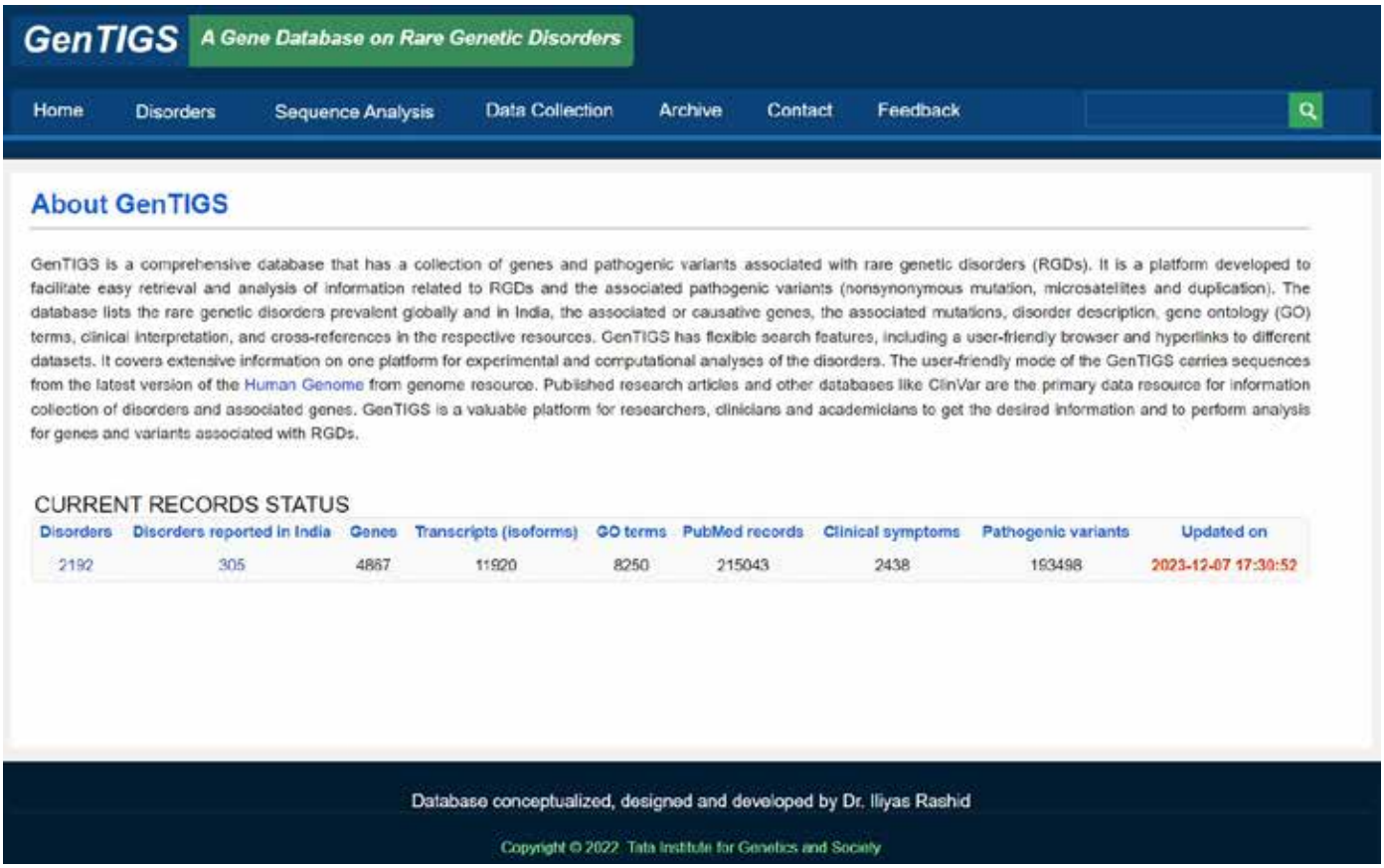
Developing a rare genetic diseases database - GenTIGS

Illyas Rashid and Shivranjani Moharir

RGDs are genetic diseases that affect a small proportion of the population and do not have sufficient diagnostic and therapeutic options. Due to India's large population, rare disorders carry a high disease burden in the country. We are developing a repository for clinical data on RGDs in the form of a database that can collate and store information on such diseases in the Indian context and focus on the genomic causes and mutations specific to the Indian population.

The database would include a wide variety of information related to RGDs from sources such as OMIM and Orphanet and will include local prevalence, affected genes, pathogenic variants, gene regulatory factors, and the role of non-coding RNAs. Clinical data (primary source) will be sourced from our partner hospitals and research organizations. Gene annotations and sequences, reports, and information on local trends will be obtained from online databases such as Ensembl and NCBI-gene databases (secondary sources) to perform a comparative analysis. The datasets will be managed and stored using a relational database management system (RDBMS).

A web-based platform will be developed by incorporating analytical and statistical tools for clinical data analysis and interpretive output. Interactive search and query features will be built in. Apart from providing information on patient care services, the analytical platform will facilitate pedigree analysis from patient to family and population level using clinical data, a novelty of this database. Custom programs are in place for automated data extraction and presentation via the user-friendly front-end of the GenTIGS web interface. The browser enables viewing and interactive searching of all the collected information on RGDs and their relevant gene(s) (PubMed and GeneID links), along with structural and functional gene information (from NCBI-GeneDB and OMIM). We are currently working on incorporating a pipeline at the back end to analyse genome and exome-level population data to identify pathogenic variants.

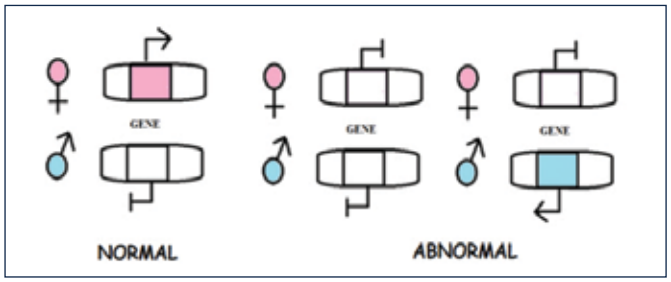


Screenshot of the GenTIGS collection viewer

Development of MS-PCR diagnostics for genomic imprinting disorders

Gayatri Rangarajan Iyer

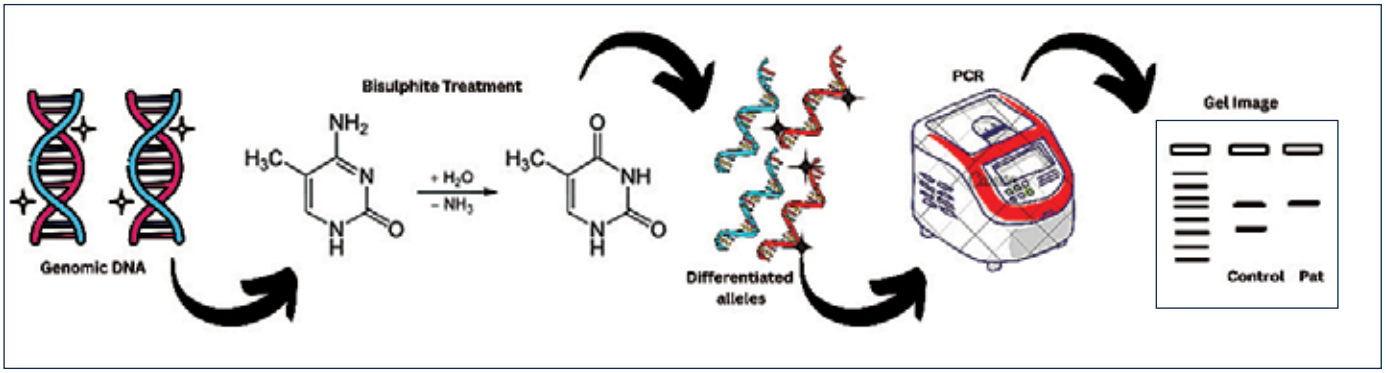
Despite the advances and application of different genomic technologies over 5 decades, the etiopathology of more than 25% of rare genetic disorders associated with intellectual disability (ID), abnormal growth and behavior is unclear emphasizing the need for exploring novel and newer mechanisms of diagnosis.



One such group of disorders is disorders of genomic imprinting. About 150+ genes in the mammalian genome are exclusively expressed from either parent depending on the parent of origin. This is achieved by the epigenetic mechanism of DNA methylation and is known as genomic imprinting.

Altered imprinting has been recognized as a cause for 10 established syndromes, four of these Prader Willi syndrome (PWS), Angelman syndrome (AS), Beckwith Wiedemann Syndrome (BWS), and Silver Russell Syndrome (SRS) are the focus of the current project. Though global incidence is stated to be 1 in 10,000 to 1,00,000, a systematic record is lacking. From the literature, the estimated Indian prevalence of the four imprinting disorders is over 3.5 lakhs. IVF pregnancies further increase the risk of imprinting disorders by 3 to 8-fold. The approximate annual addition is 25000. Imprinting disorders are underdiagnosed in India due to a lack of awareness complimented with affordability and accessibility hurdles leading to improper management. Conventional karyotyping or advanced sequencing cannot detect them as imprinting disorders are caused due to imbalance in the DNA methylation of imprinted genes. Methylation testing is the backbone for investigating these syndromes which only a few labs offer at expensive rates.

Methylation-specific polymerase chain reaction (MS-PCR) is a simple, rapid, cost-effective, low labor and equipment-intensive modality that can be easily deployed even in remote locations with robust performance. Isolated genomic DNA is first given a sodium bisulphite treatment that deaminates the unmethylated cytosines to uracil. The converted DNA sample now has differentiated methylated and unmethylated alleles in a single tube which can be amplified with the help of allele-specific primers A pilot study of 102 clinically suspected cases mentioned above showed about 28% to be confirmed as one of four known imprinting disorders by a simple methylation-based test indicating these disorders are not as rare as cited to be but require a timely referral and correct diagnostic modality to offer genetic counselling, plan prenatal diagnosis and facilitate appropriate management.



MS-PCR technique for the detection of imprinting disorders

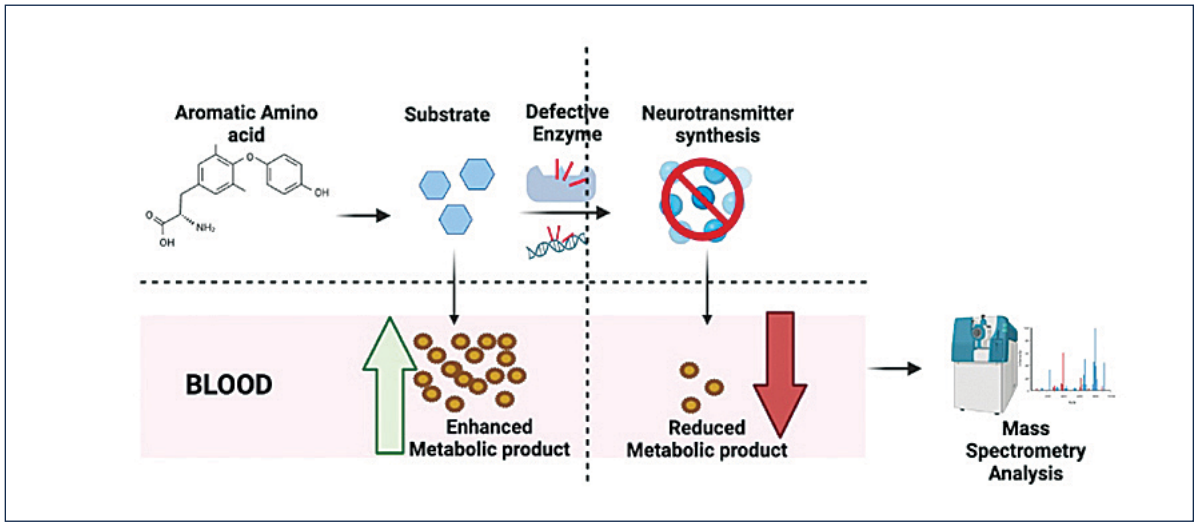
Metabolite profiling for diagnosis of monoamine neurometabolic disorders in Indian cohort

Runa Hamid

[In collaboration with IGICH, Bengaluru]

Inherited monoamine Neurometabolic disorders (mNMDs) are a group of fifteen rare genetic disorders (RGDs) caused by genetic defects in genes involved in monoamine neurotransmitter metabolism. These include genes for enzymes, cofactors, and membrane transporters of monoamine neurotransmitters (Dopamine, Serotonin, Epinephrine, and Norepinephrine pathway). Defective functioning of these proteins leads to toxic accumulations of metabolites or lack of metabolites leading to progressive neurological deterioration with an onset in the neonatal stage or early childhood. Misdiagnosis of these disorders poses a significant challenge because there is an overlap of clinical features with other neurological disorders like encephalopathy, cerebral palsy, primary movement disorders, etc. The diagnosis of these disorders is routinely made through analysis of neurotransmitters in cerebrospinal fluid by doing lumbar puncture. Collectively, the rarity, complexity, absence of definitive biomarkers, and progressive nature of these disorders pose a significant challenge for accurate diagnosis.

Our literature review indicates the presence of approximately 30 published case reports on Indian patients from across different hospitals in India. About 70 percent of these cases were genetically confirmed while 30 percent received CSF or symptom-based diagnosis. However, this data suggests that these disorders are present in our population, and it underscores their insufficient recognition. The true prevalence in India remains unclear.



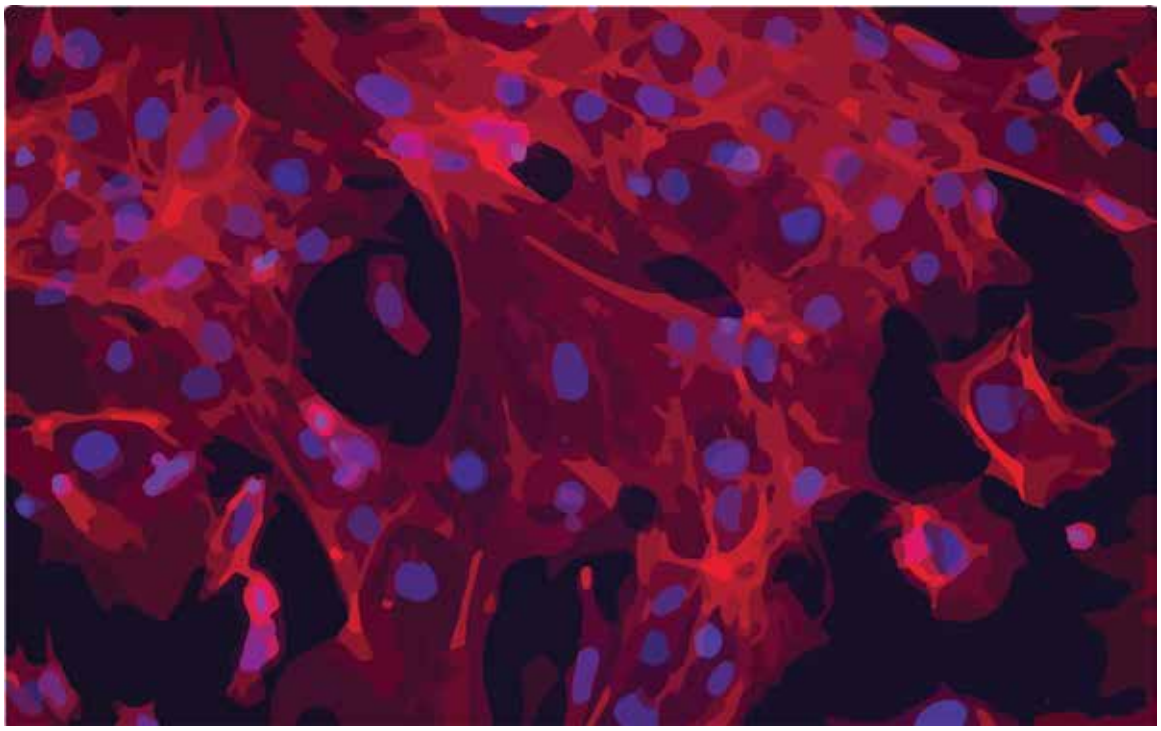
To address these challenges the project has been initiated to develop a dry blood spot based rapid and cost-effective biochemical diagnostic test based on tandem mass spectrometry. This will enable the detection of reduced or heightened metabolites of monoamine neurotransmitters in blood with high sensitivity. This method will have a predictive value for the diagnosis of mNMDs. Such a method offers advantages over the invasive method of lumbar puncture generally used for diagnosis. The developed methodology can aid in the simultaneous quantification of all the neurotransmitter metabolites present in blood plasma and can potentially serve as a multiplex diagnostic assay for mNMD disorders. The development of this method is currently in progress.

Therapeutics

It is estimated that 72 to 96 million Indians suffer from rare genetic disorders. Most of these disorders are monogenic and occur due to loss-of-function mutations in the disease-causing gene. In addition, various cancers and metabolic disorders occur as a result of loss of protein function. For a few genetic disorders and cancers, intravenous injection of therapeutic proteins is a standard and effective therapy.

However, the cost of therapeutic proteins or enzyme-replacement therapy remains prohibitively high for more than 90% of the global population. For India and other low- and middle-income countries, the cost of such therapies often exceeds the capacity of a family to afford them. Given the lack of cost-effective therapeutics for most rare genetic diseases, it is pertinent to invest our knowledge and resources to address the unmet needs of patients in the Indian context. Urgent focus areas include point-of-care production of therapeutics to reduce cost and/or innovation in R&D for a quick transition from lab to clinically treating RGD patients.

We are setting up therapeutic interventions against select rare genetic disorders using cutting-edge technology at TIGS, including repurposing small molecule drugs as well as mRNA-based therapeutics and stem cell-based therapies.



An illustration of cells in culture for disease-in-a-dish models

Spinal Muscular Atrophy: Establishing cellular assays to identify splicing modulators to treat SMA

Vasanth Thamodoran

Spinal muscular atrophy (SMA) is a rare autosomal recessive genetic disorder with an incidence of 1 in 6,000 to 1 in 10,000 live births in the USA and about 1 in 3900 to 16,000 live births in Europe. Although the incidence of SMA in India is not determined, a carrier frequency of 1 in 38 has been reported from a study conducted in Uttar Pradesh and neighboring states. Based on this report, and the prevalence of consanguineous marriages, the incidence of SMA in India is speculated to be higher than in the USA and Europe.

Deleterious mutations in the survival motor neuron 1 (SMN1) gene cause a degeneration of motor neurons, leading to muscle weakness and atrophy. SMN2 gene, an isoform of the SMN1 gene is not able to complement the defect due to the exclusion of exon 7 during splicing, resulting in truncated non-functional protein expression. Individuals heterozygous for missing or defective SMN1 gene do not exhibit any symptoms of the disease and can therefore act as carriers.

There are four types of SMA, categorized based on the onset of symptoms of the disease.

Type 1 (severe): Werdnig-Hoffman disease at birth or within an infant's first six months

Type 2 (intermediate): Dubowitz disease at 6 months to 18 months

Type 3 (mild): Kugelbert-Welander or juvenile-onset SMA after 18 months

Type 4 (adult-onset): Mid-30s

Mortality and/or morbidity are inversely related to the age of onset of disease. The median survival is 7 months, with a 95% chance of mortality for children afflicted with Type I SMA.

This project has been designed for the development of indigenous small molecule analogues of Evrysdi as oral therapy for SMA. We are working to identify analogues for the existing splicing modulators of SMN2 to bring down the cost of treatment. 13 compounds that are intermediates of Evrysdi have already been synthesized. To validate the ability of the analogues to promote SMN2 splicing, a cellular assay involving luciferase activity and assessing an increase in full-length SMN by RT-PCR will be utilized. The SMN2-luciferase construct has been generated and expression of luciferase has been validated by transient transfection. We have also optimized an RT-PCR approach to detect an increase in the levels of full-length SMN transcript. The drug molecules provided by ARR/Aurigene did not provide any lead compounds. Currently, in collaboration with Peptris, drug candidates will be screened using the same platform.

CRISPR-Cas12 based gene editing to treat hemoglobinopathies

Vasanth Thamodaran

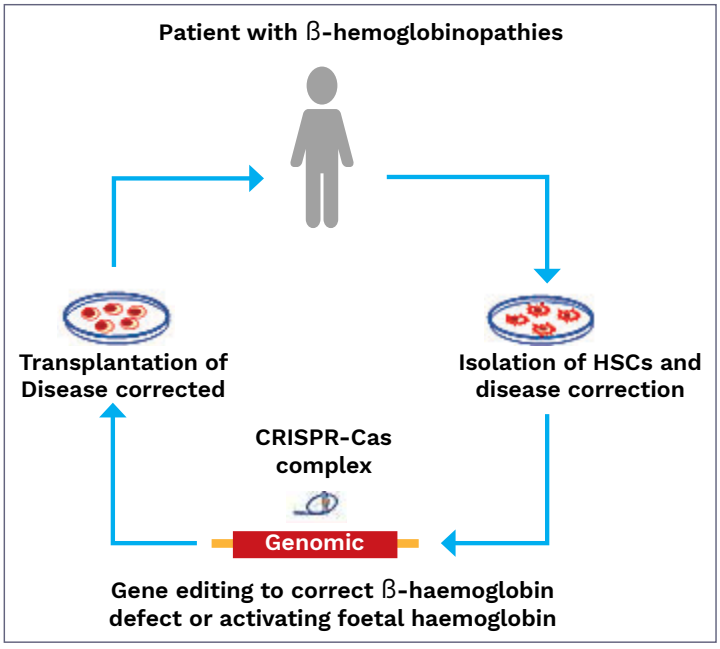
India has one of the highest occurrences of genetic disorders that affect adult β-haemoglobin production (β-thalassemia) or its functionality (sickle cell anaemia. Recently, gene-editing strategies have emerged as a safe and effective alternative to lentivirus-based gene therapy. Gene editing for treating hemoglobinopathies either involves reactivating foetal haemoglobin expression or correcting the defective β-haemoglobin. Both these strategies have been successful in clinical trials.

In the Indian context, CRISPR-Cas9 based gene editing approach to treat hemoglobinopathies has been well studied. However, the therapy can cost up to 50 lakhs INR, making this life-saving treatment less accessible. We are working on different components in gene editing-based gene therapy, where identifying alternative strategies can cut down costs.

Identification of crRNA: The expression of β-globin is suppressed by the binding of repressors BCL11A and LRF to the genomic regions -115 and -200bp upstream of the β-globin gene. The upstream element of the HBG gene was screened using CRISpick online tool and about 3 crRNAs were identified. The oligos that express the crRNA were then cloned individually in a lentivirus vector pRDA_052 and confirmed by sequencing.

Screening of optimal crRNA: To identify the crRNA that can provide efficient rescue in hemoglobinopathies, we knocked out the *β-globin* gene using CRISPR-Cas9 to mimic β-thalassemia, followed by single-cell cloning of the edited cells to get a clone with homozygous deletion. The mutant line will be transduced with the crRNA for *β-globin* activation.

