TIGS

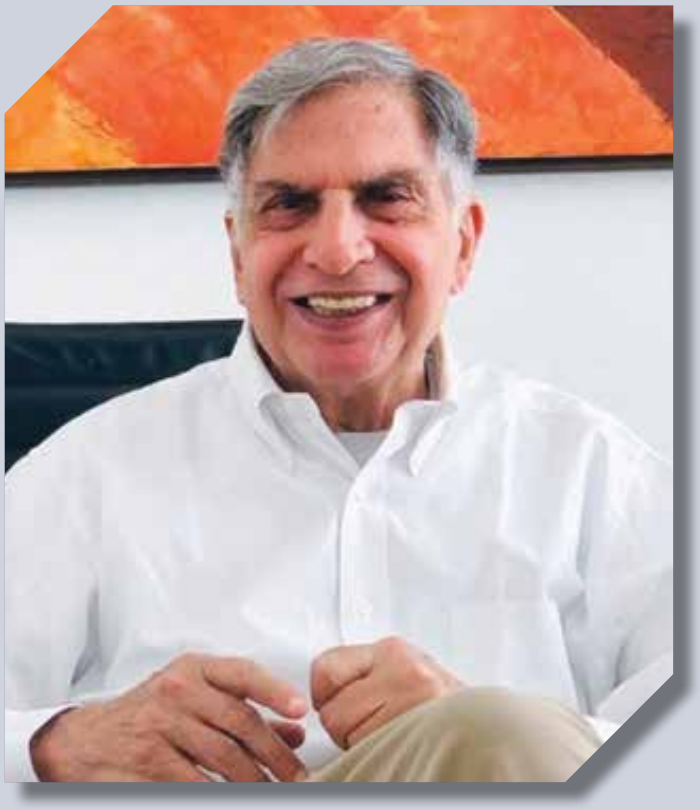
Tata Institute for Genetics and Society

Annual Report 2024

A tribute to our founder

Mr. Ratan N Tata

(1937-2024)



Mr. Ratan N Tata's visionary leadership and deep commitment to science and society laid the foundation for the Tata Institute for Genetics and Society (TIGS). He believed in the power of translational research to address humanity's most pressing challenges. His passion for applying advancements in genetics and genomics to improve healthcare, agriculture and food security has been the guiding force behind our work. Mr. Tata envisioned TIGS as a bridge between cutting-edge science and real-world impact, where research would not remain confined to the lab but would reach the people who need it the most. He recognised the power of innovation and entrepreneurship. Under his stewardship, the institute has pursued innovations in point-of-care diagnostics, state-of-the-art therapeutics and crop improvement, aligning with his lifelong commitment to socially meaningful work.

We at TIGS will always be grateful for his belief in our mission and unwavering support. As we carry his vision forward, we remain dedicated to making science work for society, ensuring that his legacy of impact-driven innovation endures.

Manoj Kumar
Managing Trustee

TIGS
Tata Institute for Genetics and Society

2024

ANNUAL REPORT

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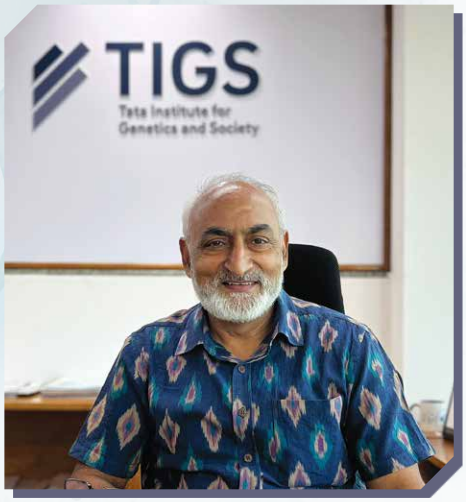
Chief Scientific Officer

Contents

Director's Message



It is with immense pride that we present the Annual Report of the Tata Institute for Genetics and Society (TIGS), reflecting a fast-paced year of transformative progress. A powerful reminder of what can be achieved through collaboration and innovation, this year has underscored our commitment to leveraging cutting-edge science and technology to tackle pressing challenges in human health and agriculture. We have taken decisive steps towards translating research into scalable, real-world applications. From novel diagnostic tools and therapeutic strategies to breakthroughs in disease surveillance and crop resilience, our teams have been at the forefront of transforming fundamental research into applied solutions.