Ex-vivo editing in hematopoietic stem cells (HSCs): We plan on working further with the crRNA that gives the highest activation of *β-globin*. Synthetic crRNA will be complexed with enAsCas12a protein (RNP) or co-transfected with mRNA expressing enAsCas12a in human adult/umbilical cord derived CD34+ cells (HSCs). After culturing the cells for 48 hours ex-vivo, the percentage of editing will be validated. The cells will also be analysed for off-target effects using NGS. A collaboration with JSS Medical College, Mysore has already been initiated to obtain umbilical cord blood to derive HSCs. To begin the screening, the Cas12 construct has been transduced into immortalised erythroid cells, and cells expressing cas12 have been selected using antibiotics. Currently, we are involved in expanding the Cas12-expressing erythroid cells. This will be followed by the transduction of sgRNA constructs that target the fetal hemoglobin repressor region.



mRNA-based therapies for the treatment of lysosomal storage disorders

Rajesh Iyer V

Lysosomal storage disorders (LSDs) are a group of monogenic rare genetic disorders that occur owing to a loss of lysosomal enzyme function. In LSD patients, intravenous administration of the functional enzyme i.e., enzyme replacement therapy (ERT) has been found to rescue disease symptoms and improve the patient's life. Though effective to a certain degree, ERT-based therapies are very costly. Globally, LSD prevalence is taken to be 1 in 7000-8000 individuals and if extrapolated, there could be more than 1 lakh LSD patients in India. More than 95% of the Indian population cannot afford these drugs. This cost is primarily due to the small market size, cost-intensive manufacturing, and purification methods to produce therapeutic proteins. The LSD patients require ERT for their entire life and owing to the absence of any indigenous drugs, very few Indian LSD patients can access these drugs via humanitarian funds. Many succumb to the disease, often due to the unavailability of these drugs. To address this emergency, we reasoned that, as an alternative to protein therapy, mRNA-encoding therapeutic proteins can be utilized to produce the therapeutic proteins in vivo. mRNA production, owing to its synthetic nature, is highly scalable with a relatively smaller footprint which ultimately leads to affordable therapeutic solutions for many diseases. Using mRNA technology, we have successfully designed therapeutic mRNAs for the treatment of two LSDs; Pompe and Fabry disease. Pompe disease occurs due to the deficiency of acid alpha-glucosidase enzyme (GAA) while Fabry disease happens due to the deficiency of alpha-galactosidase enzyme (GLA). For the treatment of Pompe and Fabry disease, we have designed & generated GAA and GLA encoding mRNA candidates and validated them using cell culture methods. We observed that the generated mRNAs can express the GAA or GLA protein for more than 96 hours in vitro. We are further developing these candidates for their in vivo validation in mice models of Pompe and Fabry disease.

mRNA-based therapy for the treatment of GNE myopathy

Rajesh Iyer V

GNE myopathy is an adult-onset progressive neuromuscular disorder that generally leads to extreme disability in a few years. The disease is caused by mutations in the bifunctional enzyme Glucosamine (UDP-N-Acetyl)-2-Epimerase/N-Acetyl-Mannosamine Kinase involved in sialic acid biosynthesis. There is no approved treatment for this disease. i

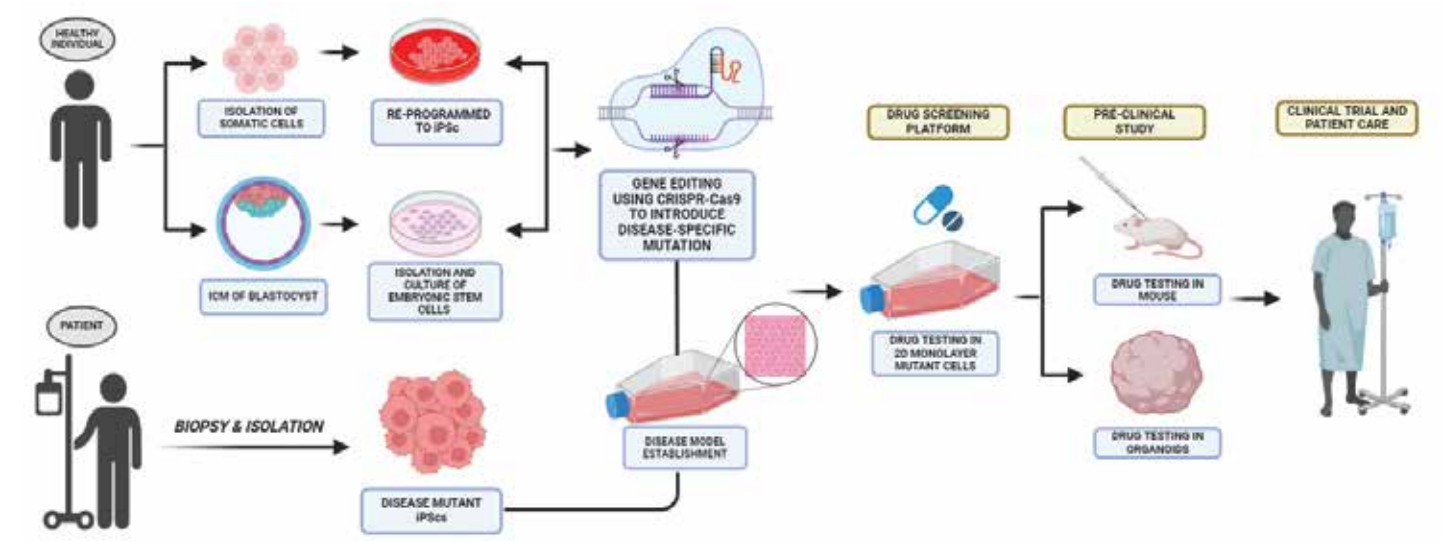
TIGS is collaborating with World Without GNE Myopathy (WWGM), a patient advocacy group, to develop mRNA therapy for GNE Myopath. Currently, the mRNA team at TIGS has generated two GNE-encoding mRNA candidates and tested them using cell culture methods. The GNE-mRNA candidates can express in cell lines for more than 4 days and efforts are now on developing muscle targeting nanoparticle formulations.

Disease Modelling & Novel Interventions

At TIGS, we are working towards creating and improving Rare Genetic Disorders (RGDs) disease models that can be utilized for screening and developing therapeutic strategies. Disease modelling provides an insightful solution for exploring interventions. Utilizing in vitro cell-based models reduces the animal burden in drug development and we are creating disease-specific systems that can be used for therapeutics testing. In conjunction with animal-based in vivo model organisms, such as mice, the disease manifestation and its progression within a controlled environment can be simulated.

The interventions that can be tested based on these disease models span from conventional drugs and biochemical assays to cutting-edge technologies like mRNA vaccines and gene therapies, bridging the gap towards tailored and transformative therapeutic solutions. We are also gathering information on Indian gene mutations - about 250 RGDs are known to be prevalent in the Indian context, however suitable stem cell models do not exist for a majority of these RGDs. These need to be made accessible and less expensive. The need of the hour is to generate pluripotent stem cell lines carrying the specific mutations for these disorders to understand their pathogeneses.

Our multidisciplinary approach places us at the forefront of research, propelling us towards the development of effective treatments and personalized solutions for individuals affected by Rare Genetic Disorders.



Human pluripotent stem cell-based disease models for testing biotherapeutics

Vasanth Thamodaran

Evolutionary conservation and ease of handling have made small mammalian models like mice and rats valuable tools for investigating human diseases and drug discovery. However, about 20% of human genes do not have orthologues in mice. Further, some disease phenotypes do not mimic the human condition. In such cases, human cell-based ***in vitro*** models are used. Conventionally, either the primary cells derived from a donor with the disorder under investigation or an immortalised cell line is used. However, primary cells cannot be maintained indefinitely and immortalised cell lines carrying genomic abnormalities may not faithfully display the disease phenotype.

The drawbacks associated with primary and immortalised cells can be overcome by using human pluripotent stem cells (hPSCs). hPSCs have the potential to differentiate into any cell type in the body and can be maintained ***in vitro*** indefinitely. Thus, a hPSC generated from an individual with a specific genetic disorder will enable ***in vitro*** derivation of cell types affected in that disorder. The cells so derived can be used in studying disease pathogenesis and drug screening. hPSCs can either be derived from an early-stage embryo or by reprogramming somatic cells to pluripotent state by expressing specific transcription factors. Somatic cell derived induced pluripotent stem cells (iPSCs) also obviate ethical concerns associated with stem cell generation from embryos.

iPSCs can be routinely derived from patient subjects and used in disease modelling studies. iPSCs present an invaluable therapeutic platform when combined with CRISPR-Cas based gene editing approaches. When obtaining patient samples is not possible, the mutation in the gene of interest can be introduced by gene editing. The gene-edited lines subsequently generated can be used ***in vitro*** to study the disease mechanisms.

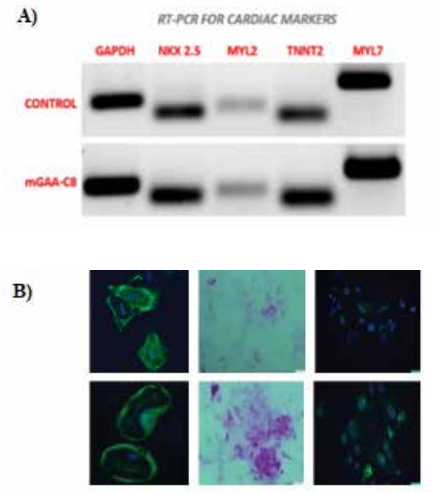
The Organisation for Rare Diseases India (ORDI) has listed about 250 rare genetic disorders (RGDs) that are prevalent in the Indian context. The lack of stem cell models for a majority of these RGDs has hindered the generation of insights on them. Thus, the establishment of pluripotent stem cell lines carrying the mutation for these disorders will enable a detailed study of RGD pathogeneses. With this goal in mind, we have initiated the following steps to develop models for a variety of disorders:

- ***Generation of mutant iPSCs***: iPSCs carrying the mutation of interest are generated by using CRISPR-Cas9 (in case of lysosomal storage disorders, DMD, and fatty acid metabolism). In case of osteogenesis imperfecta and spinal muscular atrophy, the patient cells will be reprogrammed to iPSCs.
- ***Characterisation of the mutant iPSCs***: The mutant lines will be characterised for pluripotency marker expression, trilineage differentiation potential, and genome integrity.
- ***Disease modelling:*** The mutant pluripotent stem cell lines will be differentiated to lineages that are affected in each genetic disorder e.g., cardiac and skeletal muscle lineages in the case of Pompe, and motor neurons in the case of SMA. The defects associated with these disorders will then be validated in the differentiation process.
- ***Drug testing and screening:*** Once the disease models are established, the lineages will be treated with recombinant proteins in case of lysosomal disorders or with drug molecules in case of SMA and the rescue in disease pathology will be evaluated.

Over the last few months, we have had some success in working on models for multiple disorders while others have just been initiated, at TIGS and in partnership with other institutes, as described below:

A. Lysosomal storage disorders (LSDs)

- Optimization of gene editing in iPSCs: The optimal nucleofection condition that provides efficient gene editing in iPSC/ESC was identified using guide RNAs that target the OCLN gene.
- Generation of Pompe-iPSC: Using the identified optimal nucleofection condition, the GAA gene which is defective in Pompe patients was targeted in hESC (hem20). Successful gene editing was validated by Sanger sequencing and the cells were single-cell cloned to isolate a cell line that carries homozygous mutation.
- Establishment of differentiation protocols: As cardiac and skeletal muscles are defective in Pompe's disorder, the differentiation procedures were successfully established to mimic the same (Figure 1).
- Introducing specific mutations: We have currently established an optimal protocol for introducing specific mutations using gene editing. Currently, we are generating stem cell lines with Pompe mutations that are prevalent in India.



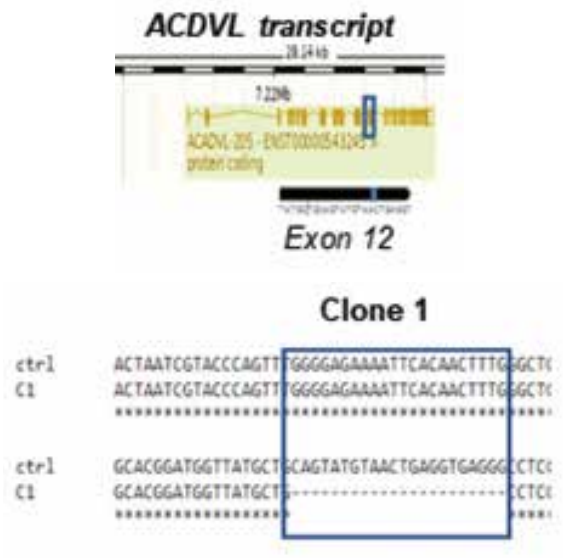
Cardiac cells displaying Pompe pathologies. A) The cells expressed all the cardiac markers and B) The cardiac cells showed signs of hypertrophy, glycogen accumulation, and lysosome dysregulation.

B. Skeletal myopathies

[in collaboration with DBT - InStem]

Very long-chain acyl-CoA dehydrogenase deficiency (VLCADD) is caused by a defect in the gene ***ACADVL***, which codes for the enzyme acyl-CoA dehydrogenase very long chain.

- Gene editing of ACADVL gene: To generate iPSC-based disease model for VLCADD, the exon 12 of ACADVL gene was targeted using CRISPR-Cas9, and one of the clones was identified as carrying a homozygous 21 bp deletion. The clone was karyotypically normal and also confirmed to be pluripotent (Figure 2).
- Investigating VLCADD in cardiac and skeletal muscle: Differentiation of VLCADD iPSC to cardiac and skeletal muscle lineages showed hypertrophy.
- Validation of the disease line: The defect in FAO in the generated line was validated by mass spectrometry. The skeletal muscle showed an accumulation of long-chain fatty acids, Indicating disruption of ACADVL gene function.



Gene editing to generate VLCADD iPSC. A. Transcript image showing the binding of sgRNA at exon 12. B. Sanger sequencing showed 21bp deletion in the C1 clone.

Rare Genetic Disorders team

Karthik K
Research Assistant

Lloyd Tauro
Research Assistant

Maheshwari B C
Research Assistant

Nimisha Goswami
PhD Student

Pooja
Research Assistant

Rupa Kumari
Research Assistant

Sancheta Kulkarni
Research Assistant

Saniya Mehraj
Research Assistant

Venkatesh Rajendran
Research Assistant

Vibhaa K K
Research Assistant

Crop Improvement

Crop Improvement

Kamal Kumar Malukani

Rambabu Ratnala

Sampath Kumar

V S Sresty Tavva

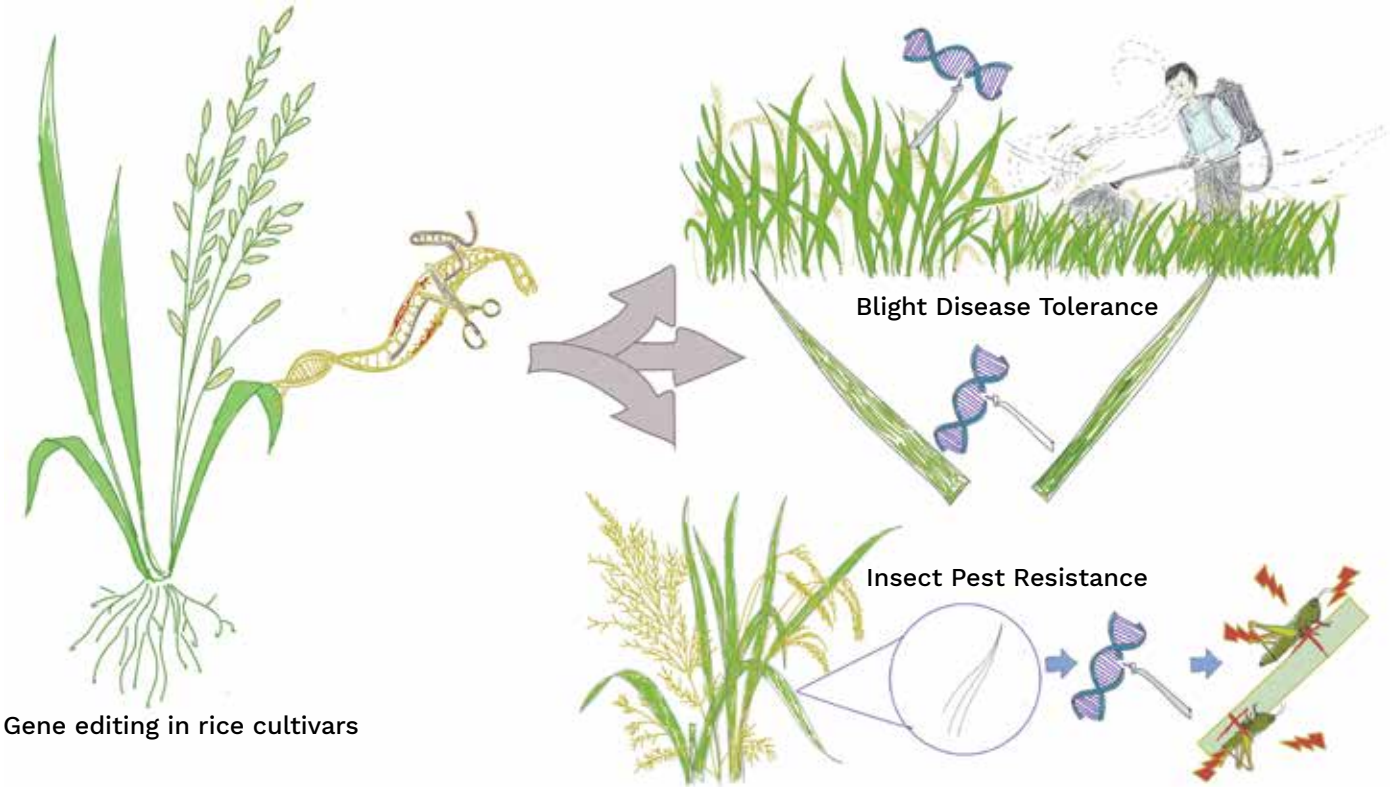
In the face of climate change and an increasing global population, food security and nutrition have become some of the biggest challenges of the day. We need to innovate and implement different approaches to improve nutritional quality of food grains, reduce crop losses due to diseases and pests, and develop varieties that can tolerate the changing environment. Promising tools are available for crop improvement, such as conventional plant breeding, mutation breeding, and genome editing technologies, which can be harnessed to achieve sustainability in agriculture.

Genome Editing

Increased agricultural production and sustainable food security is of utmost importance for the rapidly increasing global population. Successful development of crop varieties with improved agronomic traits such as high yield, and biotic and abiotic stress tolerance can have a great impact on agricultural productivity. However, the current trends in the production of agricultural food crops may not be enough to provide sustainable solutions unless innovative technologies are adopted to meet the growing needs. New breeding technologies such as genome editing by CRISPR/Cas (Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein) can be harnessed to achieve sustainability in agriculture by modifying target genes precisely. These tools can be used to create crop varieties with desired features for increasing agricultural productivity.

Developments in targeted genome editing ensure that the CRISPR components that are used to edit the selected native genes for a desirable trait and the antibiotic resistant gene used for selecting the edited line can easily be removed by segregation of the plant progeny in the next and subsequent generations. In this way, one can produce transgene-free edited plants that are indistinguishable from plants that can be obtained through conventional breeding.

Rice is one of the most important staple food crops on which over 3.5 billion people depend for daily energy consumption. With increasing water scarcity in agriculture, cultivating rice in the conventional puddled ecosystem is becoming uneconomical. Growing rice under non-puddled conditions such as direct seeding, alternate wetting and drying, and aerobic cultivation saves substantial amounts of water. However, infestation with biotic factors like weeds, pests and pathogens diminish water saving advantages of aerobic cultivation and reduce productivity under irrigated conditions. Genome editing of appropriate alleles would accelerate the process of generating rice cultivars for target environments.



Gene editing in rice cultivars

CRISPR/Cas-mediated multiplex genome editing of disease and herbicide tolerance traits in rice

V S Sresty Tavva

It is hypothesized that when biotic stress tolerance traits are introgressed into the genetic background of elite rice cultivars, it can sustain rice yields and improve crop productivity. We are working towards developing bacterial leaf blight and blast resistance through genome editing of appropriate alleles in the background of aerobic rice cultivar (KMP175) and a mega variety (MTU1010).

Bacterial leaf blight (BLB):

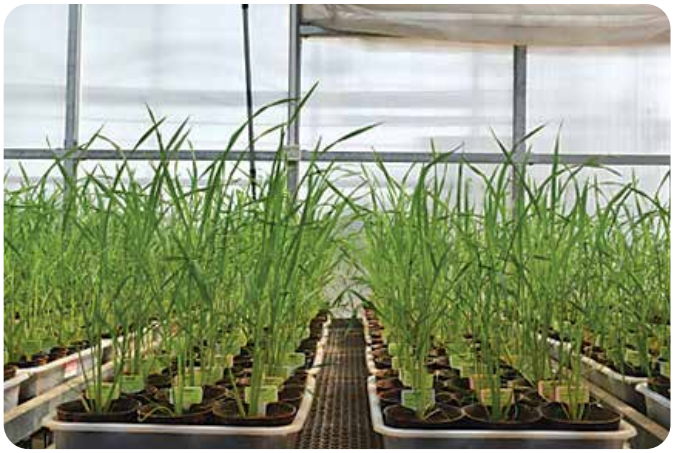
BLB caused by *Xanthomonas oryzae* pv. oryzae is one of the most devastating diseases restricting rice production. It spreads systematically through the leaf xylem tissue and infection leads to significant yield losses. More than 38 BLB genes have been identified so far, suppressing the expression of *SWEET* genes can result in the development of resistance to BLB isolates, PthXo1, PthXo2, PthXo3 and AvrXa7 (Oliva et al., 2019).

Screening of BLB edited lines: T0 rice genome edited lines generated using MTU1010 and KMP175 lines were screened by PCR amplification of the target region followed by restriction digestion or Sangers sequencing to check for the insertions and/or deletions in the target region. The selected sweet11 T0 edited lines based on molecular and phenotypic data were backcrossed with their respective wild-type parent plant (MTU1010 or KMP175) to segregate out the Cas9 and antibiotic marker genes. Appropriate screening methods are in place to ensure that the backcross seed (BC0F1) collected from selected T0 lines of both MTU1010 and KMP175 varieties are not carrying any transgenic cassettes. The selected events (BC0F2) with no transgenic cassette and having bi-allelic homozygous mutations were advanced to collect BC0F3 seed.

Rice blast: Rice blast caused by *Magnaporthe oryzae* is the most dreadful fungal disease and greatly reduces yield and grain quality (Dean et al., 2012). All blast resistance genes (Pi) encode NBS-LRR proteins, except a few genes (Pid2, Pi21 and Bsr-D1). Blast resistant genes are present in less than 10% of the rice varieties. This gives great opportunity to introduce into leading varieties. Knock-out of selected blast genes will provide broad spectrum resistance in rice.

Dual guide RNA approach was adopted to knock-out blast genes. The guides designed were fused separately with U6 gRNA scaffold in pUC19 backbone. All these gRNA scaffolds were further subcloned into CRISPR construct consisting of UBI:Cas9, 35S:Hyg and 35S:Dsred cassettes. We have transformed blast SDN1 constructs into MTU1010 and KMP 175 lines. Stable events were transferred to greenhouse and screened for mutations in the target regions. Based on the mutation data, selected T0 lines were backcrossed with their wild-type plant to get rid of transgenic cassette. BC0F1 lines derived from selected T0 events were genotyped and identified the lines carrying mutations in heterozygous condition.

The selected BC0F1 heterozygous lines were subjected to both self-pollination and a second round of backcrossing to collect BC0F2 and BC1F1 seeds. Blast challenge assay will be performed on BC0F2 or BC0F3 lines.



Backcross population derived from BLB resistant genome edited rice lines.

Table 1: Genotyping of sweet11 BC0F1 and T1 lines to confirm mutation status and its inheritance from T0 lines

T0 event ID	Mutation status in T0 events		BC0F1 or T1 ID	Mutation status in BC0F1 or T1		Zygosity
	Allele 1	Allele 2		Allele1	Allele2	
12.1	-GTACACCA (8bp)	CCTACTGT	F1.12.1.1	-CCTACTGT	WT	Heterozygous
			F1.12.1.2	-CCTACTGT	WT	Heterozygous
			F1.12.1.4	-CCTACTGT	WT	Heterozygous
			F1.12.1.5	-CCTACTGT	WT	Heterozygous
			F1.12.1.6	-CCTACTGT	WT	Heterozygous
			F1.12.1.7	-CCTACTGT	WT	Heterozygous
			F1.12.1.8	-CCTACTGT	WT	Heterozygous
			F1.12.1.9	-TACTGTACA	WT	Heterozygous
			F1.12.1.11	-CCTACTGT	WT	Heterozygous
12.10	-CCTACTGT (8bp)		F1.12.10.3	-CCTACTGT	WT	Heterozygous
			F1.12.10.4	-CCTACTGT	WT	Heterozygous
			F1.12.10.6	-CCTACTGT	WT	Heterozygous
			F1.12.10.10	-CCTACTGT	WT	Heterozygous
12.08	-TAC (3bp)	WT	12T1_008_01	-TAC	WT	Heterozygous
			12T1_008_03	-TAC	WT	Heterozygous

Table 2: Analysis of T0 blast gene edited lines

T0 Event ID	Mutation type identified by PCR followed by DrdI digestion at guide1 (CR7)	Allelic status by Sanger's sequencing	
		Allele 1	Allele 2
12	Bi-Allelic	CCAAGG(+A)C	CCAAGG(-ACAG)
30	Bi-allelic	+A	+G
33	Mono-allelic	+A	Wt

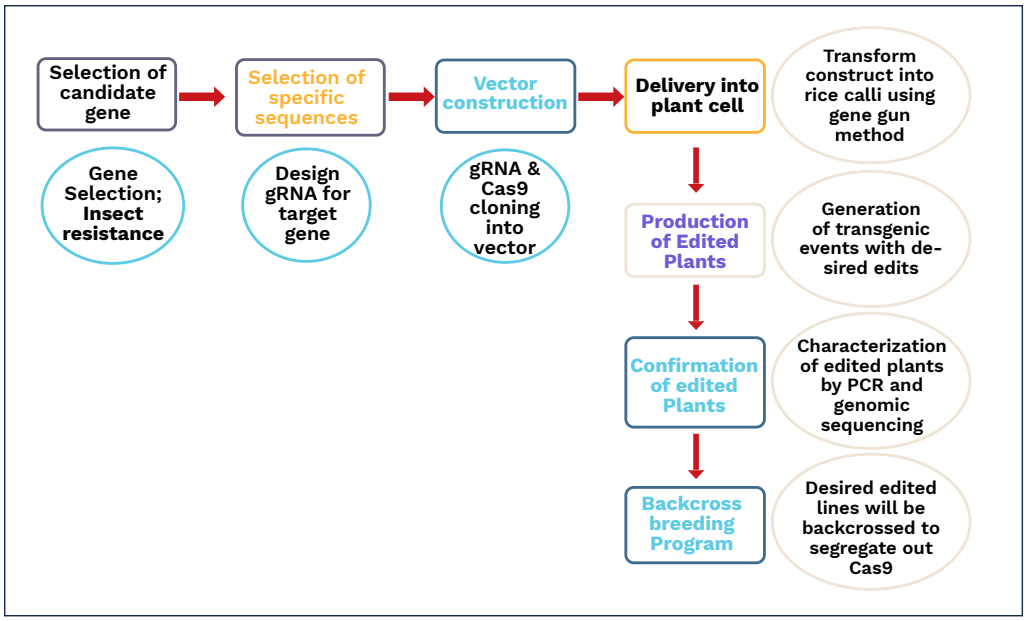
Genome editing of rice cultivars to develop insect pest resistance

Rambabu Ratnala

To ensure global food security for continuing population growth, it is vital to control the various insect pests that damage rice. The brown planthopper (BPH) and stem borer are two of the most serious pests in rice production.

The brown planthopper (BPH), ***Nilaparvata lugens*** (Stål) (Hemiptera: Delphacidae), is a planthopper species that feeds on rice plants (***Oryza sativa L.***). This insect is the most significant rice pest, causing direct damage to rice through feeding and the transmission of two viruses. Under favourable conditions, up to 60% yield loss is common in susceptible rice cultivars attacked by BPH.

The striped stem borer (***Chilo suppressalis***), which is a chewing insect, feeds on newly formed tillers and stems, causing "dead hearts" and "white heads," resulting in significant yield losses. Both BPH and SSB are difficult to control using chemical pesticides. So far, no SSB resistance germplasm source or resistance genes have been identified in rice. The development of insect-resistant rice varieties is seen as a viable and ecologically sustainable approach for controlling these devastating insect pests. Here, we deploy a CRISPR/Cas9-mediated genome editing strategy to knockout the CYP gene, which shows increased resistance to BPH and SSB insect pests (Figure).



Experimental design and workflow for generating genome edited lines

We couldn't succeed with the previous experimental design and constructs. Therefore, a change in strategy is being evaluated, including replacement of the Cas9 as well as design of four new guides to make sure that each guide has a restriction site for preliminary screening for easy characterization of plant transformants.

We have adopted a dual guide RNA approach to edit the target gene and cloned improved Cas9 and new guides in plant binary expression vector, which is already used in the lab. So far, approximately 1000 calli in 7 batches have been transformed with new constructs through biolistic gene gun method. Now they are in different stages of tissue culture and transformation. We will be sending first batch of T0 plants by the end of this month for further analysis.

Mutation Breeding

Food crops, such as rice, have been domesticated for thousands of years. Cultivation of specific rice varieties generation over generation for selected traits leads to loss of other beneficial traits and narrows down the genetic variability over time. Generating genetic variability through mutagenesis is an important tool to develop new varieties with different traits. Mutagenesis can be performed on a desirable genetic background and the mutant lines can be screened for beneficial traits like high nutrient content, disease resistance and high yields. The mutations associated with the beneficial phenotypes can be mapped by next generation sequencing (NGS) or micro-satellite markers to ensure propagation and distribution of pure lines.

Enhancing crop traits and yields via genetic approaches

Generation of homogenous hermaphrodite pointed gourd (Parwal) lines and their agronomic evaluation in field conditions

V S Sresty Tavva

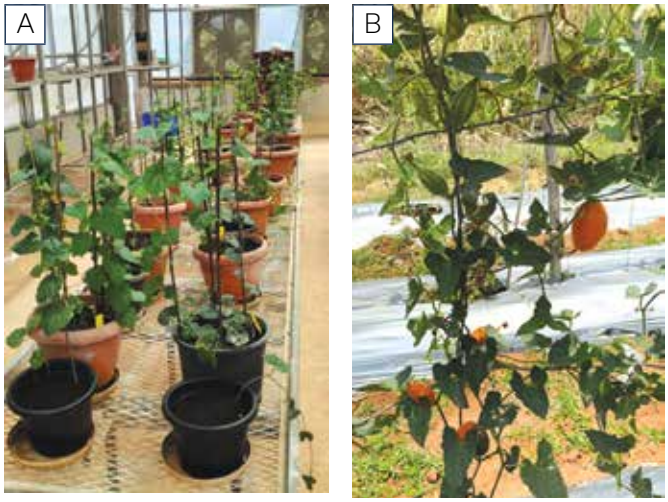
Trichosanthes dioica, also known as pointed gourd, is a dioecious species with male and female flowers observed in separate individual plants. It is mostly cultivated in the eastern and northern parts of India. The fruits are green with white or no stripes. These striped, green vegetables also called as parwal is rich in many nutrients, various antioxidants, Vitamin A, B1, B2 and C. On the other hand, Pointed Gourd is rich in fibre and low in calories which help in reducing and maintaining weight. Due to its dioecism, cross pollination is inevitable for fruit setting. Hand pollination in female flower is widely practiced and must be completed preferably by 5:30 AM. Though pointed gourd vegetable has several health benefits, the production happens at very low scale due to the plant being dioecious and the pollination must be completed very early in the morning.

The aim of this project is to generate hermaphrodite (flowers containing both female and male organs) pointed gourd (Parwal) lines and evaluate their agronomic performance under both greenhouse and field conditions. The mutant line developed through EMS mutagenesis produces both hermaphrodite and female flowers; so, it is required to first study the flowering pattern and extent of fruit setting under greenhouse and field conditions. Since Parwal is a perennial and a vine (creeper) plant, detailed analysis can only be done on field grown plants. Therefore, TIGS is collaborating with University of Agricultural Sciences, GKVK, Bengaluru to carryout field experiments and to generate and evaluate hermaphrodite parwal plants. We have set the following objectives:

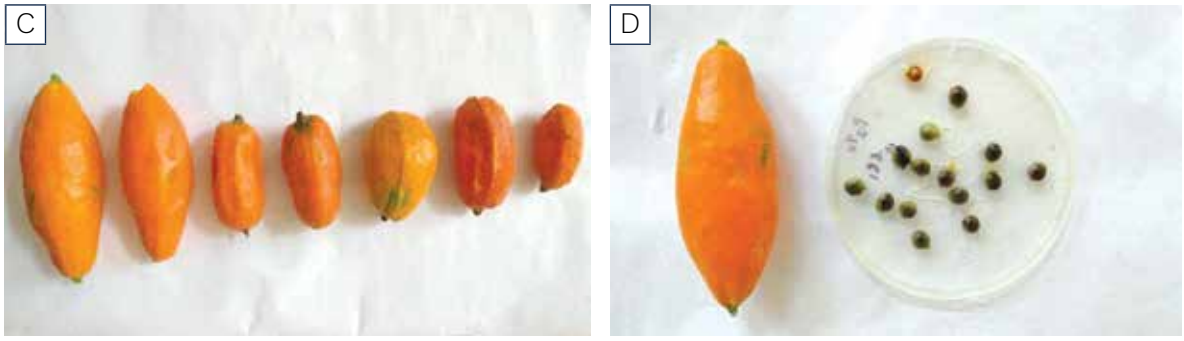
- The Parwal mutant lines received from Tata trust produce both hermaphrodite and female flowers and the desired phenotype needs to be segregated. We are assessing the flowering pattern and the extent of fruit setting in mutant pointed gourd line under field conditions.
- Fruits and seed from hermaphrodite flowers are to be collected and screened for the progeny to identify lines that produces only hermaphrodite flowers. We will collect data on Distinctness, Uniformity and Stability (DUS) characters of homogenous hermaphrodite lines for at least two seasons in the field.

Observations from greenhouse and field grown plants (first season):

Hermaphrodite phenotype was not observed under greenhouse conditions. We have observed both female and hermaphrodite flowers on few of the mutant population under field conditions. None of the progenies have only hermaphrodite flowers. Fruits from female flowers were big and looks like regular parwal in the market. Fruits from hermaphrodite flowers were not of marketable size.

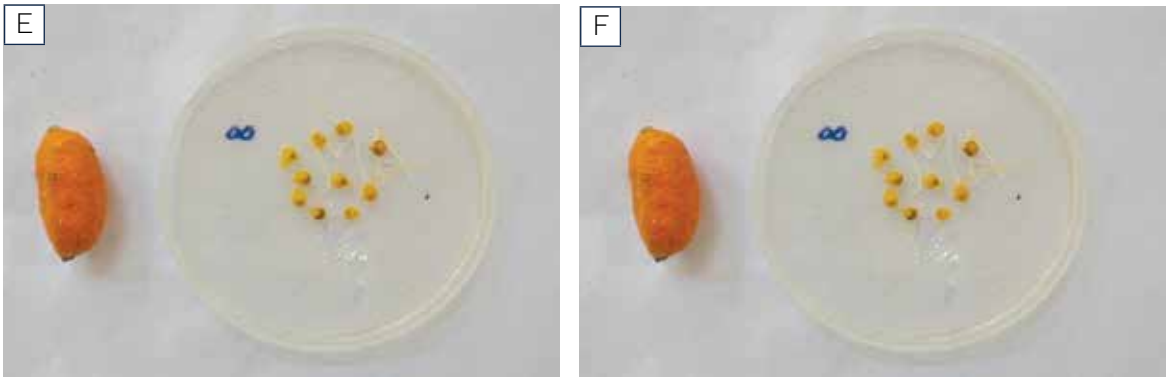


Pointed gourd lines that are being assessed for hermaphrodite trait under both greenhouse (A) and field (B) conditions.



C) Parwal fruits of different sizes collected from female and hermaphrodite lines

D) Marketable size parwal fruit collected from female plants



E and F) Parwal fruits collected from hermaphrodite lines; small and not marketable size

Development of rice varieties with low glycaemic index and enhanced level of protein, iron and zinc

Kamal Kumar Malukani, Shivranjani Moharir

[in collaboration with CSIR-CCMB]

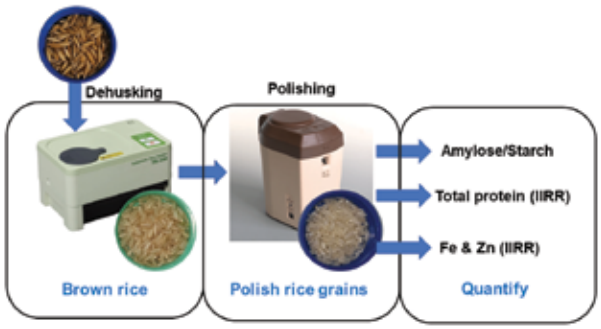
Most of the traditionally grown varieties of rice are rich in carbohydrates but do not provide adequate amounts of micronutrients such as iron, zinc, and proteins. We aim to screen rice lines generated by mutagenesis for beneficial traits like low glycaemic index, and high iron, zinc, and protein content. We are testing rice mutant lines previously developed by CSIR-CCMB in collaboration with ICAR-IIRR as well as freshly mutagenized rice lines.

As part of the collaborative work, we have generated a new mutagenized population in the background of Improved Samba Mahsuri (ISM), the bacterial blight tolerant, low GI rice variety. These lines will be advanced at CCMB, Hyderabad, and Indian Institute of Seed Science, Bengaluru till the fourth generation to stabilize the traits and then screened for nutrition content.

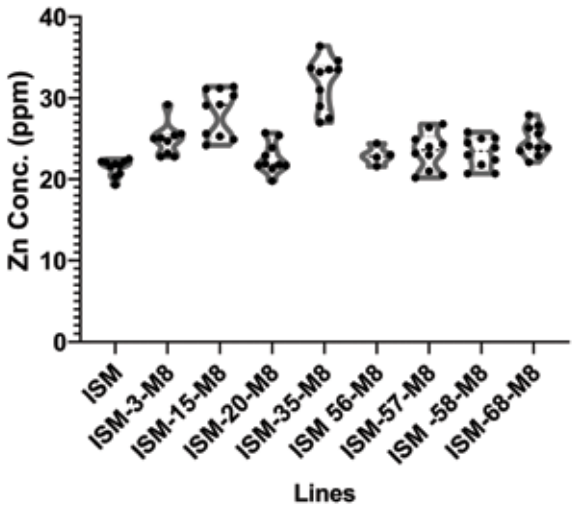
Parallelly, we have screened over 200 previously selected mutant lines, varieties, or landraces for iron and zinc concentration in the grains. In the first screening, some mutants in the M6 generation showed higher zinc in the grains than their parents. These are all high-yielding mutants in the background of ISM. We screened the same lines in subsequent generations. We observed 8 lines that show higher Zinc than the parent (ISM) in three successive generations. Three of these appear to be pure lines where all tested plants show higher zinc than the parents while the others appear to segregate for the high zinc character.

Background	Trait	No. of lines
Samba Mahsuri (SM)	Elite rice variety	45
Improved Samba Mahsuri (ISM)	Bacterial blight tolerant SM	53
93R	Early flowering SM mutant line	57
Various varieties		58
	Total	213

Table showing the rice varieties tested for zinc and iron content.

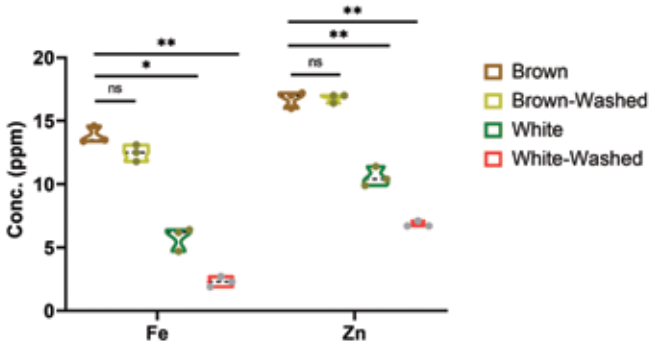


Workflow for nutrient quantification.



Zinc content in polished rice of 8 mutant lines that show higher zinc than the parent (ISM)

While testing for the iron and zinc content in rice grains, we tested in unpolished rice that comes right after dehusking and in polished white rice which is generally consumed form of rice. We observed polishing leads to a severe loss of iron and a significant loss of zinc. Washing rice before cooking is a traditional practice in India. We observed washing also leads to significant loss of iron and zinc particularly in polished rice and less so in brown rice.



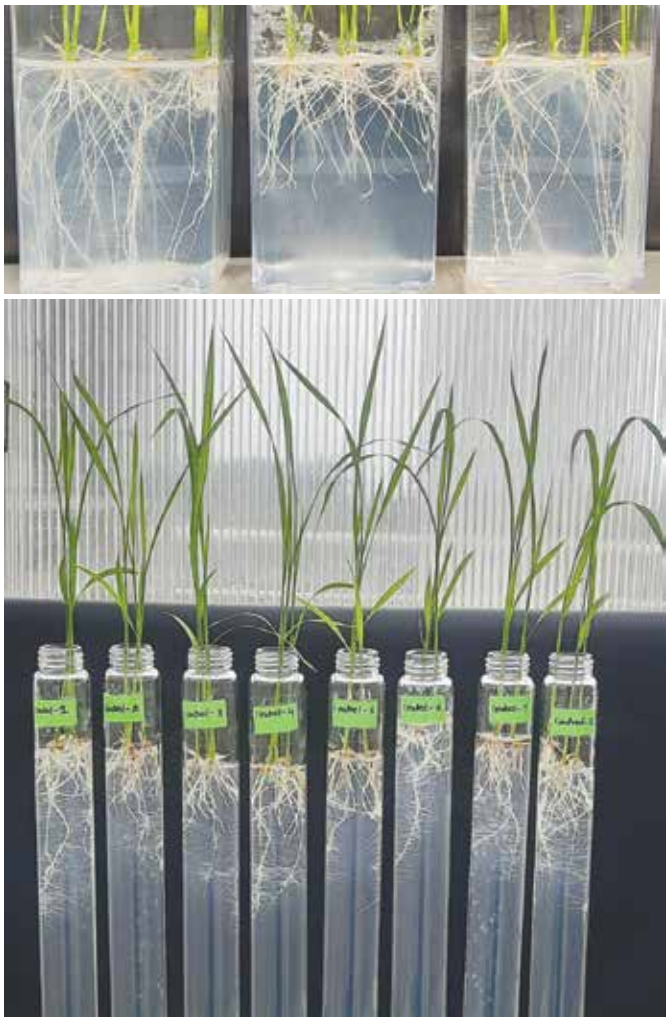
Change in iron and zinc content in rice grains after washing and polishing.

Investigating plant growth promoting compounds in crops

Kamal Kumar Malukani

[In collaboration with University of California, San Diego]

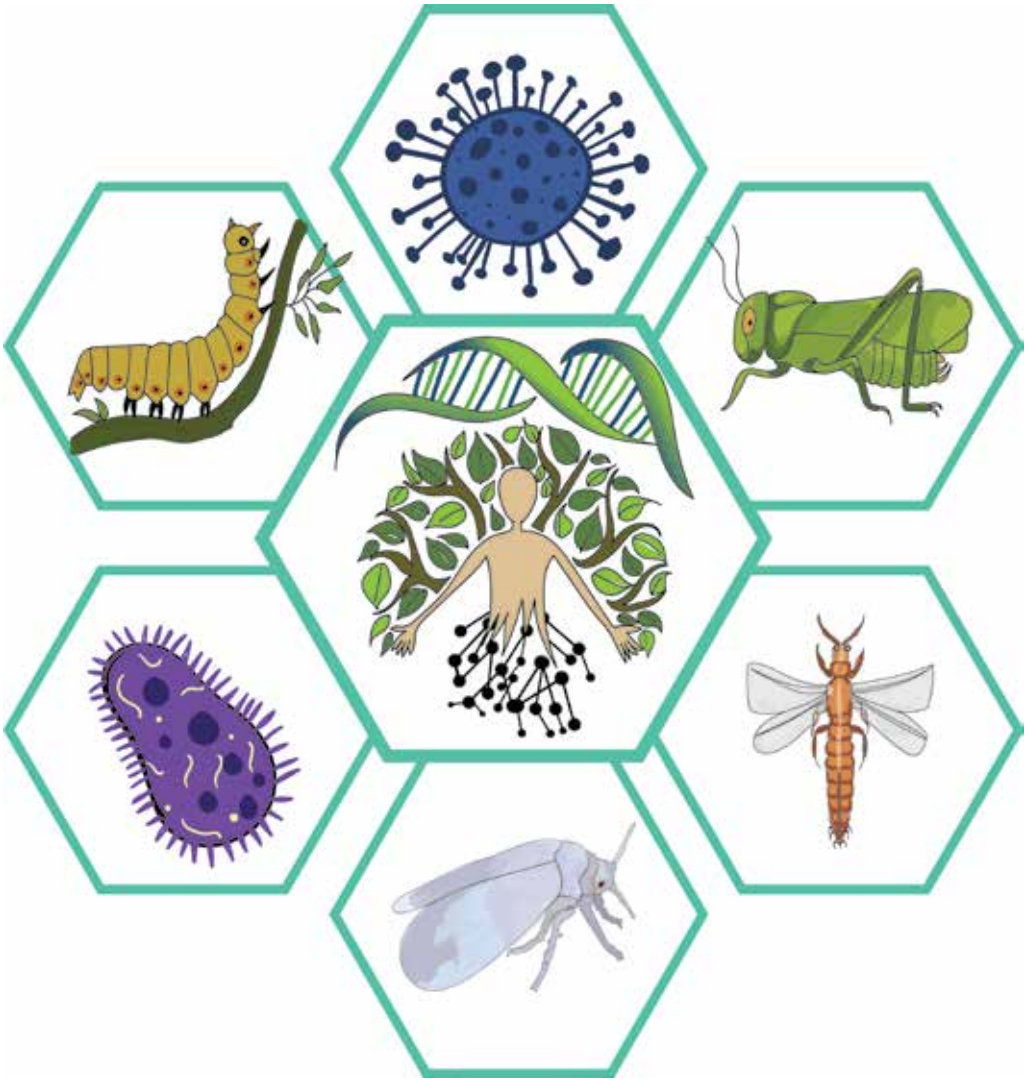
Drought is one of the major abiotic stresses affecting the yield of crops. There are different strategies to enhance drought tolerance in plants. One of these is enhancing the plant root length. A Deeper root will be able to absorb water from deep soil which is helpful during drought conditions. Our collaborator at the University of California, San Diego has identified two plant secondary metabolites involved in root growth development. Treatment of seedlings with either of these metabolites enhances root growth in rice and tomato seedlings. We are testing if these metabolites also increase root growth in adult rice plants and if pretreatment of these compounds also increases root growth in plants. If the compounds do induce root growth in plants, they will be tested for providing tolerance against drought.



Setup used for testing the effect of secondary metabolites on root growth.

Disease and Pest Management

Climate change and rapid rise in the population of plant pests has led to increased usage of insecticides over the last several decades. This has, in turn, led to the evolution of insecticide resistance in pests, making pest management an ever-increasing challenge. At present, the chemical control method is the most widely accepted pest management method across the globe owing to its ease of application, cost effectiveness, availability, and widespread adaptation. However, due to high toxicity, insecticide resistance, increasing government regulations and awareness among consumers, we may soon see considerable decline in usage of chemical-based insecticides/pesticides. At TIGS, we aim to develop new Integrated Pest Management (IPM) programs with a focus on insects affecting Indian agriculture.



Integrated pest management programs to improve nutrition security

Developing feasibility studies for management of Coffee Stem Borer through innovative methods

Sampath Kumar

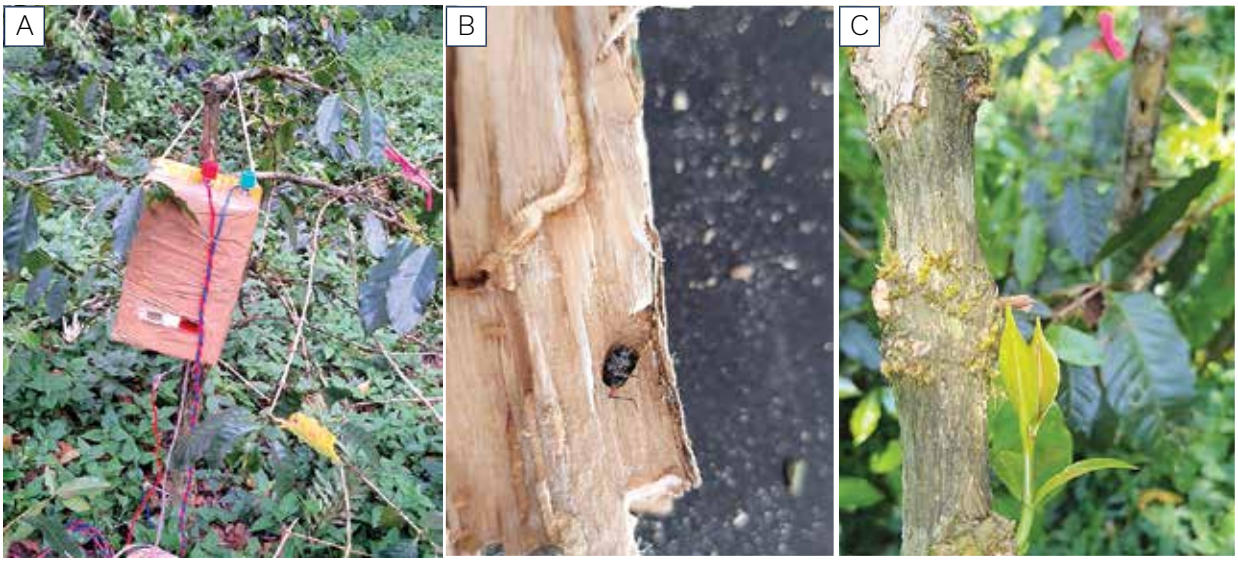
[In collaboration with Central Coffee Research Institute, Chikmagalur and Indian Institute of Science, Bangalore]

Coffee Stem Borer is a notorious pest that causes severe economic losses. One of the major limitations in developing methods to kill this pest is its cryptic life cycle. The immature stages of the borer live deep inside the stem and targeting the pest with chemical insecticides is not possible. Many other methods - physical and biological - developed till now have not been very effective in managing the pest.

In association with CCRI and IISc, we are trying to develop a novel method of using Electromagnetic Pulse (EMP) to arc the borer within the plant and kill them. Additionally, we are working on developing targeted microwave resonating frequencies for selectively killing the borer pest but not the coffee plant. We have set out the following specific objectives:

- Exploring the feasibility of using EMR frequencies in managing stem borer infestations
- Evaluating the impact of the novel physical control measures on the growth and development of the plant.

We have identified that the electric current approach on plants depend on several factors, such as Current intensity, Frequency, Duration, Polarity, Waveform, Plant species, Developmental stage, and Environmental conditions. Based on this we are working on a third prototype. We have now customized power energizer that converts AC power into a brief high voltage regulated pulse frequency. Currently standardization of the duration of the pulse is in progress. We found high voltage electric pulses of load peak (in excess of 10,000 volts and rapid drop) through the wood at a frequency of 1 KHz (one pulse per second) is causing no harm to the plant. Since we are working with 5µA current circuit (prescribed safe limit for humans is 10µA) and there is no harm to humans or animals due to the prototype. Ten coffee plants have been subjected to electric shock treatment for 6 hours and are being longitudinally monitored for their growth and other physiological parameters.



A) 3rd Prototype on coffee plant B) Adult borer ready for emergence C) monitoring of coffee plant post electric exposure

Surveillance of Fall Armyworm in Karnataka and its susceptibility against different insecticides

Sampath Kumar

[In collaboration with University of Agricultural Sciences, GKVK, Bengaluru]

The Fall Armyworm (*Spodoptera frugiperda*) is a Lepidopteran insect belonging to the family Noctuidae. Although the fall armyworm (FAW) can feed on various kinds of food, with a host range of more than 80 plant species, its main preferences are grass plants. In particular, crops of economic importance such as maize, millet, sorghum, rice, wheat, and sugarcane are the preferred food sources of this pest.

FAW is an invasive pest and between 2018-2022, it has spread throughout the nation causing not only severe economic losses but also raising food security concerns. Thus, it is essential to develop an effective and flexible approach to manage it. Application of various insecticides should be based on scientific evidence. Collaborating with the University of Agricultural Sciences, GKVK, we aim to develop environmentally safer synthetic as well as bio-pesticides. We would also be evaluating the resistance among this pest. The base-line insecticide susceptibility data is available with UAS, Bangalore; tracking the pest in real time and evaluating the susceptibility data would provide insights into the possibility of resistance to insecticides that might be developing within the pest.

We have defined three key objectives:

i. Address the gap in knowledge regarding resistance status of FAW

ii. Develop novel combinations of bio-pesticides

iii. Support farmers in mitigating the threat posed by FAW.

Since the fall season this year, we have developed protocols for conducting field surveys related to assessment of damage, yield loss and insecticide usage patterns. Our approach includes surveillance in major corn growing areas of Karnataka and assessing the rate of infestation and crop loss due to FAW. We have set-up the infrastructure and developed protocols for maintaining field collected FAW under lab conditions for conducting bioassay studies. We found the incidence of FAW throughout the year and their densities varied according to the stage of the crop and pesticides used for the control. The commonly used insecticides were Emamectin benzoate, Chlorantraniliprole, Spinetoram, Spinosad and Chlorpyrifos and Lamda-cyhalothrin without being aware of their dilutions and a randomly following the dosages as prescribed by dealers or shop vendors. Further the insecticide bioassay results indicated that, among different insecticides, Emamectin benzoate, Spinetoram, Spinosad and Chlorantraniliprole recorded significant mortality even at lower dosages than the recommended dosages, suggesting that these insecticides can be used at lower concentrations than actual recommended dosages for the control of fall armyworm. Contrary to this, insecticides such as Chlorpyrifos and Lambda cyhalothrin recorded significant mortality of fall armyworm at dosage higher than the recommended dosages suggesting that certain populations might be developing resistance against these molecules at a faster rate compared to other molecules. Our work would make a significant impact in sensitizing the correct usage of insecticides and withheld the development of insecticide resistance.

Heavy infestation of Fall Armyworm

Egg mass of fall armyworm

Rearing of fall armyworm on leaves of castor

Early and Late instars of fall armyworm

Pupae

Female and male of fall armyworm

Mass Rearing of Fall Armyworms

Leaf dip assay to study insecticide resistance

Crop Improvement team

Chandra Girish M
Senior Research Associate

Syam Sura
Senior Research Associate

Ashok K
Research Associate

Gargi Prasad S
Research Associate

Vennapusa Ramanjaneya Reddy
Research Associate

Dileep Kumar N T
Research Assistant

Deepika G T
PhD Student

Harshitha DM
Research Assistant

Kamalakar
Research Assistant

Manjari T C
Research Assistant

Manoj R Y
Research Assistant

Sahana P
Research Assistant

Karthur Veerarjun T T
Lab Assistant

Technology Platforms

Technology Platforms

Harvinder Kour Khera

Rajesh V Iyer

Satyaprakash Pandey

Vasanth Thamodaran

Setting up an effective public health system to prevent, detect, and respond to adverse health events requires good surveillance in conjunction with sensitive, economical, and readily available diagnostic options. The availability (or lack thereof) of diagnostic healthcare in rural India is a pressing issue. There is also a dearth of good, well-functioning licensed laboratory services for point-of -care diagnostics. Diagnostics remain a challenge in our country of 1.3 billion people. Major hurdles in this area include high-cost and need for skilled and trained personnel. Therapeutic platforms can facilitate proof-of-concept studies for the development of innovative treatment strategies. The specificity of bio-therapeutic platforms makes them popular for the treatment of some diseases refractory to small molecule therapy. Translational research towards the development of new and improved diagnostics and therapeutics is therefore the need of the hour.

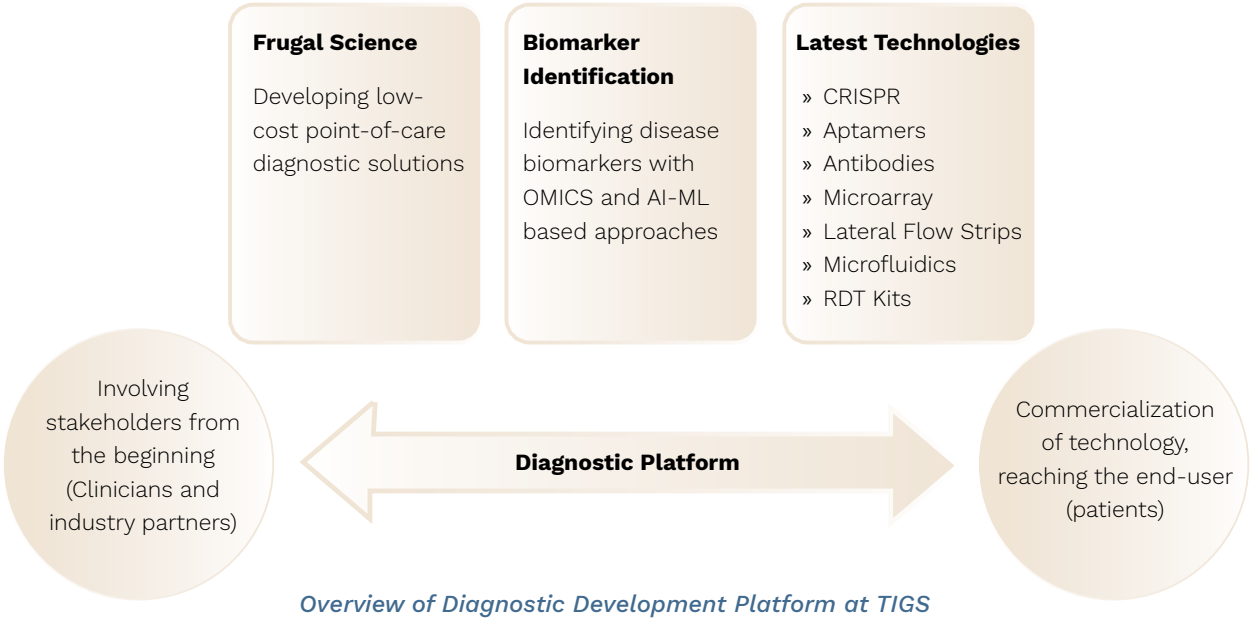
Finally, since most of these technologies were created in the West, the cost of reagents and equipment is considerable. Another of our focus areas, therefore, is the indigenization of technologies used in nucleic based diagnostics development.

TIGS is working to develop multiple platforms, that include instrumentation and knowledge expertise, in order to accelerate early research for quick transition to the development of a treatment modality. Once developed, these platforms will be open and available as a shared resource for multiple stakeholders to work in a disease-agnostic manner.

Diagnostics Development Platform

Molecular diagnostics provides powerful tools for early and more accurate diagnosis of diseases, paving the path towards personalized medicine. Accurate diagnosis is the key to the right treatment, and early diagnosis of a disease is critical for saving lives. The absence of cost-effective diagnostic methods and delayed or inaccurate diagnosis remain a healthcare challenge in our country. To address the existing diagnostics gap, we are developing a platform for diagnostic solutions for various infectious and rare diseases using the latest cutting-edge technologies such as CRISPR, digital PCR, isothermal amplifications (LAMP and RPA) as well as next-generation sequencing (NGS) panels.

The diagnostics platform is focused on developing low-cost, point-of-care diagnostic solutions suitable for field applications in India. The aim is to provide innovative solutions for early diagnostics that are rapid, robust, affordable, and accessible to the remotest part of the country.



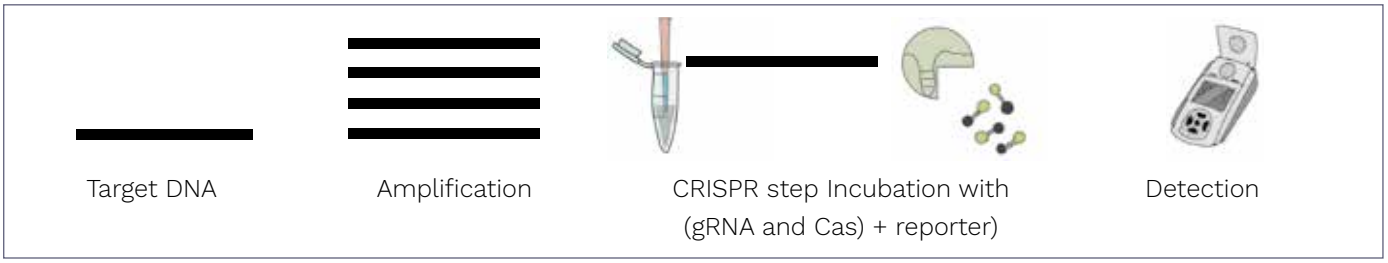
Overview of Diagnostic Development Platform at TIGS

Indigenization of Enzymes for developing Advanced Diagnostics in India

Harvinder Kour Khera

The CRISPR-based diagnostic assays for various infectious and rare diseases being developed at TIGS provide point-of-care solutions that can be taken for clinical validations. The platform has a keen focus on both indigenization and bolstering the stability of reagents.

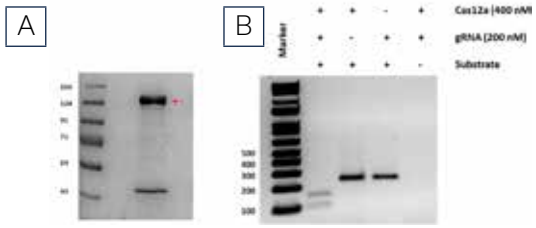
Indigenization of diagnostics is crucial for India due to its potential to address specific healthcare challenges and promote self-reliance. Customizing diagnostic solutions to the country's diverse population, prevalent diseases, and unique environmental conditions ensures more accurate and culturally relevant results. Additionally, indigenous diagnostic technologies can be tailored to meet the affordability requirements of a large population with varying economic backgrounds. This approach not only facilitates timely and accessible healthcare but also



Cas based detection; DNA is extracted from the samples followed by targeted amplification. The amplified DNA is incubated with Cas and single-stranded reporter DNA and detected via measurement of the fluorescence released.

mitigates dependencies on foreign technologies and markets. Furthermore, investing in local research and development fosters innovation and expertise within the country, contributing to the growth of the healthcare sector. In the context of diseases endemic to India, such as certain tropical infections, having diagnostic tools designed for local needs makes them affordable, enhance the effectiveness of disease management and public health initiatives

The diagnostics development platform has a keen focus on both indigenization and bolstering the stability of reagents. Currently, at TIGS, we are working for optimization of inhouse production of enzymes important for molecular diagnostics. Our efforts have led to streamlining the production of various Cas enzymes such as Cas9, Cas12, Cas13, and Cas 14 at a lab scale. By optimizing indigenization strategies, we've successfully slashed reagent costs by half, and we aim to further reduce costs by indigenizing polymerases.



A) SDS-PAGE analysis of purified LbCas 12a. B) In vitro cleavage analysis of purified LbCas 12a

Enhancing Stability for the development of RNA based colorimetric sensor

Synthetic biology's rapid design-to-production cycles offer a solution, introducing engineered gene circuits that diversify molecular detection, create dynamic sensors, and enable portable diagnostic tools. Toehold switch-based diagnostics emerge as a promising, inexpensive, rapid, and highly sensitive alternative to RT-qPCR, especially beneficial in resource-limited regions. These devices, adaptable to paper-based platforms, offer potential for widespread use in low-resource settings. Ensuring stability and functionality under varying environmental factors poses a challenge in their practical implementation for diagnostic purposes. To address this, our study focuses on preserving cell fee expression systems under extended temperature stress through lyophilization. Lyophilization emerges as a crucial method, potentially ensuring prolonged stability and convenient transportation of diagnostic components.

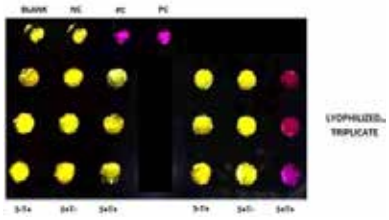


Photo from a cell phone camera showing colour readouts of paper-based IVTT assay of S17 with lyophilized IVTT, post incubation at 37°C for 2hrs.

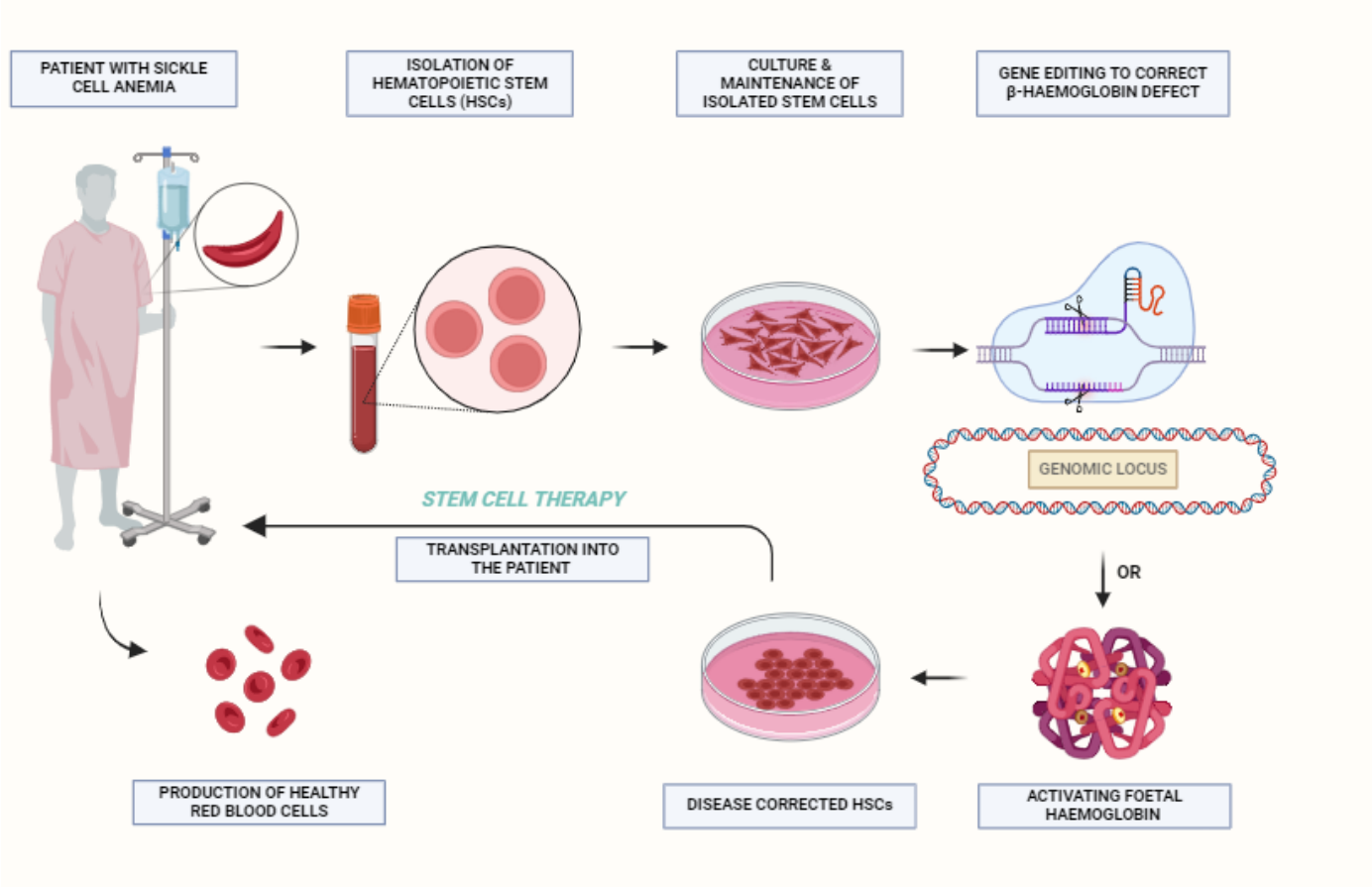
Cell-Based Therapeutics Platform

Small animal models such as mice have been a valuable tool to study human diseases and develop therapeutic interventions. However, about 20% of the human genes do not have orthologues in the mouse model. In addition, model organisms do not always completely display the disease pathologies associated with rare genetic disorders. Thus, a human based disease model can provide a better picture on disease mechanisms and development of efficient therapies. Human pluripotent stem cells, either embryonic stem cells (ESCs) or induced pluripotent stem cells (iPSCs) with their ability to differentiate to any cell types in the human system. This ability enables investigations on cell types such as neurons that are difficult to access in a living individual. Further, when an iPSC is generated from a patient with a genetic disorder, the disease model can provide insights on human specific disease pathologies.

iPSCs developed from patients have enabled the investigation of disease mechanisms in the lab without dependence on animal models. Further, the mutation from a specific patient may not represent the most prevalent disease variant. At TIGS, we develop human pluripotent stem cell-based disease models for rare genetic disorders by using gene editing or by reprogramming patient derived somatic cells. Using genome editing, it is now possible to disrupt a gene function by introducing the mutation of interest and to correct a disease-associated mutation. Therefore, to study a specific genetic disorder, the mutation of interest can be introduced in the target gene in a pluripotent stem cell derived from a normal donor.

Once generated, the cell line can be differentiated into appropriate lineages. As the cells differentiated from patient iPSCs also show the disease phenotype, they are very valuable in drug screening and testing various therapeutics as a disease-in-a-dish model. This also circumvents difficulties in obtaining case-by-case patient samples, including ethical concerns and accessibility.

The developed disease-in-a-dish platform will be useful in investigation of disease pathogenesis to identify drug targets. The targets will be further validated for their ability to rescue disease phenotypes using novel or existing drug molecules. The platform will also be used to evaluate interventions like mRNA biotherapeutics. After evaluation, the identified intervention can be preclinically validated in mouse or organoid-based disease models. In addition to drug discovery and evaluation, we also focus on developing cell-based therapeutics using stem cells. Towards this goal, we have been indigenizing some of the reagents used in stem cell-based therapies to reduce treatment costs.

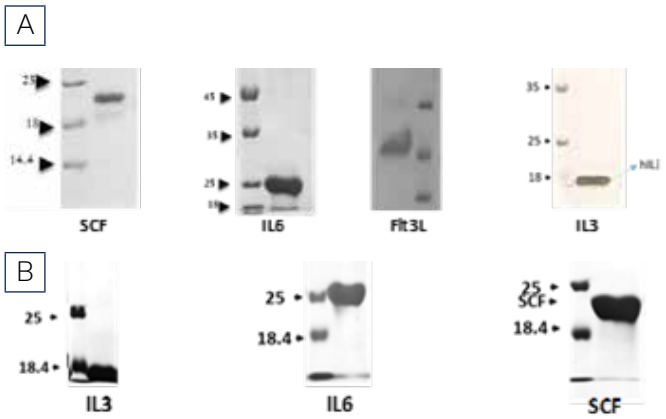


In-house production of growth factors for *ex vivo* expansion of Hematopoietic stem cells (HSCs)

Vasanth Thamodaran

The medium used for culturing stemcells is prohibitively expensive with 80% of the cost attributed tocytokines (FLT-3L, SCF, TPO, IL-3,and IL-6). We aim to bring down the cost of cell-based therapy/gene therapy for hemoglobinopathies by in-house production of growth factors required for ex-vivo expansion of hematopoietic stem cells.

We have successfully expressed the growth factors IL3, IL6, SCF,and FLT3L in bacteria, refolded and purified. In addition, three growth factors -IL3, IL6,and SCF -were over expressed in cytoplasm and purified. The growth factors were also validated using cell lines to check the growth-promoting activity. The validation showed that soluble cytoplasmic growth factors can promote cell proliferation severalfold.



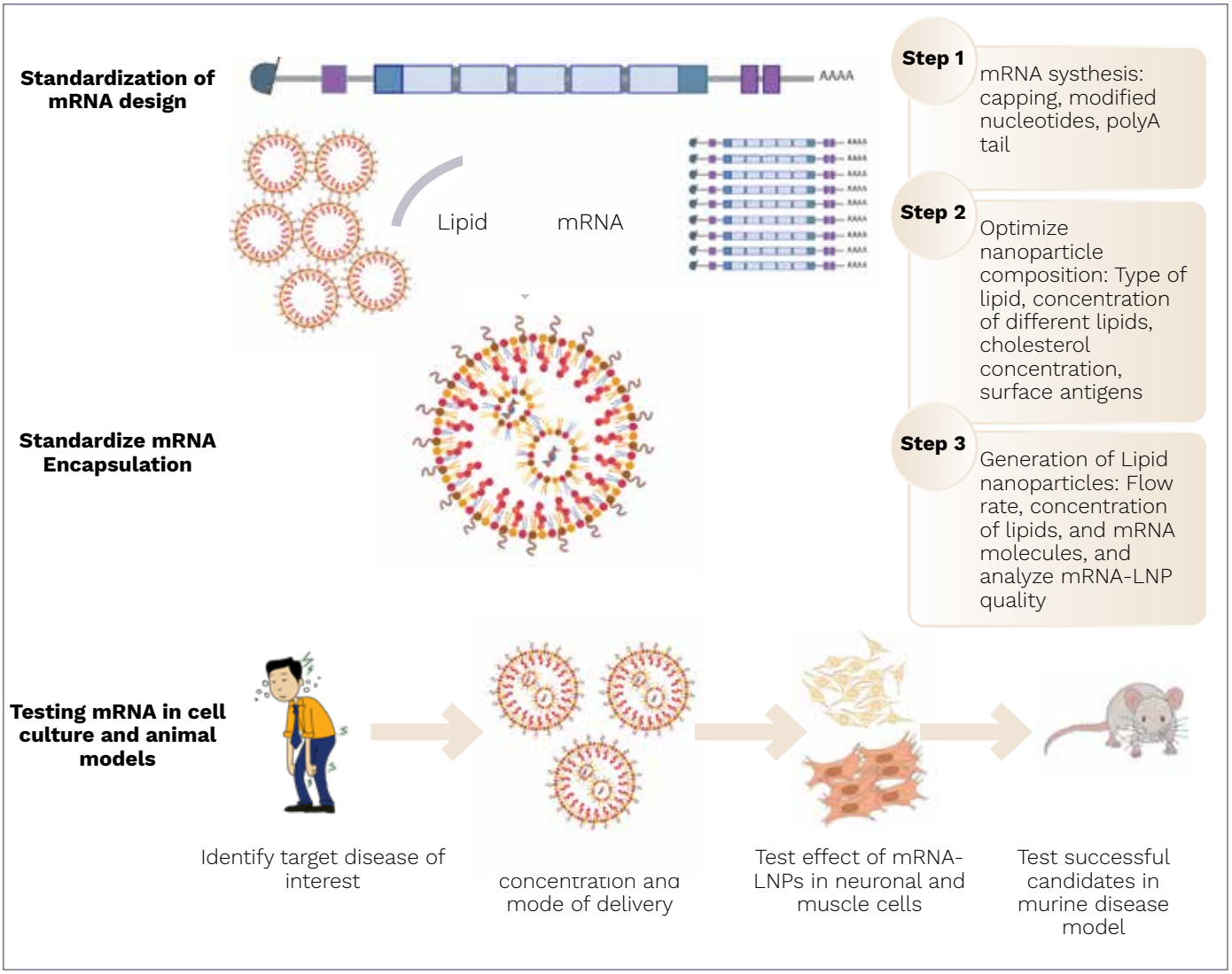
Human recombinant growth factors expressed and purified from E.coli. A) Micrographs showing gel images of refolded and purified growth factors, SCF, IL6, FLT3L and IL3. B) Micrographs showing gel images of purified proteins, IL3, IL6,and SCF, that are overexpressed in the cytoplasm.

mRNA-based Biotherapeutics Platform

The TIGS mRNA laboratory strives to develop an affordable and disease-agnostic mRNA biotherapeutic platform technology for treating rare genetic disorders. The advent of the messenger RNA (mRNA) vaccine for SARS-CoV-2 has laid the foundation stone for mRNA-based therapeutic technology. mRNA biotherapeutic technology is a cutting-edge science being developed worldwide to combat genetic as well as systemic diseases. In this platform, mRNA encoding the therapeutic protein is complexed with lipids to form lipid nanoparticles and is injected parenterally into the patient's body. The internalized mRNA expresses the therapeutic protein in the hepatic, muscle, or blood cells of the patient and mediates symptomatic treatment. The mRNA therapy bypasses the protein expression and purification steps required for the current recombinant protein-based biotherapeutics, thereby reducing the cost of treatment substantially. The platform nature of mRNA technology allows rapid as well as parallel product development for the treatment of many genetic diseases. The work being done in developing the mRNA platform directly connects to the TIGS vision of using cutting-edge science to solve societal problems.

mRNAs are a fast-emerging class of biotherapeutics. mRNA therapies offer a new opportunity for targeted treatment of challenging diseases and flexible manufacturing, as demonstrated by the rapid development of mRNA vaccines against COVID-19. They are non-infectious, non-integrating, and cell-free, offering both rapid and readily scalable production with high productivity.

The mRNA team at TIGS, following the depicted preclinical development pipeline, has begun working towards improving the purification of synthesized mRNA and developing alternative lipid formulations for improved encapsulation and stability, using specialized devices for encapsulation and high throughput assessment of lipid formulations.



Generation of lipid nanoparticles for *in-vivo* delivery of mRNA

Rajesh Iyer V

We have successfully generated mRNA-lipid nanoparticles (mRNA-LNPs) using a customizable microfluidic device. The size of mRNA-LNPs was found to be below 100 nanometres with a net negative surface charge. These mRNA-LNPs were highly efficient in transfecting mRNA encoding the green fluorescent protein into HEK 293 cells. Upon microscopic examination, we found that under in vitro conditions, more than 95% efficiency of HEK 293 transfection can be achieved by using 250 nanograms of mRNA-LNPs.

Future outcomes

We have prospective mRNA candidates for numerous rare diseases, which are ready for packing into nanoparticles and testing in rodent models. Following proof of efficacy in animal models, we envisage a toxicological study to demonstrate that our therapy is safe for humans. Post toxicity studies, we want to initiate human clinical trials, where a small cohort of rare disease patients would be administered the drugs to demonstrate safety as well as efficacy. The clinical and industrial collaborations required for the above work are already being set in place to expedite the clinical application of the therapy.

Technology Platforms team

Aathira M K
Research Assistant

Lakshmy Venugopal
Research Assistant

Lenifer Helen D Souza
Research Assistant

Palash Ghosh
Research Assistant

Pooja D B
Research Assistant

Praveen P
Research Assistant

Sabari Kannan G
Research Assistant

Swetha Mariam Stanley
Research Assistant

Research Facilities

Facilities

Sunita Swain
Insectary

V S Sresty Tavva
Greenhouse

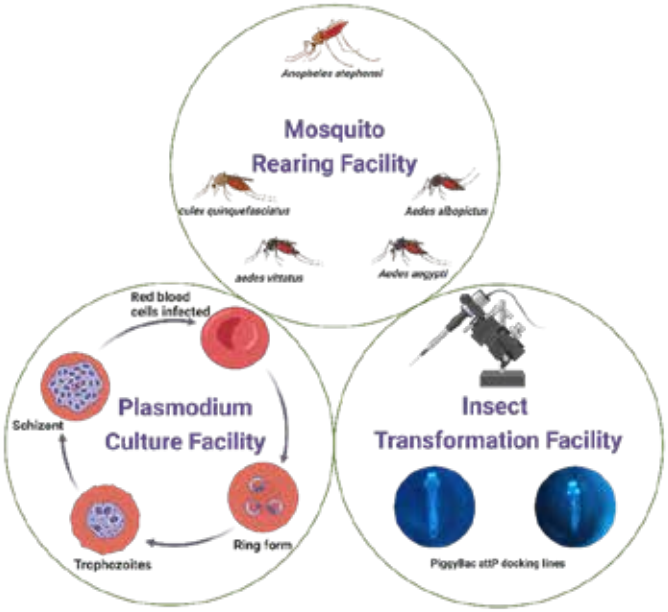
Satyaprakash Pandey
Technology
Implementation

Insectary

Sunita Swain

Mosquitoes, extensively studied for their crucial role in disease transmission, encompass more than 3,500 species globally. While this diversity is vast, only a select few species have the ability to carry pathogens responsible for human diseases. As a result, scientific studies have predominantly focused on these specific mosquito species.

The TIGS mosquito-rearing facility aims to be a national-level hub for major mosquito vectors in India, particularly those within the Indian subcontinent. It has three major components.



I. Mosquito rearing facility: It houses mosquito lines (Anopheles, Aedes, Culex) for vector-related research, including competence, behaviour, genetics, and host-parasite studies. The facility also creates isofemale and mutant lines for specific experiments.

II. Parasite Culture Facility: It supports research on Plasmodium falciparum, aiding studies on parasite biology, drug testing, and vaccine development.

III. Insect Transformation Facility: It facilitates bio-manipulation in insect pests and vectors for diverse studies.

In collaborative efforts, we are partnering with Integri-biotech to develop a Tele-Epidemiology Based Vector Identification and Disease Prevention System (Tevi-Dps), for real-time AI-based mosquito surveillance.

Another collaboration with inStem focuses on investigating the impact of odors on mosquito immunity and vector competence. The in-house projects involve the creation of mutant Aedes lines for repellent screening and the establishment of a human pluripotent stem cell-derived liver organoid model for studying malarial pathogenesis. Additionally, our endeavors focus on inducing refractoriness to Plasmodium infection in Anopheles stephensi through Wolbachia trans-infections.

Within our training programs, the TIGS insectary facility successfully organized the national-level workshop titled “Mosquitoes Up Close: Exploring Biology to Practical Techniques” from November 28th to November 30th, 2023. The workshop elicited a very positive response

from enthusiastic participants, esteemed speakers, and the dedicated TIGS team, who played integral roles in the successful execution of this event. These three days featured engaging sessions led by field experts, hands-on experiences designed to enhance participants' skills in mosquito studies, and networking opportunities that facilitated meaningful connections within the entomological community.

As a part of BliSc cluster, our initiatives encompass orientation programs, training modules, and services focused on mosquito-related research.

Numerous outreach programs were executed, involving 42 students, 3 faculties on National Science Day, 25 participants from the Simons Monsoon School, and 54 international and national ambassadors of the Sustainability Ambassadors of Global Exchange program. These endeavors play a pivotal role in advancing knowledge and management of vector-borne diseases.

Dr. Soumya Swaminathan's Visit

With TIGS SAB Members

Insectary Workshop hands-on session

Greenhouse

V S Sresty Tavva

TIGS has a state-of-the-art greenhouse facility for growing transgenic and non-transgenic plants under controlled conditions. The greenhouse is carefully designed to avoid any unintentional transmission of recombinant or synthetic nucleic acid molecules through plant pollen and to avoid any escape and establishment of genetically engineered (GE) plants into the natural environment. The Standard Operating Procedure (SOP) to conduct experiments on transgenic and non-transgenic plants in controlled conditions is designed as per the DBT guidelines.

The initial screening of genetically engineered events takes place in the greenhouse after plant transformation and regeneration of whole plants in vitro. The primary transformants and their derivatives are usually grown for early trait evaluation and event screening purposes. We have proper screening and labelling procedures in place for the accurate identification of plants which is very critical to maintaining plant product integrity during research activities in containment facilities. TIGS greenhouse is also equipped with a pollination chamber to perform crosses between selected GE plants and wild-type parent controls. The pollination chamber is designed to generate the heat and humidity required to perform crossing experiments.

Currently, we are evaluating genome-edited rice lines and EMS mutagenized pointed gourd lines in the TIGS greenhouse facility.

A few glimpses from the Greenhouse at TIGS

Technology Implementation

Satyaprakash Pandey

Enabling the technologies developed at TIGS to reach to society

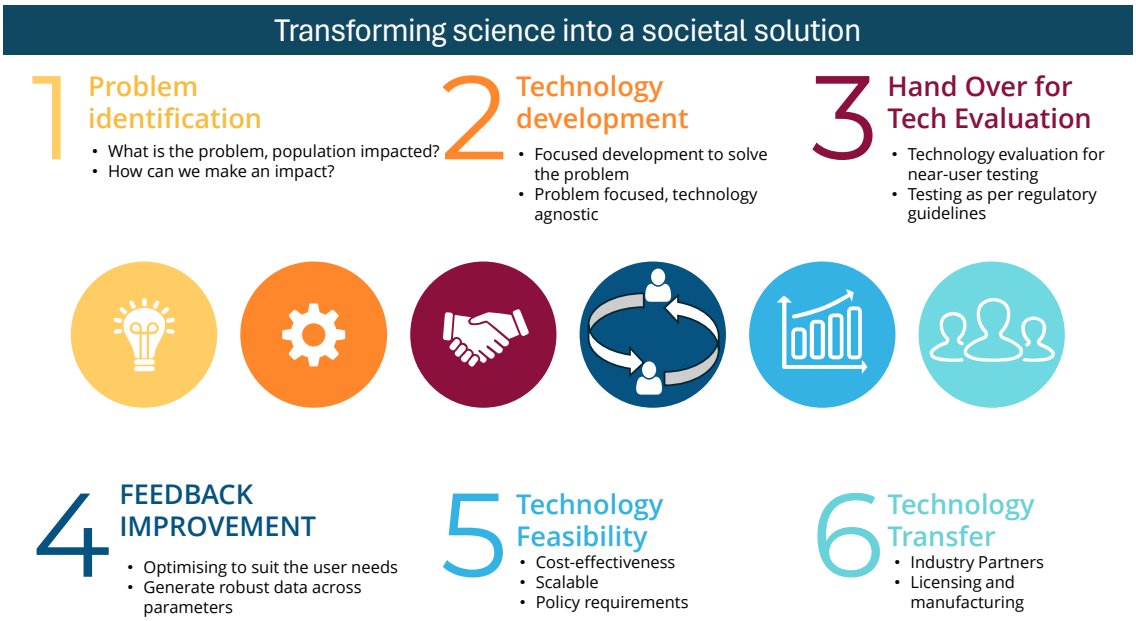
The mission of TIGS is to develop cost-effective, high-quality, cutting-edge scientific technologies towards solving societal problems.

The purpose of the technology implementation team is to take the technological solutions developed at Tata Institute for Genetics and Society (TIGS) to the stakeholders and end-users, especially in the healthcare and medical diagnostic market.

The technology implementation team is a combination of product development and commercialization domain with its major roles as follows-

- **Technology evaluation**- assess the developed technology for its performance evaluation as per the established guidelines. Generate the data using International Standards and panels to evaluate the performance of the assay in controlled field settings.
- **Affordability and Accessibility**- Develop strategies to optimize for ease of use, technology/infrastructure availability and cost-effectiveness of the developed solutions for broader coverage.
- **Technology transfer**- Identify a suitable partner and support for product reports to commercialize the assay by handing over the SOPs and technology for scalability.

To achieve the goal, it is important to note that every step will require collaboration between multiple stakeholders and strong knowledge of the multiple guidelines and approval requirements. The team actively engages important stakeholders, such as clinicians, industry partners and Government labs, from the beginning of the development of the technology. Regular feedback from the partners results in continuous improvement of the developed technology which is incorporated in our developed solution to improve its robustness, ease of use, and adherence as per the regulatory agencies and Government bodies.



Facilities Team

Chaitali Ghosh
Assistant Insectary Manager

Naveen Kumar
Research Associate

Chethan Kumar R
Research Assistant

Pooja D B
Research Assistant

Soumya Gopal Joshi
Research Assistant

Soumya Mogaveerthi
Research Assistant

Joydeep Roy
Laboratory Assistant

Sanjay M
Green House Assistant

Chandrashekhar Pradhan
Green House Assistant

Community Engagement and Policy Stewardship

Community Engagement and Policy Stewardship

Saveetha Meganathan

The Community Engagement and Policy Stewardship program at TIGS aims to integrate scientific advancements with a holistic approach to community engagement and policy stewardship. This approach aligns with the GoI Science, Technology and Innovation Policy 2013 principles, which include open science, transparency, extended engagement through public and expert consultations, promoting scientific temper, closing the gender gap, and translating science to societal needs.

TIGS is committed to achieving health equity and nutrition security by addressing community concerns through clear science communication and societal interface practices. Proactive community engagement involves amplifying concerns through consistent and clear science communication. Exploratory/action research projects lead to policy advocacy, funding opportunities, and system strengthening, ultimately positively impacting lives.

TIGS is committed to building socially conscious and ethically bound research programs to develop humanitarian technologies that will benefit and serve Indian society. It also aims to build trust with communities, network with humanitarian groups, develop global coalitions, and enable efficient technology transfer to stakeholders.

Community Engagement

Demystifying Rare Genetic Diseases: Building Understanding and Empowering Communities

Genetic disorders, while often categorized as "rare," pose a significant challenge in India due to its vast population. This translates to a high disease burden, impacting countless individuals and families. Recognizing this urgency, the National Policy for Rare Diseases (NPRD) 2021 emphasized the need for awareness, early diagnosis, and improved treatment options.

The Tata Institute for Genetics and Society (TIGS) is actively involved in accelerating diagnostics, therapeutics, and public awareness regarding rare genetic diseases (RGDs). Through our "Demystifying Rare Genetic Diseases" project, we strive to:

- **Increase awareness and understanding:** Empower clinicians and the general public with accurate information about RGDs.
- **Accelerate diagnosis:** Raise awareness to facilitate timely and accurate diagnosis for patients.
- **Empower individuals:** Provide reliable information and resources to those affected by RGDs.
- **Foster collaboration:** Promote knowledge exchange among experts, clinicians, and science communicators.
- **Enhance genetic literacy:** Improve the public's understanding of genetics and its role in health.

Building a 360-degree engagement platform:

To achieve these goals, we are developing the "Rare Genetic Diseases" portal, a one-stop platform for comprehensive information and resources:

- **Blogs:** Written by RGD researchers, clinicians, and genetic counselors, offering diverse perspectives and expertise.
- **Podcasts:** The "Demystifying Rare Genetic Diseases Podcasts" series features conversations with experts to raise awareness and curate factual knowledge.
- **Posters:**
  - **NPRD, 2021:** Highlighting key points, strategies, and recommendations from the National Policy for Rare Diseases.
  - **Geotagged Disease Posters:** Tailored for both clinicians and the public, covering various RGDs and facilitating data collection on user engagement.
- **Multistakeholder engagement:**
  - **Rare Genetic Diseases Research Summit (REDRESS):** An annual event bringing together diverse stakeholders for collaboration and knowledge exchange.
  - **Innovative events:** Exploring formats like hackathons to encourage creative solutions and community involvement.
- **Interactive learning:**
  - **Videos:** Engaging videos explaining complex concepts in an accessible manner.
  - **Gamification:** Educational games for high school students to enhance genetic literacy in a fun and interactive way.
  - **Outreach activities:** Organizing awareness campaigns and educational sessions at colleges.

By building this comprehensive platform and engaging various stakeholders, TIGS aims to demystify RGDs, empower individuals and communities, and contribute to significant advancements in diagnosis, treatment, and overall well-being for those affected by these conditions.

Policy Stewardship

Anti-Microbial Resistance: A Silent Pandemic

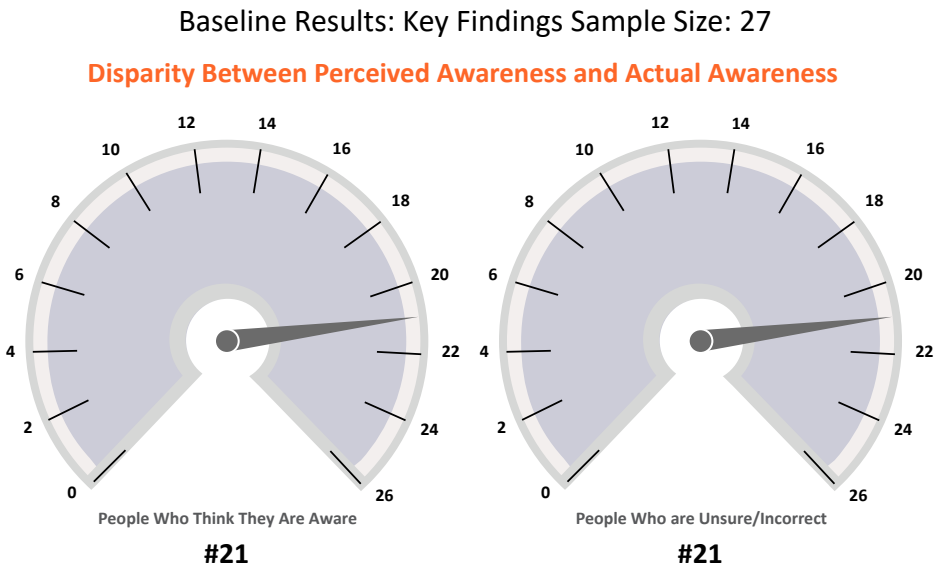
Antimicrobial resistance (AMR) is a global health crisis, threatening the effectiveness of antibiotics, antifungals, and other antimicrobials used to combat infections. AMR renders once-effective drugs useless, leading to longer illnesses, increased healthcare costs, and higher mortality rates. An estimated 1.27 million deaths globally were directly linked to bacterial AMR in 2019, with millions more impacted indirectly. Without effective interventions, AMR could push us back to a pre-antibiotic era, jeopardizing advancements in medicine and public health. AMR is a complex challenge requiring a multi-pronged approach. By implementing effective policies and fostering collaboration, we can mitigate the threat of AMR.

In this milieu, a dissertation project was designed and completed to understand the effectiveness of science podcasts to communicate the information on Antimicrobial Resistance to the public. A short survey was done with the students of St. Joseph's University's social work department. The study showed that even though people perceive their awareness of AMR to be sufficient, in reality, there are major gaps in understanding of AMR.

The role of podcasts in communicating information on AMR requires further research with a long-term empirical evaluation of the potential benefits of podcasts in causing behavioural change through the Information Education Communication (IEC) model. Future Science communication studies could explore standardised and tested models to communicate information to various communities

The majority of the end-line survey respondents said that they were informed about the podcast and they would intervene if someone they knew, were to use antimicrobial medicines without a valid prescription. While this marks the effectiveness of the podcast it was also noted that the respondents have answered incorrectly to questions related to AMR which signposts a sufficient information gap related to AMR information.

(Antimicrobial Resistance Awareness The Importance of Science Communication and The Potential of Podcasts. Master's in Science Communication Dissertation by Ananthapathmanabhan, The University of Sheffield. Supervised by Saveetha Meganathan from TIGS and Marion Germain from the University of Sheffield)



Key findings- Disparity between perceived and actual awareness

Haemoglobinopathies in India: Policy Perspectives

Haemoglobinopathies, a group of inherited disorders affecting the hemoglobin molecule's synthesis or structure, include conditions like thalassemia and sickle cell disease.

Beta-thalassemia major is one of the main public health concerns. The 2011 Census notes that 3-4% of the total Indian population are thalassemia carriers. In India, an estimated 100,000 individuals struggle with beta thalassemia, mainly due to common mutations. These inherited blood disorders cause severe anemia, organ damage, and reduced life expectancy. Regular blood transfusions and expensive medications become a life-long struggle for patients and their families.

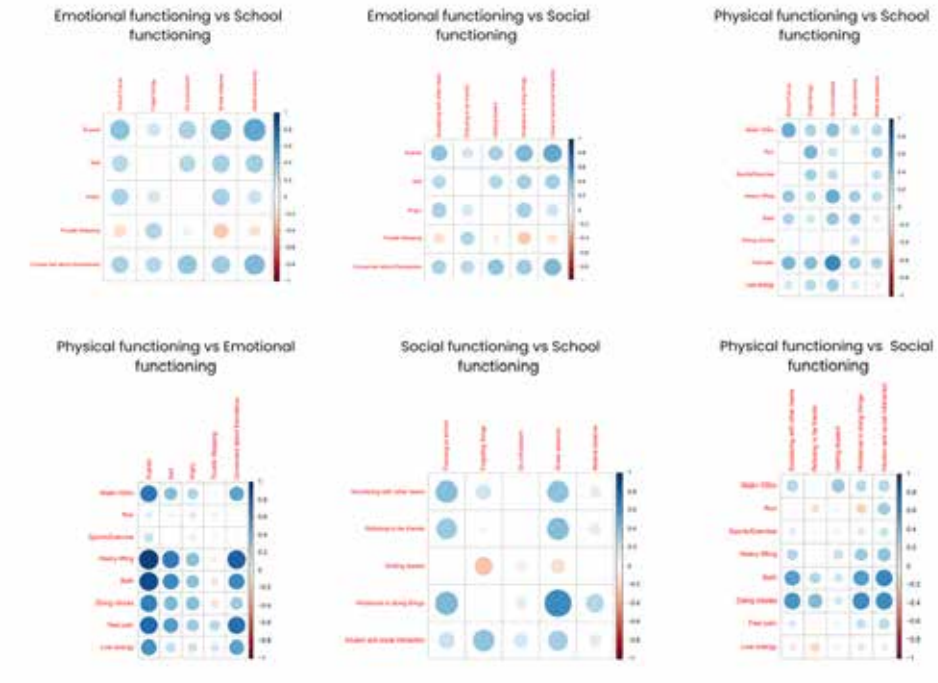
In this background a dissertation project was designed and completed to understand the Quality of Life (using the Pediatric Quality of Life questionnaire (PedSQL)), along with the secondary research on available treatment and management, and screening programs in the Indian context for thalassemia. For our study, we gathered primary data from individuals aged 7-18 with beta-thalassemia major in Banglore, India.

Through the questionnaire designed to assess the quality of life, we looked at the co-dependencies between physical, social, emotional and school functioning. For example, we found a positive correlation between thalassemia patients experiencing pain and them not being able to do schoolwork. By interpreting such relationships, we gained insights into how each aspect of the questionnaire influences one another, providing a comprehensive understanding of the factors impacting the quality of life for beta-thalassemia major patients in India.

In this matrix, blue indicates a positive correlation, red signifies a negative relationship, and no color indicates no connection between variables.

Understanding these aspects is valuable for making informed decisions about healthcare policies and gaining a better understanding of what patients themselves experience and need which can further inform care protocols and policy decisions.

(A study to assess the Quality of Life (QoL) of Beta-thalassemia major patients in India. Master's in Public Health Dissertation by Esha Srivastava, Indian Institute of Public Health, Gandhinagar. Supervised by Saveetha Meganathan from TIGS and Senthilkumar Natesan from Indian Institute of Public Health, Gandhinagar)



Correlation analysis using between different variables of the questionnaire

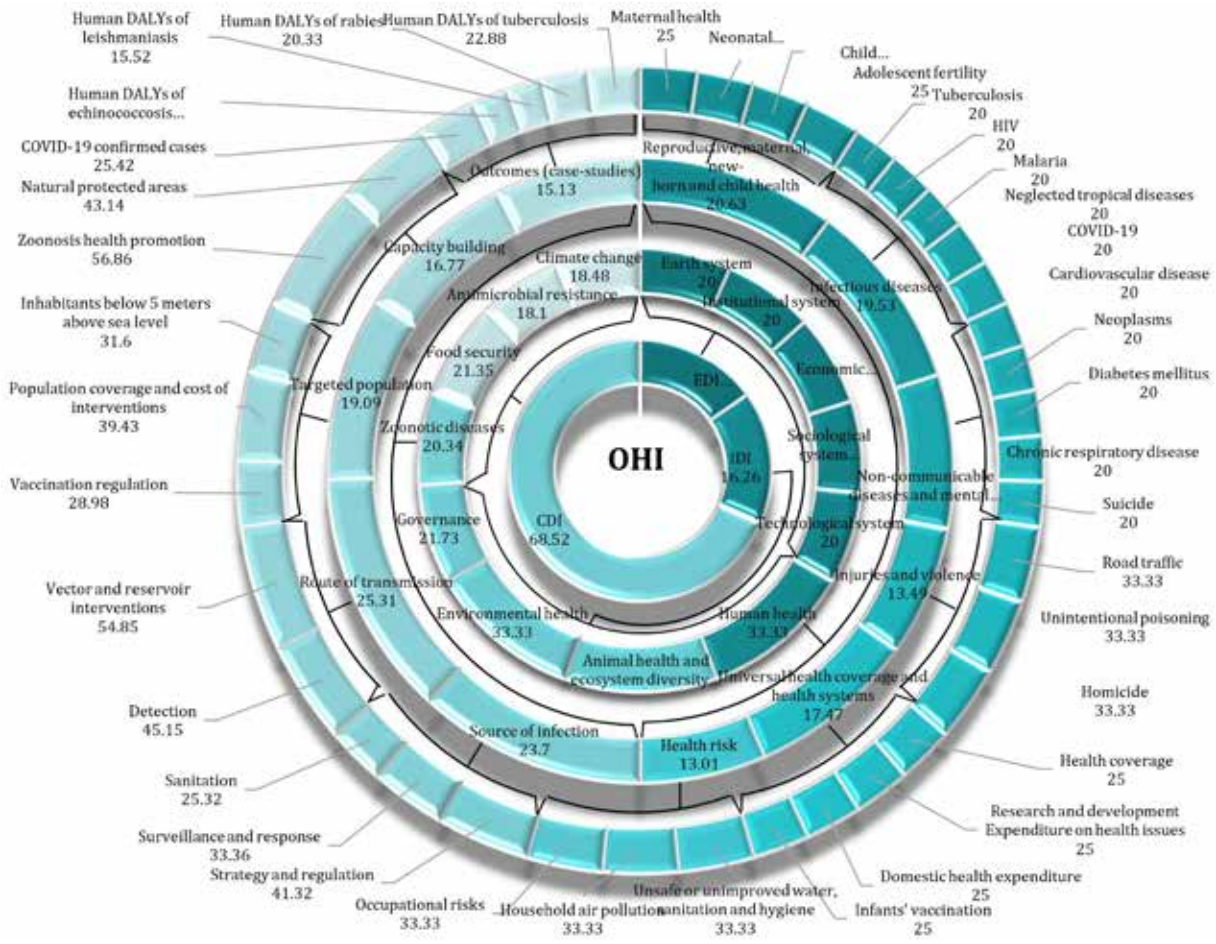
A One Health Index Framework for India

"One Health" is an integrated, unifying approach to balance and optimize the health of People, Animals and the environment. The one-health approach enhances global health security by promoting collaboration at the human-animal-environment interface. There is a need to create a single health index that simplifies complex health data, making it accessible to policymakers, healthcare providers, and the public.

To develop the One Health Index, a statistical framework was developed using which a One Health Index was calculated for India. To determine the lack of data and data gaps in India, indicators that contributed to One Health were assessed.

This framework brings to light the areas where improvement is necessary to bring a change in the OHI and thus according to the weights and the scores for each indicator, we can get indicator-based ranks and administer attention accordingly. The establishment of an index holds significant promise in various aspects of public health. This tool can play a crucial role in monitoring health trends, assessing the effectiveness of interventions, guiding policy-making processes, facilitating resource allocation, and pinpointing disparities that require targeted interventions. Additionally, adopting a unified approach to One Health emerges as a powerful strategy for addressing the intricate and interconnected health challenges that society faces.

Despite these potential benefits, the standardization of impact indicators poses a notable challenge, highlighting the need for a concerted effort to establish consistent metrics for comprehensive health assessments. This endeavour is essential for ensuring the reliability and comparability of data across diverse health initiatives and interventions.

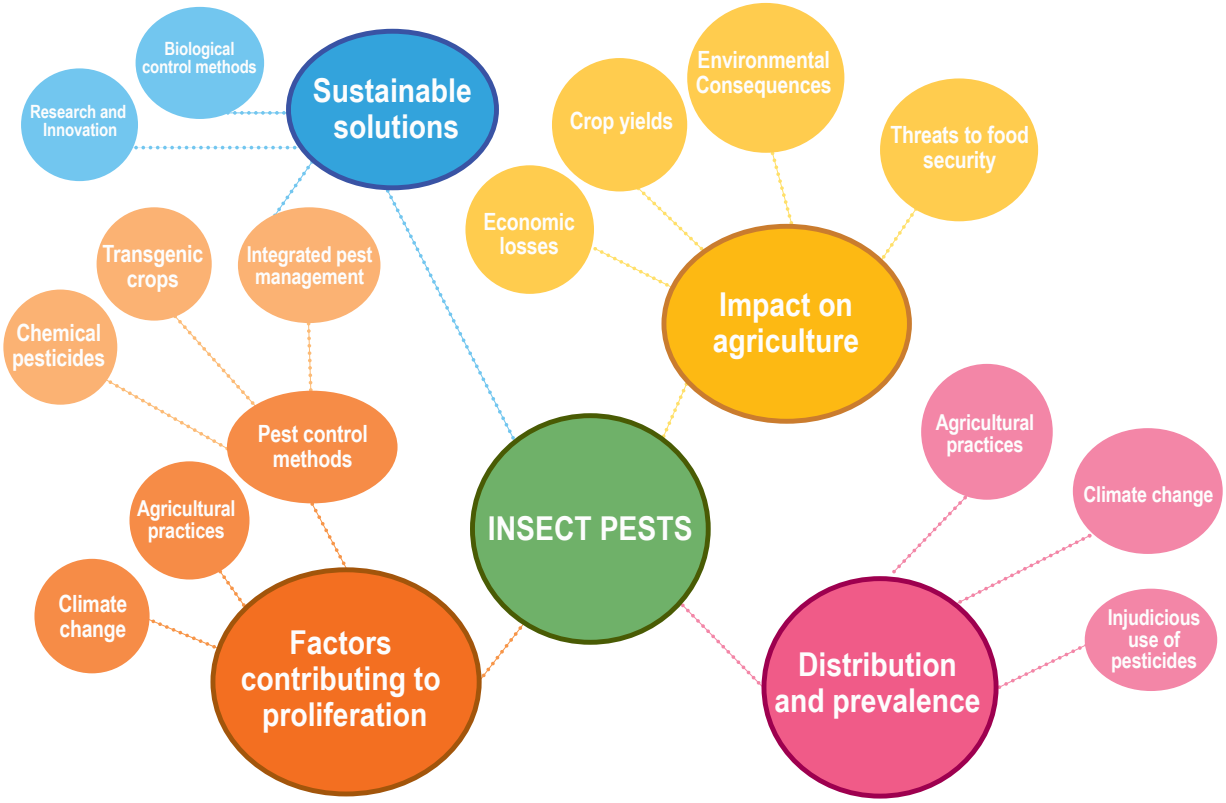


One Health Index

Insect pests and their Impact on Agriculture in India

Insect pets have been a major constraint in agriculture. Huge losses have been incurred due to the damage caused by insect pests. This project aims to provide a comprehensive overview of insect pests and their implications for agriculture in India. Recognizing the profound impact of climate change on insect pest dynamics is imperative. Policies should mandate thorough investigations to comprehend these dynamics, pinpointing vulnerable regions and crops. Armed with this knowledge, adaptive solutions can be proposed to mitigate the risk of excessive chemical pesticide use. Addressing the injudicious use of pesticides for insect pest control necessitates a policy perspective that underscores the crucial need for a comprehensive assessment framework. Policies must advocate for systematic studies, meticulously gauging the extent of pesticide misuse, and considering factors such as application frequency, dosage, and adherence to safety standards. This in-depth analysis lays the groundwork for targeted initiatives that not only promote responsible pesticide usage but also safeguard both agricultural productivity and environmental health.

In the context of crafting policy recommendations, Integrated Pest Management (IPM) emerges as a strategic imperative. Policies should actively endorse the adoption of IPM strategies, prioritizing biological control, resistant crop varieties, and a diminished reliance on chemical interventions. This holistic policy approach harmonizes with sustainable agricultural practices, ensuring the resilience of India's diverse farming ecosystems.



Insect pests: Conceptual framework

Community Engagement team

Arpit Katiyar
Research Assistant

Esha Srivastava
Research Assistant

Suguna Ganesh
Consultant

Ananthapathmanabhan MS
Intern

Anika Bajpai
Intern

Hemanth S
Intern

Priya Raghu
Intern

Shweata N Hegde
Intern

Collaborative Networks

Multi Stakeholder Engagements

Collaborations form an integral part of our work at TIGS, allowing rapid implementation of scientific innovations in line with our mandate. Sharing of infrastructure and expertise significantly reduces costs of taking technology to society. We develop partnerships with multiple stakeholders for application-oriented research to be dispersed where it is needed. To take forward the outcomes of such research, we have developed networks with institutes and universities at both the national and international level across all three research programs to accelerate application-oriented projects.

TIGS is an integral part of the Bangalore Life Science Cluster (BLiSC), boosting our capacity for leveraging advancements in science and technology for social transformation. We operate within an ecosystem that encourages research of top global standards, allowing access to world-class infrastructure as well as continuous interactions with industry and academic partners. While we collaborate extensively to find solutions to problems, we also recognise the significance and need for developing key facilities and technology platforms in-house to facilitate these activities and these are shared for R&D support as a part of BLiSC.

We also partner with industries/start-ups and hospitals as well as with NGOs and patient groups across the city and beyond, to develop low-cost point of care diagnostics for infectious and inherited diseases, keeping patient needs at the forefront. To ensure stakeholder buy-in from the beginning, we enlist the support of government and municipal/ administrative agencies to make a path for innovative research to reach its target, such as implementing disease surveillance and One health initiatives.

Public health surveillance has gained enormous significance in light of the COVID-19 pandemic. Comprehensive surveillance calls for monitoring the prevalence of pathogens, and is the first step in disease control and elimination. It requires continuous, systemic collection, analysis, and interpretation of health-related data through sampling of individuals as well as their environment. Analysis of infectious pathogens and their load, combined with clinical disease sampling, can support predictive disease models and enable preventive action. One Health approaches that encompass environmental monitoring will be the way ahead to monitor for infectious pathogens and prevent future pandemics. TIGS is a leading partner in multiple such initiatives, both at the state and national level.

We also engage in policy advocacy in healthcare by interacting with relevant regulatory arms of GOI, and contribute to evidence-based policy recommendations within the government's framework, for example in the areas of wastewater surveillance for pathogen monitoring, disease vector control and insect genetic modification.

We have been working towards bringing together stakeholders trying to address the difficult problem of providing solutions to those suffering from rare genetic disorders, where diagnostics and therapeutics are extremely expensive to create. Our collaborative effort towards a National Rare Genetic Diseases Research Summit (REDRESS) is a step in this direction.

Bangalore Life Science Cluster (BLiSC)

The Bangalore Life Sciences Cluster (BLiSC) is an innovative institutional model for cutting-edge scientific research, where existing centres of excellence are used for the development of new centres with challenging new mandates. The vision of the cluster is to have an integrated multi-disciplinary and interactive bioscience and technology research enterprise, which will result in path-changing scientific discoveries, and the translation of these into tangible technological advances. It is envisioned that these synergistic associations at the cluster will have a far greater impact on life sciences research than the sum of individual contributions from each institution.

The Tata Institute for Genetics and Society (TIGS) is a non-profit research institute that aspires to develop solutions to challenges in human health and agriculture using applications of cutting-edge science and technology in genetics and genomics.

Centre for Cellular and Molecular Platforms (C-CAMP) is an initiative of Department of Biotechnology, Ministry of Science and Technology, Government of India, with a mandate to be an enabler of cutting-edge life science research and innovation.

The National Centre for Biological Sciences (NCBS), located in Bangalore, is part of the Tata Institute of Fundamental Research.

The Institute for Stem Cell Science and Regenerative Medicine (inStem), an autonomous institute under the Department of Biotechnology, Ministry of Science and Technology, Government of India, is dedicated to the study of stem cell and regenerative biology.

Bengaluru One Health City: Integrating human and animal health with surveillance and disease ecology in a global urban centre

One Health recognises the interconnectedness between environment, animal, and human health. To this end, TIGS is a leading partner in a transdisciplinary collaborative effort to propose and implement research, policy, and programmes at a local and regional scale in Karnataka. The goal is to build a Bengaluru One Health Platform – a network of practitioners and scientists who will evaluate the value of shared environment, biodiversity and livestock monitoring for pathogens in the changing milieu of a large and active Indian city. This network will engage with and inform policy makers, city planners and the health authorities which is critical for the smooth implementation of scientific knowledge. TIGS and NCBS have developed a comprehensive framework for developing the Bengaluru One Health City.

Establishing a sustainable innovation ecosystem requires a well-connected network of educational and research institutions, entrepreneurs, private enterprises, government agencies, investors and citizens/society. This need has led to the establishment of regional innovation clusters in many parts of the world, which bring together capital, expertise, and talent to foster technological breakthroughs that have tremendous impact on society. The state of Karnataka and the city of Bengaluru play a critical role in India's economic growth, with their unique combination of a talented base of scientists and engineers, academic institutions, multi-national companies and a vibrant start-up ecosystem. The Bengaluru S&T (BeST) cluster envisions the establishment of a unique innovation culture that would strengthen this ecosystem, and further cement the region's position as a global innovation powerhouse. The BeST Bengaluru Science and Technology cluster was is now also formalized by the PSA office in 2022. Bengaluru Science and Technology Cluster (BeST) https://www.bestkc.in/thematic-areas/

The Bruhat Bengaluru Mahanagara Palike (BBMP) consented on 23.12.2021 to collaborate with BeST and the stakeholders drawn from various city-based institutions to undertake pioneering work in the area of One Health and disease ecology, environmental surveillance models and disease risk, public health and and infectious disease, antimicrobial resistance tracking, innovation, public engagement, education and outreach. The constellation of this consortium with experts will lead to science evidence and knowledge, and also co-creation of intervention strategies, adaptive risk management of zoonotic outbreaks in Bengaluru City. Since BBMP is responsible governance organization and primary implementation stakeholder, BBMP will be the end user of knowledge and data generated by the One Health Bengaluru City consortium.

Under the leadership of BBMP, Special Health Commissioner, a One Health Cell has been initiated. One Health Cell is intended to follow One Health Framework to promote activities at human-animal-environment/ ecosystem interfaces by providing generic guidance for comprehensive response to prevent, prepare, detect, respond to, and recover from events especially pandemic and AMR, and assure human and animal health security.

The BeST One Health cluster is co led by TIGS and NCBS along with partners BBMP, Biome Trust, ATREE, Azim Premji University, IISc, ARTPARK, Ashoka University, IIPH, Molecular Solutions, Initiative for Climate Action, Echo Network among others.

[Co-led by Dr. Farah Ishtiaq from Tata Institute for Genetics and Society and Dr. Uma Ramakrishnan from National Centre for Biological Sciences]

A multi city consortium for developing pathogen surveillance programs

Public health surveillance systems must generate disease information that drives action, and these data must be of sufficient quality, quantity and resolution to reduce disease burden.

TIGS is a key partner in a unique pan-India initiative for environmental surveillance and developing innovative strategies for pathogen monitoring. A consortium of four city clusters – Bengaluru, Hyderabad, Pune and New Delhi – has been established with generous support and a three-year seed fund from the Rockefeller Foundation. Conceptualized during the pandemic, the consortium has already set up an advanced SARS-CoV-2 surveillance platform, incorporating viral genome sequencing and wastewater based detection and surveillance.

We are currently developing new technologies and disease-agnostic surveillance platforms to monitor and predict the spread of infectious diseases such as respiratory illnesses (COVID-19, influenza, tuberculosis), vector-borne diseases (dengue, chikungunya, scrub typhus etc), and anti-microbial resistance (AMR) in India.

The disease surveillance data will be monitored in real time via shared data pipelines and interactive data dashboards serving researchers and policymakers as well as the general public.

A major outcome of our work in this consortium is to develop sustainable environmental surveillance models that can be handed over to relevant agencies for large scale implementation. By initiating an early warning system at a regional level, this program will be a crucial step towards strengthening the public health surveillance network in India and to mitigate future pandemic risks.

Partners in the Alliance for Pathogen Surveillance Innovations (APSI-India) include Tata Institute for Genetics and Society (TIGS) and National Centre for Biological Sciences (NCBS) in Bengaluru, CSIR-Institute of Genomics and Integrative Biology (IGIB) and the Ashoka University in Delhi-NCR, Pune Knowledge Cluster, CSIR-National Chemical Laboratory (NCL) and Indian Institute of Science Education and Research (IISER) in Pune and the CSIR-Centre for Cellular and Molecular Biology (CSIR-CCMB) in Hyderabad, along with other academic and clinical partners across the country.

Rare Genetic Diseases Research Summit (REDRESS)

The annual Rare Genetic Diseases Research Summit (REDRESS) 2023 was successfully held on the 24th and 25th of November. It was a remarkable event which brought together all stakeholders ranging from researchers, clinicians, students, policy makers, patient advocacy groups, funding agencies, industry, and start-ups on one platform to deliberate on the status of Rare genetic diseases in India and suggest way forward in addressing this challenge. The event was organised by TIGS and the Organization for Rare Diseases India. We were fortunate to have onboarded Indian Council of Medical Research (ICMR), The National Consortium for Research and Development on therapeutics for Rare Diseases as a knowledge partner for the event.

The event unfolded on a poignant note with the Keynote address by Dr. Meenakshi Bhat, Centre for Huma Genetics, Bengaluru on Rare Disease, Genetics and Society: One Family's Journey. The talk highlighted the insurmountable challenges that RGD afflicted patients & families grapple with daily. The talk reinforced the idea that progress in Rare Genetic Diseases (RGD) field is a collective effort requiring multidisciplinary collaboration, government support and a relentless commitment to make a difference in the lives of such individuals.

Sessions on RGD landscape and diagnostics in India, Basic and clinical research, and Enhancing RGD therapy and research environment were held over 2 days. Each session focused on showcasing cutting-edge research as well as the lived experiences narrated by patient advocacy groups.

The exchange of insights between researchers, government and patient advocacy groups is the uniqueness of REDRESS. The synergy between participants and speakers fueled a comprehensive understanding of RGD challenges, highlighting the need for effective strategies for diagnosis, treatment, and support.

REDRESS also included Panel discussions on the Rare Disease Policy and Insurance, where insights on the recent National Rare Disease Policy, 2021 were shared and the challenges to claim insurance when diagnosed with rare diseases was discussed.

Another area where stakeholders from industry and PAGs deliberated was on the Indian orphan drug market and required changes in this space. The event concluded with a session on 'Progress and the way Forward' that summed up the insights, stories, and future directions for collaborations.

Vibrant poster sessions were also held, with over 60 posters being presented by medical students, student researchers and startups highlighting their work on RGD's.

Group photo of the participants from REDRESS 2023

Partnerships

TIGS partners with many industries/start-ups and hospitals as well as with NGOs and patient groups across the city and beyond, to develop low-cost point of care diagnostics for infectious and inherited diseases, keeping patient needs at the forefront. To ensure stakeholder buy-in from the beginning, we enlist the support of government and municipal/administrative agencies to make a path for innovative research to reach its target, such as implementing disease surveillance and One health initiatives.

Below are the partnerships developed in 2023

TIGS and DBT – CDFD – April 18 2023

TIGS and DBT – Centre for DNA Fingerprinting and Diagnostics, Hyderabad sign an MoU to initiate projects in diagnostics, screening, and mRNA therapeutics for Rare Genetic Diseases in a cost-effective and accessible manner. From L to R: Dr. Ashwin Dalal, Head Diagnostics Division, DBT – CDFD, Dr. Rakesh Mishra, Director, TIGS, Dr. K. Thangaraj, Director, DBT – CDFD, Dr. Surabhi Srivastava, CSO, TIGS and Dr. Shivranjani Moharir, Senior Scientist, TIGS

TIGS – ICAR NIVEDI – April 27 2023

TIGS signed an agreement with ICAR - National Institute of Veterinary Epidemiology and Disease Informatics, Bengaluru to initiate projects on surveillance and monitoring of livestock diseases, including zoonotic diseases, Epidemiology and disease informatics. From L to R: Dr. Sanjay Lamba, Scientist, TIGS, Dr. Harvinder Kour Khera, Scientist, TIGS, Dr. Pankaj Gupta, Sr. Program Manager, TIGS, Dr. Rakesh Mishra, Director, TIGS and Dr. Baldev Raj Gulati, Director, ICAR NIVEDI and other scientists from ICAR – NIVEDI.

TIGS – EIPL May 17 2023

TIGS and Enhanced Innovations Private Limited signed an MoU to work on a diagnostics kit to detect Sars-CoV-2. The agreement was signed by Dr. Rakesh Mishra, Director, TIGS, and Mr. Prerit Mittal, EPIL along with Dr. Surabhi Srivastava (R), CSO, TIGS, Dr. Pankaj Gupta (L), Sr. Program Manager, TIGS and Dr. Harvinder Kour Khera (L2), Scientist, TIGS.

TIGS – Sepio Health - June 27 2023

TIGS and Sepio Health signed an MoU to work on insect and pest repellent clothing for farm use. The MoU was signed by Dr. Rakesh Mishra, Director, TIGS and Dr. Praveen K Vemula, Sepio Health.

TIGS – ICAR IISS – July 20 2023

TIGS and ICAR - Indian Institute of Seed Science, Mau signed an MoU to conduct joint collaborative research in seed science & technology and crop improvement. From L to R: Dr. Sanjay Singh, Director, ICAR – IISS and Dr. Rakesh Mishra, Director, TIGS.

TIGS – CUTN – July 25 2023

TIGS and Central University of Tamil Nadu,Thiruvarur signed an agreement to identify bacterial strains responsible for Scrub Typhus and to develop targeted treatment strategies. The MOU was signed by Dr. R Thirumurugan Registrar CUTN and Dr. Rakesh. K. Mishra, Director TIGS in the presence of Prof. M. Krishnan, Vice Chancellor, CUTN and staff from both institutions.

TIGS – NIAB – August 16 2023

TIGS and the National Institute of Animal Biotechnology, Hyderabad signed an MoU to work towards interdisciplinary research in tackling complex challenges in Animal Biotechnology with a specific focus on Zoonotic diseases. The agreement was signed by Dr. G. Taru Sharma, Director, NIAB and Dr. Rakesh Mishra, Director, TIGS in the presence of scientists and staff from both institutions.

TIGS – GBRC – September 1 2023

Gujrat Biotechnology Research Centre, Ahmedabad and TIGS signed an MoU to work on joint projects to address societal issues in healthcare and agriculture using biotechnology. The MoU was signed by Dr. Rakesh Mishra, Director, TIGS and Dr. Madhvi Joshi, Joint Director, GBRC, Ahmedabad.

TIGS – NBAIR – September 12 2023

TIGS joined hands with the ICAR - National Bureau of Agricultural Insect Resources (NBAIR), Bengaluru to harness the power of genetics and molecular biology and develop sustainable and eco-friendly methods for controlling insect pests in agriculture. The MoU was signed by Dr. Rakesh Mishra, Director, TIGS and Dr. S N Sushil, Director, ICAR – NBAIR.

List of collaborators

Academy of Scientific and Innovative Research, Ghaziabad
Institutional Collaboration to offer joint PhD program

Ashoka University, Sonipat
Co-operation in the field of RGDs

Bangalore Baptist Hospital, Bengaluru
Research and academic activities in the area of Infectious Diseases and RGDs

Bangalore Life Sciences Cluster, Bengaluru
Institutional Collaboration along with the other institutes of the cluster

Bruhat Bengaluru Mahanagara Palike, Bengaluru
Joint colloboration for surveillance of infectious diseases

Central University of Tamil Nadu, Thiruvarur
Vector-borne diseases from the Kaveri delta, developing Q-RTPCT based molecular assay

Centre for Cellular and Molecular Platforms, Bengaluru
Institutional Collaboration to work on various projects

Centre for Human Genetics, Bengaluru
Research and academic activites in the area of Infectious Diseases and RGDs

Christian Medical College, Vellore
Establish cellular models for disease mechanisms, translational research, collaborative research and training

CSIR – Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow
Joint collaboration in the areas of Vector control using organic aromatic oils

CSIR - Centre for Cellular and Molecular Biology (CCMB), Hyderabad
To run collaborative projects in Crop Improvement and Rare Genetic Disorders

DBT - Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad
Co-operation in the field of RGDs

DBT - Institute for Stem Cell Science and Regenerative Medicine, Bengaluru
Institutional Collaboration to work on various projects

DBT - National Institute of Animal Biotechnology, Hyderabad
Joint collaborative work on Infectious diseases in animals, Brucellosis, Leptospirosis, JEV, Toxoplasmosis

Dr. Shyama Naranga Foundation, Motor Neurone Disease (MND) Trust, Bengaluru
Organizing joint programs, scientific events and creating awareness about RGDs, such as MND/ALS.

Dystrophy Annihilation Research Trust, Bengaluru
iPSC from patient samples, to establish cellular models to understand DMD

Enhanced Innovations Private Limited, New Delhi
To develop a CRISPR-based integration system for detection of Covid-19

Gujarat Biotechnology Research Centre, Gandhinagar
To conduct joint research in the areas of Healthcare and Agriculture

ICAR- National Institute of Veterinary Epidemiology and Disease Informatics, Bengaluru
Surveillance and monitoring of livestock diseases, diagnostic and disease informatics

ICAR-Indian Institute for Seed Science (IISS), Mau
Joint collaborative projects on Crop Improvement and Mutation Breeding

ICAR-National Bureau of Agricultural Insect Resources (NBAIR)
To work on projects relating to Crop Improvement and Pest Management

IIT Banaras Hindu University (BHU), Varanasi
Joint research in disease biology and genomics - iPSC-based disease models

Institute of Bioinformatics and Applied Biotechnology (IBAB), Bengaluru
Joint Collaborative Research in Bioinformatics and Capacity Building

Integri Biotech, Mumbai
Synergizing artificial intelligence with mosquito surveillance for prevention of vector-borne diseases

JSS Medical College, Mysuru
Optimizing ex-vivo HSCs culture and gene editing

Kamineni Academy of Medical Sciences and Research Centre, Hyderabad
Joint research in Rare Genetic Disorders

Macquarie University, Sydney
Development of novel synthetic biology approaches to improve waste management, bioremediation, and biomanufacturing with Hermetia illucens

Magstik Private Limited, New Delhi
Joint collaboration in the field of Crop Improvement

National Centre for Biological Sciences, Bengaluru
Institutional Collaboration to work on various projects

Nordic Centre in India, New Delhi
Institutional Collaboration?? SAGE program

Organization for Rare Diseases India, Bengaluru
Organizing joint programs, scientific events and creating awareness about RGDs

Peptris Technologies, Bengaluru
AI based drug screening for SMA

Sepio Health, Bengaluru
Protective Fabric to Prevent Pesticide-induced Toxicity in Farmers

University of Agricultural Sciences, (UAS - GKVK), Bengaluru
Joint collaboration in the field of Crop Improvement

University of California, San Diego
Collaborative work in Crop Improvement - Investigating plant growth promoting compounds in crops

World Without GNE Myopathy, New Delhi
Research work on GNE Myopathy

Management and Administration

Director's Team

Rakesh K Mishra
Director

Surabhi Srivastava
Chief Scientific Officer

M K Sham Bharadwaj
Communications Coordinator

Hemanth Rao
Executive Secretary

Gottivedu Jyothirmai
Office Coordinator

Govardhan
Office Assistant

Program and Lab Management Team

Pankaj Gupta
Senior Program Manager

Kokilavani Varadharajan
Assistant Lab Manager

Namratha A
Senior Executive, Accounts

Sangeetha Ramdass
Executive, Procurement

Vinutha KS
Assistant Manager, Procurement

Vidyasagar YS
Lab Assistant

Human Resources Team

Naveen P
Senior Manager, HR

Likith Kumar V
Assistant Manager, HR

Medappa PK
Assistant Manager, IT

Finance and Accounts Team

Karthik Krishnan
Chief Financial Officer

Jyothi A
Assistant Manager,
Accounts

Hardik Solanki
Assistant Manager,
Accounts

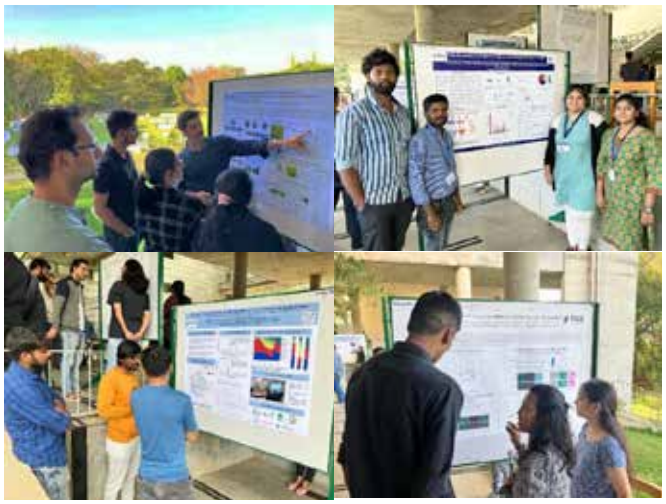
Pushpalatha V
Senior Executive,
Finance

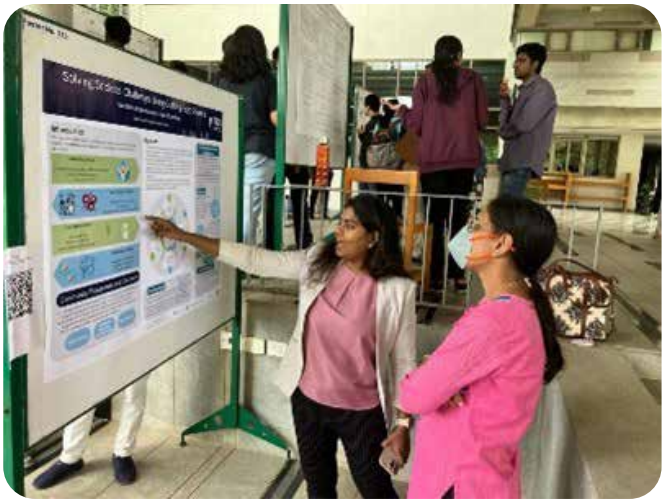
Knowledge Dissemination

Talks

Talk by Dr. Farah Ishtiaq on Understanding of Holobiome at Holobiome Symposium, Kolkata. January 8 2023

Talk by Dr. Rakesh Mishra at the Chromatin, RNA and Genome Conference at IISc Bangalore. January 10 2023





TIGS researchers presented their work at the NCBS Annual talks 2023. January 23 - 25 2023

Talk by Dr. Farah Ishtiaq on Wastewater surveillance and tracking emerging diseases using wastewater at the Remediation of wastewater symposium, Kolkata. February 19 2023

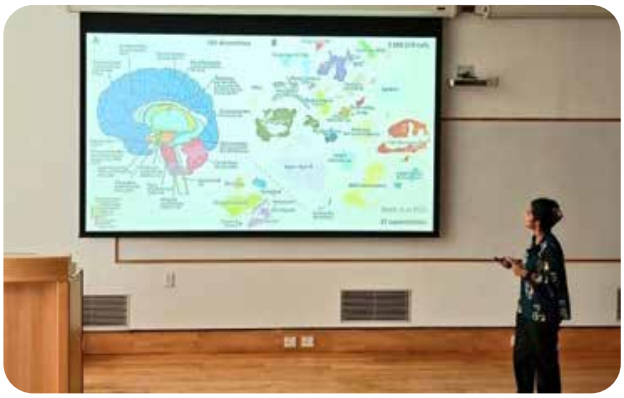
Talk by Dr. Surabhi Srivastava on Need for Data Dashboards for Tracking Emerging Diseases via Wastewater Surveillance at Centre for Cellular and Molecular Biology, Hyderabad. March 4 2023

Dr Sanjay Lamba delivered a talk at the Department of Mathematics, School of Advanced Sciences, Vellore Institute of Technology, Vellore on 'Wastewater-based Epidemiology – A Powerful Tool in Health Surveillance: From Data to Policy'. April 3 2023

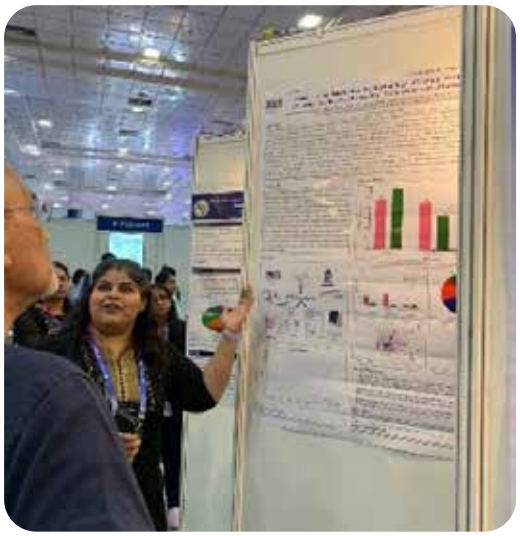
Dr. Farah Ishtiaq presented her work on the importance of Environmental Surveillance in India at C-CAMP InDx Round table on Avian Influenza - Outbreaks, Diagnosis and Surveillance. May 20 2023

Dr. Surabhi Srivastava spoke of the importance of wastewater surveillance at the LV Prasad Eye Institute, Hyderabad for the first AMR Frontline Workshop, an initiative by Superheroes Against Superbugs for the Alliance for Pathogen Surveillance Innovations (APSI-India). June 22 2023

Dr. Rakesh Mishra spoke at the Rare Diseases summit 2023, an initiative of IHW council. June 24 2023



Talk by Dr. Sonia Sen on the neurogenesis of neural stem cells at the Physics of Life 2023 conference. June 24 2023



Poster Presentation by Dr. Mansi Malik on 'Simultaneous detection and epidemiology of Dengue serotypes and Chikungunya in urban Bengaluru: A molecular surveillance approach.' at CIDSCON,13th Annual conference of clinical infectious diseases held at Chennai. 6 – 9 July 2023

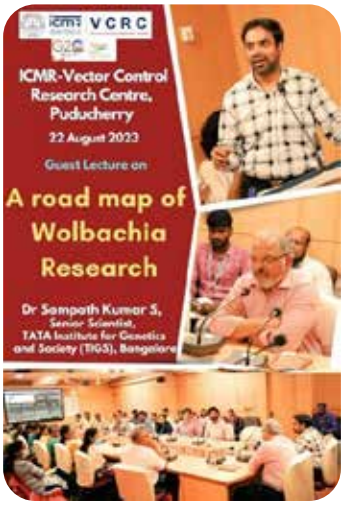
Talk by Dr. Rakesh Mishra on the approach of TIGS and BLiSC in disease surveillance at the Roundtable on One Health, Disease Surveillance and Pandemic Preparedness, G20-Chief Scientific Advisors Roundtable (CSAR) side event, organised by PKC at Pune. July 10 2023

Talk by Vasanth Thamodaran on Human Pluripotent stem cell model to study Pompe's disease at the 8th Annual international conference on 'Genetics and Genomics in Health and Disease' organised by the Board of Genetic Counselling India and University of Hyderabad. July 7-9 2023

Talk by Dr. Saveetha Meganathan on Practical Ethics and Clinical genetics in the context of vulnerable and disadvantaged populations at the 8th Annual international conference on 'Genetics and Genomics in Health and Disease' organised by the Board of Genetic Counselling India and University of Hyderabad. July 7-9 2023

Talk by Dr. Farah Ishtiaq on Environmental Surveillance of Bangalore wastewater bodies at Sugarrush with Science, organised by C-CAMP, Bengaluru. August 4 2023

Talk by Dr. Farah Ishtiaq on Island biogeography and population genomics to understand colonisation patterns in Anopheles stephensi organised by ICMR – NIMR and MERA India. August 18 2023



Talk by Dr. Sampath Kumar on A roadmap of Wolbachia research at ICMR – Vector Control Research Centre (VCRC), Puducherry. August 22 2023

Dr Farah Ishtiaq (first from R), was an invited Panellist at the Building Back Better Surveillance Systems Workshop organised by TIGS and GLC4HSR on 31st Aug 2023

Dr. Shivranjani Moharir (3rd from left) participated in the panel discussion on 'Integrated Surveillance Platforms For 'Onehealth' at the 'Building back better surveillance systems workshop organised by TIGS and GLC4HSR. September 1, 2023

Perspectives talk by Dr. Sonia Sen at the Developmental Biology Journal Club - September 13

Dr. Jay Prakash Shukla, participated as an expert member in the workshop on "PATHWAYS TO A DENGUE FREE-WARD" organised by OneHealth Bengaluru City (OHBC) consortium. September 15, 2023

Dr. Kamal K Malukani delivered a talk on the Biofortification of rice using mutation breeding at the 20th International symposium on rice function genomics organized by the University of Agriculture Sciences, Bengaluru (3-5 Nov 2023). November 4 2023.

Panel Discussion on Demystifying Vaccines led by (from L to R) Dr. Arati Ramesh,TIGS, Dr. Monalisa Chatterji, Sekkei Bio, Dr. Swetha Raghavan, NCBS, Dr. Rajesh Iyer, TIGS, Dr. Chitra Pattabiraman, IDRF. November 7, 2023.

Dr. Arati Ramesh giving an overview on mRNA biology and its history. November 7, 2023

Presentation by Dr. Surabhi on "APSI: A Pan India Consortium for monitoring pathogens via wastewater surveillance" at the International Conference Towards a Global Wastewater Surveillance System for Public Health, Frankfurt, Germany. November 17th 2023

Other talks

1. Dr. Sanjay Lamba delivered a talk on **Epidemiology with R** at the 'Workshop on Statistical Modeling with R' held at the Indian Institute of Information Technology, Allahabad, India on January 14, 2023.
2. Dr. Sanjay Lamba was invited to give talk at the 'Workshop on Fundamentals of Mathematical Biology' held at the Indian Institute of Information Technology, Allahabad, India. He spoke on **SARS-CoV-2 Infection Dynamics and Genomic Surveillance Reveals Early Variant Transmission in Urban Wastewater.** May 11, 2023
3. Dr. Harvinder Kour Khera gave a talk on **'Community based adaptions for climate resilience in India: A pathway to achieving sustainable development goals'** at the National Seminar organized by Government Degree College for Women, Kathua (JKUT). 19th May 2023
4. Dr. Sanjay Lamba acted as a Resource Person and delivered a talk on **SARS-CoV-2 Infection Dynamics and Genomic Surveillance to Detect Variants in Wastewater – A Longitudinal Study in Bengaluru,** India at the 'Five-day Virtual Faculty Development Program on Data Analytics Software in Real World Problems' held at the Division of Mathematics, School of Advanced Sciences, Vellore Institute of Technology, Chennai. May 3, 2023.
5. Dr. Sanjay Lamba was invited to talk on **'Mathematical Modeling of Regulation of Nitrogen Metabolic Pathway'** at the "Three-day Virtual Faculty Development Program on Introduction to Mathematical Biology: From Theory to Applications" held at the Department of Mathematics, School of Advanced Sciences, Vellore Institute of Technology, Vellore on June 7, 2023.
6. Dr. Farah Ishtiaq was invited as a speaker at USAID RISE National-level NGS Networking Workshop. She delivered a talk on **Genomic Surveillance of Pathogens in Wastewater: A smart tool beyond COVID-19.** July 13 - 14 2023
7. Dr. Mansi Malik delivered a talk on **'Molecular surveillance and epidemiology of Scrub typhus from patients presenting acute febrile illnesses in Bengaluru',** India' at the Asia Pacific meeting for Rickettsial diseases, Mahabalipuram, Chennai. September 23 - 24 2023
8. Dr. Farah Ishtiaq was an invited speaker at the Lakshadweep Knowledge Summitt, IIT Gandhinagar. She delivered a talk on **Island Biogeography and Human Practices Drive Ecological Connectivity in Urban Mosquito Species.** December 4 – 6 2023
9. Dr. Farah Ishtiaq was invited to speak on **'Role of Genomic Surveillance in Community Health Using Wastewater'** at the Society for Biologists in Chemistry, BITS Pilani, Goa: December 18 – 20 2023

Awards and Recognitions

Best turbo talk award to Dr. Mansi Malik at the 15th Conference on Vectors and Vector borne diseases held at Goa University. February 15 - 17 2023

Dr. Kamal Kumar Malukani received the second-best poster award at the International Conference on Current Trends And Future Prospects Of Plant Biology (CFTPPB-2023) organized by the University of Hyderabad. February 23 – 25, 2023

Dr. Farah Ishtiaq was featured among the 35 young women scientists as Future Hopes in Vigyan Vidushi: 75 Women Trailblazers of Science published by VigyanPrasar

Here's the full list of young women making significant contributions to science: https://bit.ly/3zEPRQp

Dr. Shivranjani Moharir – Secured the India Alliance Early Career Fellowship 2022 – 2023

Dr. Pankaj Gupta received the NCURA National Conference Award during their 65th Annual meeting at Washington D.C. USA.

Dr. Mansi Malik Won first prize for the oral presentation as well as the best talk award in the category of molecular virology for her work on 'A novel molecular assay to detect various pathogens from clinical samples presenting undefined pyrexia' at MICROCON 2023, the 46th Annual conference of Indian association of medical microbiologists at Lucknow from November 23 - 26 November 2023.

Webinars and Podcasts

Surveillance of Vector Borne Diseases: Exploring Newer Horizons (Webinar) – June 28 2023

Vector-borne diseases have plagued human lives for centuries now. Recent advances in molecular biology, and genetics have enabled understanding of infection dynamics of various pathogens causing morbidity and mortality worldwide. Disease control and prevention involves both vector management and clinical alleviation and thus, surveillance and ecological studies play a crucial role in knowing the hotspots of both the vector and the infection in time and space. Novel methods for indexing vector population and advanced diagnostics and therapeutics to timely detect and treat affected population is the need of the hour.

This webinar 'Surveillance of Vector-borne diseases: Exploring newer horizons' focus on the need and methods of surveillance of vector-borne diseases. We were glad to have Dr. Pragya Yadav, Scientist-F and Group Leader, Maximum Containment Facility and Dr. Ashwani Kumar, Director, ICMR-Vector Control Research Centre (VCRC), Puducherry take part in this webinar to provide valuable insights.

Snapshot of speakers and scientists from TIGS during the webinar

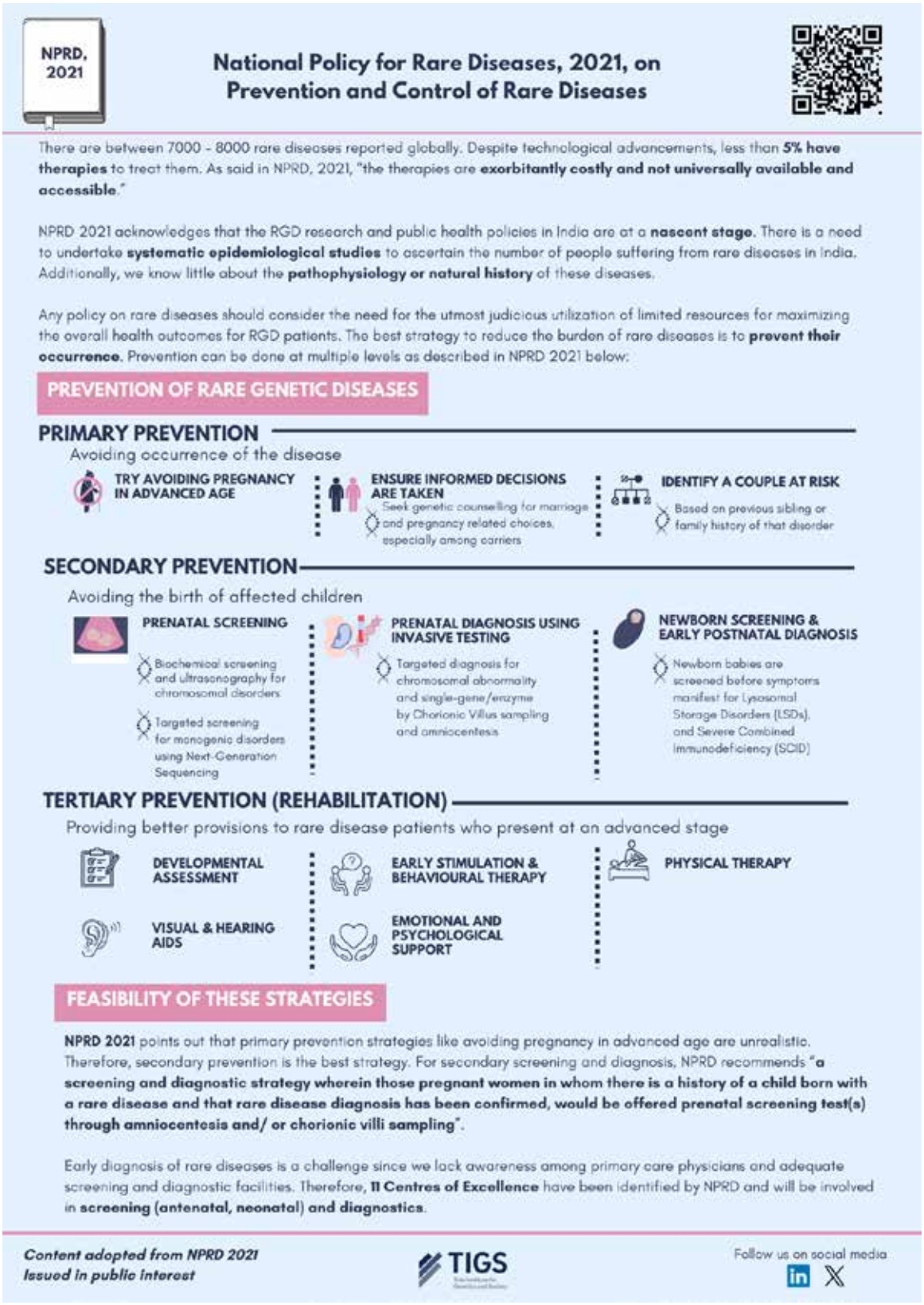
Demystifying Rare Genetic Diseases (Podcast) - June 28 2023

Conversations@TIGS is back with a new series: "Demystifying Rare Genetic Diseases". Through this series, we aim to increase awareness about Rare Genetic Diseases and curate factual knowledge through conversations with experts.

In this episode, Dr Rakesh Mishra, Director, TIGS talks about the challenges of Rare Genetic Diseases in the Indian context, the urgency of accelerating diagnostics and therapeutics for these conditions and the emerging trend in the field.

NPRD, 2021 Resources

National Policy for Rare Diseases (NPRD), 2021, is the latest policy addressing the challenges of rare diseases in India. Through our Demystifying Rare Genetic Diseases project, we are shining a spotlight on the key points, strategies and recommendations mentioned in NPRD, 2021.

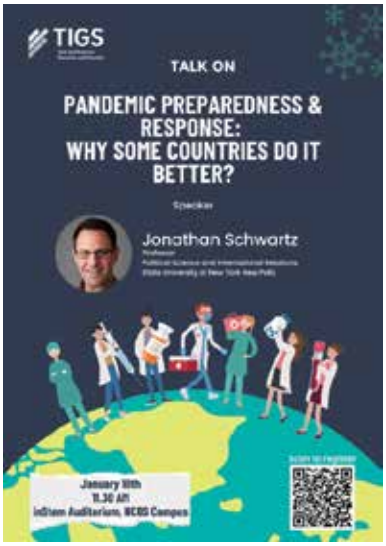


Workshops and Public Lectures

Talk by Dr. Jonahan Schwartz – January 10 2023

Why do some jurisdictions more effectively respond to crises than others? Dr. Jonathan Schwartz talk focused specifically on pandemics, first reviewing alternative explanations for relative pandemic response effectiveness before delving into the potential benefits arising when local community actors work in concert with the state. Using Collaborative Governance and One Health literatures, the talk described the underlying arguments that pandemic response capacity is best fostered by building long-term collaboration between state and community actors at the local level.

Dr. Jonathan Schwartz, a Professor of Political Science at New Paltz, State University of New York has been conducting research on pandemic preparedness and response in East Asia for almost 20 years now. We were pleased to host him at TIGS and deliver a talk titled 'Pandemic Preparedness and Response: Why some countries do it better?



Talk by Prof. Anil Koul - March 21 2023

Prof. Anil Koul, Professor in Translational Discovery at the London School of Tropical Medicine and Hygiene visited TIGS and delivered a talk on 'Discovery of novel therapeutics against tuberculosis and other neglected diseases - Role of innovation in public health'. The talk focused on the role of public health R&D to address some of major public health challenges, including drug resistant tuberculosis. The discovery of Bedaquiline has helped us in addressing one of the serious public health issues of multi-drug-resistant tuberculosis. Similarly, we need to tackle neglected diseases like dengue and other future pandemic threats through innovation and proper access framework.

Dr. Anil Koul on "Discovery of novel therapeutics against tuberculosis and other neglected diseases - Role of innovation in public health" at BLiSC campus. March 21 2023

Talk by Dr. Soumya Swaminathan - May 19 2023

We were honoured to host Dr. Soumya Swaminathan, Chairperson, M S Swaminathan Research Foundation (MSSRF), Chennai and Ex-Chief Scientist, WHO to TIGS for a short visit. As part of it, she interacted briefly with our scientists about the work being carried out at TIGS and gave an inspiring and insightful talk on 'Lessons from the Pandemic for Science and Public Health' at the Bangalore Life Sciences Cluster campus.

Dr. Soumya Swaminathan delivering her talk on Lessons from the Pandemic for Science and Public Health at BLiSC campus. 19 May 2023

Talk by Dr. Gagandeep Kang - June 20 2023

Dr. Gagandeep Kang, renowned physician-scientist of India, and a Professor at the Chrisitan Medical College, Vellore visited TIGS and had discussions with our scientists. As part of the visit, she delivered a talk on "Next targets for Vaccines", where she highlighted a few diseases which are currently posing a threat to humans and the need to target them using vaccines.

Talk by Dr. Reena Kartha - June 28 2023

Drug repurposing involves identifying alternative uses for approved or investigational drugs beyond their initial medical indications. This strategy accelerates drug development and minimizes the risk of failure. Moreover, it can uncover novel mechanisms of action, targets, and pathways for further exploration. Dr. Reena Kartha illustrated this approach with pertinent examples from her laboratory's studies on inherited metabolic disorders during her talk at TIGS.

We were pleased to host Dr. Reena Kartha, Associate Professor of Experimental and Clinical Pharmacology at the University of Minnesota, USA visit TIGS and share valuable insights into Drug repurposing for inherited metabolic disorders.

Talk by Dr. Madhvi Joshi - June 30 2023

Dr. Madhvi Joshi, Scientist and Joint Director, Gujarat Biotechnology Research Centre visited TIGS campus and gave a talk on 'Leranings from Past: Extending wastewater-based epidemiology beyond COVID'. It was an insightful session on wastewater based epidemiology during COVID19 and how those learnings can be used to generate baseline data for emerging contaminants (pathogens and key pollutants) for future use.

Sustainability Ambassadors Global Exchange (SAGE) Program

We were excited to host the senior and junior ambassadors of the Sustainability Ambassadors Global Exchange (SAGE) Program, Orgnanised by Echo Network, Nordic Centre in India and TIGS. The ambassadors had engaging and interactive sessions with our scientists on our research programs, overview about TIGS and how we choose problems to address them using cutting edge science and technology. They also got to visit our facilities and interact with their teams to know about the work we do and why we do it.

SAGE program ambassadors visit to TIGS. August 8 – 9 2023

Building Back Better Surveillance Systems
August 31 – September 1 2023

Surveillance plays a pivotal role in public health, serving as a crucial epidemiological tool. It entails the continuous, systematic collection, analysis, and interpretation of health-related data. These data serve as an early warning system, and to identify potential outbreaks that could escalate into public health crises. Surveillance permits the assessment of intervention impact, aiding in tracking progress towards predefined goals. Lastly, it guides priority-setting and informs public health policies.

In humanitarian crises, the risk of infectious disease transmission and other health emergencies intensifies. A robust disease surveillance system is indispensable for swiftly detecting outbreaks, preventing widespread dissemination, and saving lives, particularly in conflict zones or post-natural disaster scenarios.

In today's world, amid escalating global health threats, such as pandemics, epidemics and outbreaks public health surveillance is paramount. The data on disease patterns, health indicators and overall public health system performance, which empowers civic bodies and health authorities to identify risks, detect emerging threats, and implement timely public health interventions.

The two-day workshop, "Building Back Better Surveillance Systems." Co-hosted by the Global League for Communicable Diseases Surveillance and Response (GLC4HSR) and the Tata Institute for Genetics and Society (TIGS), marks a significant step towards strengthening public health surveillance systems in a post-pandemic era. It seeks to dive deep into surveillance systems through the perspective of lessons gleaned from recent pandemics.

The workshop entailed engaging presentations from groups leveraging newer surveillance methods, in-depth panel discussions exploring the strengths and weaknesses of these approaches, and collective efforts towards building better surveillance systems that can seamlessly integrate technological innovations.

Participants from the 2-day workshop on 'Building Back Better Surveillance Systems'. August 31 and September 1 2023

Insectary workshop on Mosquitoes Up close: Exploring Biology to Practical Techniques. November 28 – 30 2023

The Insectary facility at TIGS successfully organised a 3-day workshop, 'Mosquitoes Up close: Exploring Biology to Practical Techniques' from November 28 – 30 2023. The aim of the workshop was to provide a comprehensive and unique blend of invited talks and practical hands-on sessions on mosquito biology, collectont, taxonomy and rearing. The workshop also ensured that participants get a holistic view of the past and current advances in Vector research, which would aid the participants in many ways to explore their journey in the mosquito world.

Highlights of the workshop

1. Engaging sessions led by experts, offered insights into cutting-edge research in mosquito biology and vector research.
2. Practical hands-on experiences provided participants with valuable skills for their mosquito studies.
3. Networking opportunities that facilitated meaningful connections among professionals and participants in the field of entomology.

Snippets from the workshop November 28 – 30 2023.

Publications

1. **Chaitali Ghosh, M. Soumya, Naveen Kumar, Chethan Kumar R, Soumya Gopal Joshi, Sampath Kumar, Suresh Subramani, Sunita Swain** Aeroplane wing, a new recessive autosomal phenotypic marker in the malaria vector, Anopheles stephensi Liston, Heliyon, Volume 10, Issue 1, 2024, DOI: https://doi.org/10.1016/j.heliyon.2023.e23693.

2. **Farah Ishtiaq,** Wastewater-based surveillance of vector-borne pathogens: a cautionary note, Trends in Parasitology, December 2023, DOI: https://doi.org/10.1016/j.pt.2023.12.005.

3. **Stanley SM, Khera HK,** Chandrasingh S, George CE, **Mishra RK.** A comprehensive review of dengue with a focus on emerging solutions for precision and timely detection. Int J Biol Macromol. 2024 Jan;254(Pt 1):127613. DOI: 10.1016/j.ijbiomac.2023.127613. Epub 2023 Oct 22.

4. Kour, N., Singh, J., **Khera, H.K.** Increasing Prevalence of Antibiotic-Resistant Genes in Wastewater: Impact on Public Health. In: Shah, M.P. (eds) Genomics of Antibiotic Resistant Bacteria in Industrial Wastewater Treatment. Springer, Cham. DOI: https://doi.org/10.1007/978-3-031-44618-4_5

5. **Khera HK, Mishra R.** Nucleic Acid Based Testing (NABing): A Game Changer Technology for Public Health. Mol Biotechnol. 2023 Sep 11. DOI: 10.1007/s12033-023-00870-4

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Events

Dr. Jonahan Schwartz during his talk on Pandemic preparedness and response: Why some countries do it better. January 19 2023

Dr. Rakesh Mishra and Dr. Farah Ishtiaq from TIGS were part of the One Health National agenda meeting held at IISc, Bengaluru. February 10, 2023

TIGS members participating in 2023 Racefor7 event. February 28 2023

Racefor7 is an annual event organised to raise awareness on Rare genetic diseases and to highlight the diagnostic and treatment challenges of patients and their families.

On National Science Day 2023, students of Biotechnology from St. Josephs University, Bangalore visited TIGS and DBT – inStem. Our scientists interacted with them on the importance of science and how it can have a significant impact on human health and agriculture. The students also had a tour of our research labs and facilities. February 28 2923

Group photo from the official BeST cluster launch at Bengaluru with all collaborating partners. 3rd March 2023

Scientists from TIGS visited the Tata Digital Nerve Centre (DiNC) at Kolar, Karnataka. DiNC is a unique and innovative delivery model designed to connect, communicate, coordinate, and deliver care by leveraging people, infrastructure, and a robust digital platform. It connects the sub centre, primary health centre and the district hospital to provide an integrated and well-connected health care system. March 7 2023

Dr. Soumya Swaminathan visited TIGS and interacted with our scientific staff. A few glimpses from her visit. May 19 2023

Glimpses from the visit by Dr. Gagandeep Kang at BLiSC campus. June 20 2023

Dr. Reena Kartha delivering the talk on Drug repurposing for inherited metabolic disorders during her visit to TIGS. June 28 2023

Dr. Madhvi Joshi's talk on Learnings from Past: Extending wastewater-based epidemiology beyond COVID. June 30 2023

Sustainable Ambassadors Global Exchange (SAGE) program ambassadors visit to TIGS. August 8 – 9 2023

We were glad to host Dr. Arvind Virmani, Member, NITI Aayog to TIGS and Bangalore Life Sciences Cluster (BLiSC) campus. Interactions were held on how synergistic associations between the four cluster institutions is fostering innovations and research in the campus. As part of the visit Dr. Virmani also visited few of our research facilities to showcase or work at TIGS.

Few glimpses from Dr. Arvind Virmani's Visit to BLiSC campus. August 24 2023

Few Glimpses from the 2 day workshop on Building back better surveillance systems, organised by Access Health International and Tata Institute for Genetics and Society on August 31 and September 1 2023.

From L to R: Dr. Uma Aysola, Director, Communications, Relations, & Partnerships, ACCESS Health International, Dr. N Krishna Reddy, CEO, ACCESS Health International, Dr. Anil Kumar, Principal Advisor, National Centre for Disease Control, Union Ministry of Health & Family Welfare. Dr. Rakesh Mishra, Director, TIGS, Dr. K V Trilok Chandra, Special Commissioner (Health),Bruhat Bengaluru Mahanagara Palike (BBMP), Bengaluru and Dr. Farah Ishtiaq, Principal Scientist, TIGS during the Inaugural session of the workshop. August 31 2023.

From L to R: Dr. Rakesh Mishra, Director TIGS, Dr. Sindura Ganapathi, PSA Fellow, Office of PSA, GoI, Dr. Priya Nagaraj, CEO, Pune Knowledge Cluster. Dr. Madhvi Joshi, Joint Director, GBRC, Ahmedabad, Dr. Farah Ishtiaq, Principal Scientist, TIGS during the session on 'Wastewater surveillance and other applications of molecular technologies in surveillance'. August 31 2023

From L to R: Dr. Arindam Ray, Senior Program Officer (Vaccine Delivery), Bill and Melinda Gates Foundation, Dr. Harpreet Singh, Scientist and Head, Division of Biomedical Informatics & Chief Data Officer, Indian Council of Medical Research and Dr. Raghu Dharmaraju, President, ARTPARK during the session on 'Data-driven surveillance and other applications of digital technologies in surveillance'. September 1 2023

From L to R: Dr. Sanjiv Kumar, Chairman and Managing Trustee, Three Domain Health Leadership Foundation, Prof. Uma Ramakrishnan, Professor, National Centre for Biological Sciences, Bengaluru, Dr. Anil Kumar, Principal Advisor, National Centre for Disease Control, Union Ministry of Health & Family Welfare, Dr. Shivranjani Moharir, Senior Scientist, Tata Institute for Genetics and Society, Dr. Sudipto Roy, Scientist E, Indian Council of Medical Research, Dr. Vijay Yeldandi, Vice President (Medical Education and Professional Development), Continental Hospitals, Hyderabad during the session on integrated surveillance platforms for One health' September 1 2023

From L to R: Dr. Krishna Reddy N, ACCESS Health International, Dr. Anil Kumar, Principal Advisor, National Centre for Disease Control, MoHFW, Ms. Asha Jyothi,Policy Catalyst, Swasti, The Health Catalyst and Dr. Yoong Khean Khoo Scientific Officer, Duke NUS Centre for Outbreak Preparedness and Centre of Regulatory Excellence, Singapore during the session on integration of new age methods: A governance and policy perspective. September 1 2023

Students of Biotechnology from lady Doak women's college, Madurai visited NCBS and TIGS campus, they toured various research facilities and engaged with scientists and staff working in the areas of insect behaviour and tissue culture facilities. September 29 2023

Glimpses from the Rare Genetic Diseases Research Summit (REDRESS) 2023. 23rd – 24th November 2023

From L to R - Dr. B S Charan (Online), Add Director General, Directorate of Health Services, Government of India Mr. Prasanna Shirol, Executive Director, ORDI and Dr. Rakesh Mishra, Director TIGS during the inaugural session for REDRESS 2023

A few key organisers of REDRESS 2023. From L to R - Dr. Runa Hamid, TIGS, Mr. Samir Sethi, ORDI, Dr. Nabendu Sekhar Chatterjee, ICMR, Dr. Rakesh Mishra, TIGS, Mr. Prasanna Shirol, ORDI and Dr. Saveetha Meganathan, TIGS

Dr. Meenakshi Bhat, Professor, Mazumdar Shaw Research Chair, Centre for Human Genetics, Bengaluru delivered the Keynote address on 'Rare Disease, Genetics and Society: One Family's Journey'.

Dr. Meenakshi Bhat, Professor, Mazumdar Shaw Research Chair, Centre for Human Genetics, Bengaluru with Dr. B K Thelma, University of Delhi

Speakers of the session RGD landscape and Diagnostics in India. From L to R Dr. Swarkar Sharma, University of Jammu, Dr. Subasree Ramakrishnan, NIMHANS, Bengaluru, Dr. Amlin Shukla, ICMR, New Delhi, Dr. Ashwin Dalal, Diagnostics Division, DBT - CDFD, Hyderaba, Mr. Vikas Bhatia, MERD India Foundation and Dr. Ratna Dua Puri, Sir Ganga Ram Hospital, New Delhi,

Speakers of the session Basic and Clinical Research - I. From L to R Dr. Srinivasrao Repudi, DBT - inStem, Bengaluru, Dr. Karthik Bharadwaj, CSIR - CCMB, Hyderabad, Dr. R V Shaji, CMC Vellore, Dr. Binukumar B K, CSIR IGIB Delhi, Dr. Anju Shukla, KMC, Manipal, Dr. Radha Rama Devi, Rainbow Hospitals, Dr. Aravind Ramanathan, DBT - inStem, Bengaluru and Dr. Rakesh Mishra, TIGS, Bengaluru

Panelists of the discussion on Rare Genetic Disease Policy and Insurance. From L to R Prof. Viswanath Pingali (online), IIM Ahmedabad, Dr. Neerja Gupta (online), AIIMS New Delhi, Mr. Prasanna Shirol, ORDI, Dr. Sanjeev Jain, NIMHANS Bengaluru, Dr. Shakila Shakila N, DoHFW, Government of Karnataka and Mr. Nabendu Das, Centogene

Speakers of the session Basic and Clinical Research – II. From L to R Ms. Parvathy Krishnan (online), Krishnan Family Foundation, Dr. Alka Chaubey (online) Bionano Genomics, Inc., Dr. Pratibha Bhalla (online) University of Texas Southwestern Medical Center, USA, Dr. Ravi Manjitya, JNCASR, Bengaluru and Dr. Rakesh Mishra, TIGS.

Speakers of the session Enhancing RGD Therapy and Research Environment. From L to R Dr. Anuranjan Anand, JNCASR, Bengaluru, Dr. Ajay Singh (online), Gennova Biopharmaceuticals, Pune, Ms. Kirtida Oza, Sjogrens's India, Dr. Nabendu Sekhar Chatterjee, Indian Council of Medical Research, New Delhi, Dr. Rita Sarin, Intellectual Property Rights Consultant, Ms. Moumita Ghosh, CureSMA foundation of India and Dr. Sadhna Joglekar, Novartis India, Hyderabad

Panelists of the discussion on Indian Orphan Drug Market: Opportunities. From L to R Prof. K Thangaraj (Session chair) CSIR - CCMB, Hyderabad, Mr. Samir Sethi, Indian Rett Syndrome Foundation, Dr. Charu Gautham, IQVIA, Ahmedabad, Dr. Anil Kukreja AstraZeneca, Bengaluru, Ms. Sharmila Mulpur, National Insurance Company, Bengaluru, Mr. Parameshwaran Sitaram, Sanofi Specialty Care, New Delhi, Dr. Monika Pahuja ICMR HQ, New Delhi and Mr. Sri Harsha, Indian Prader-Willi Syndrome Association.

Speakers of the concluding session Progress and way forward in RGD Field. From L to R Prof. Vijay Chandru, NCBS, Dr. Deepa Bhat, JSS Mysuru, Dr. Thanngaraj K, CSIR - CCMB, Hyderabad, Dr. B K Thelma, University of Delhi and Dr. Radha Rama Devi, Rainbow Hospital, Hyderabad.

Few glimpses from the poster sessions

Mosquitoes Up close: Exploring Biology to Practical Techniques - Participants attending lectures, learning from field visits, and conducting hands on experiments in the lab, along with the Insectary team. November 28 – 30 2023

#TIGS in the News

Why environmental surveillance for avian influenza is vital

PREMIUM

Birds infected with avian influenza virus shed large quantities of virus in their faeces as well as in their saliva and nasal secretions for about a week

February 18, 2021 08:45 pm | Updated 08:45 pm IST

FARAH ISHTIAQ

BBMP to set up Metropolitan Surveillance Unit to identify potential disease outbreaks

The Hindu Bureau
BENGALURU

As part of the BBMP's public health strategy, the civic body is working on set-

The unit that will be fully funded by the Centre will help the civic body in putting in place a structured

reporting units - private and the government," he said.

The BBMP has already set up a 'One Health Cell' to address public health

Industry · 2 Min Read

COVID-19 in endemic stage, still need to monitor viral load, new variant: Top expert

COVID-19 in endemic stage, still need to monitor viral load, new variant: Top expertwas more significant than the third wave and would have had a big problem. However, it did not

A Bengaluru group is knee-deep in wastewater—looking for secrets on future diseases

Ecologist Farah Ishtiaq and her team are tracking viruses and diseases through Bangalore's underbelly. Their wastewater-based epidemiology project is catching attention.

nature > nature india > comment >

SANDHYA RAMESH | 1 March, 2023 13:42 pm IST

COMMENT | 15 June 2023

Ignoring wastewater is a wasted opportunity to improve disease response

As the COVID-19 emergency status fades, sewerage surveillance should be maintained

Farah Ishtiaq

From sewer to safety: top scientist moots wastewater monitoring in new STPs

V. Geetanath
HYDERABAD

Telangana government's decision to set up 31 Sewerage Treatment Plants (STPs) for dealing with wastewater generated by

the population," says Tata Institute for Genetics and Society director Rakesh Mishra.

Used for detecting polio

The scientist, a former di-rector of CSIR-Centre for

priate measures if someth-ing unusual is noticed in the samples.

"Wastewater monitor-ing has become important because treated water from the outlet is often used for irrigation, planta-

"The biggest advantage is that it is cheap, non in-trusive, won't disturb any person, and will give a real reflection of the health sta-tus as we found out during COVID. The protocols have turned out robust and di-

Mosquito surveillance must include non-residential urban environments

In contrast to WHO's door-to-door larval surveillance protocol, the study found environments with non-residential locations too harbour ideal breeding sites

June 24, 2023 09:20 pm | Updated June 25, 2023 03:47 pm IST

R. PRASAD

COMMENTS SHARE

Tata Institute for Genetics and Society inks MoU with CUTN

July 26, 2023 07:10 pm | Updated 07:10 pm IST – TIRUVARUR

THE HINDU BUREAU

Top institutes ink pact to keep watch on zoonotic diseases

National Institute of Animal Biotechnology, Tata Institute of Genetics and Society join forces to study animal diseases of viral, bacterial origins; collaboration likely to bolster 'One Health' concept

August 28, 2023 12:11 am | Updated 04:46 pm IST – HYDERABAD

Wastewater study detects a large, silent wave in Bengaluru

R. Prasad

The XBB.1.16 Omicron recombinant first detected in India on December 25, 2022 has be-

from 28 sewage treatment plants spread across Bengaluru by the Tata Institute for Genetics and Society (TIGS) has revealed the true extent of

toms are obvious. In many instances, the infected remain asymptomatic.

Wastewater testing is an active form of environmental

RESEARCH HIGHLIGHT | 14 August 2023

Discarded storage containers may be aggravating Bengaluru dengue outbreaks

Unplanned waste disposal makes fertile breeding ground for *Aedes* mosquito larvae

BF.7 variant of COVID-19 not worrisome for India, assures senior scientist Rakesh Mishra

Rakesh Mishra, Director, Tata Institute for Genetics and Society, Bangalore, however cautioned that wearing face masks and avoiding unnecessary crowds is always advisable

healthpost

WEDNESDAY • 13 SEPTEMBER, 2023

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Interview: Dr Rakesh Mishra

Our research is aimed at making treatment for rare genetic diseases affordable

Gunjan Sharma | Monday, May 1, 2023

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Design and Illustrations by: The Pen & Mouse, www.penandmouse.in

Tata Institute for Genetics and Society
Bangalore Life Science Cluster (BLiSC), inStem Building, NCBS Campus,
GKVK Post, Bellary Road, Bengaluru-560065, India
T: +91 80 6194 8158 | E: info@tigs.res.in | www.tigs.res.in