Our Infectious Diseases program has been a cornerstone of pandemic preparedness and One Health initiatives. On the inherited diseases front, our Rare Genetic Disorders program is focused on developing novel diagnostic solutions, India-specific disease models, and filling the gap in accessible information resources, offering hope for affordable therapies and better management options. Our Crop Improvement program has achieved a crucial milestone where our disease-resistant rice varieties are ready for open field trials. We have also expanded our genome editing approach to develop better varieties of millets and pulses.

Our technology platforms - diagnostic development, mRNA therapeutics, cell based therapeutics & 'disease in a dish' models, crop genome editing and NuTIGS platform for nutritional profiling - have significantly matured to deliver solutions in the fastest possible time and meet diverse challenges. In order to take laboratory findings to the society rapidly, we have created a pipeline of technology evaluation and implementation operating seamlessly across all programs. We have also been actively working towards bridging the gap between research and public awareness. These efforts highlight our commitment to scientific excellence with societal relevance, ensuring that innovation is accessible and impactful.

The privilege of being part of the Bangalore Life Sciences Cluster (BLiSC) and the support from our stakeholders, partners, and the broader scientific community has been instrumental in helping us come a little closer to realizing our vision.

As we look to the future, we remain guided by our mission to harness the transformative power of science for societal impact. We express our heartfelt gratitude to all who have contributed to TIGS's journey, and we look forward to another year of innovation, collaboration, and meaningful contributions to humanity.

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.

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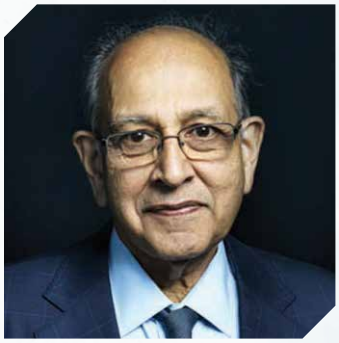

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Scientific Advisory Board

TIGS has a biannual review with the Scientific Advisory Board (SAB), consisting of leading experts in the field, academic as well as from industry. The board meets 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.

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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. TIGS is a unique initiative of the Tata Trusts that supports application of cutting-edge science and technology in genetics and genomics to address some of India's most pressing issues. We work on developing scientific approaches for disease prevention, improving access to affordable and quality diagnostics and therapeutics, and nutrition security through sustainable models for agriculture.

TIGS works with a vision of synergizing visionary philanthropy and outstanding science to serve humanity. All our research programs are designed for societal relevance with clearly defined deliverables that are directly implementable. As a program driven organization, we ensure our stakeholders are on board from the start. Research programs at TIGS are focused on three broad areas:

1. ***Infectious Diseases Program:*** Combating the spread of infectious diseases requires multiple strategies aligned to a One Health approach. The Infectious Diseases program focuses on disease monitoring, developing environmental surveillance and novel diagnostics to understand the prevalence of disease-causing pathogens and trends of antimicrobial resistance. We explore novel approaches to controlling vector-borne diseases based on understanding disease ecology, with a special emphasis on mosquito behavior and population control to alleviate the impact of diseases transmitted by them.
2. ***Rare Genetic Disorders Program:*** Rare genetic disorders (RGDs) individually affect a small percentage of people but translate to a large disease burden given India's huge population. Affecting mostly children, families often suffer through a long diagnostic odyssey for disease confirmation which delays the scope for early interventions. Even where the genetic cause is known, many RGDs do not have affordable therapeutic or management options. TIGS focusses on developing accessible diagnostic assays for screening patients and carriers of such diseases as well as to indigenize and develop low-cost and effective therapeutic interventions.
3. ***Crop Improvement Program:*** Food and nutrition security have become some of our biggest challenges in the face of climate change, deteriorating soil health and increasing resistance in crop pests. The Crop Improvement program incorporates scientific techniques such as genome editing, mutation breeding, and eco-friendly pest management, to enhance productivity, disease and climate resilience, and nutritional content. TIGS is developing enhanced varieties of staple food crops with desired agronomic features for increasing agricultural productivity and to ensure a sustainable, diverse and nutritionally adequate food supply for the country's large population.

In order to facilitate the implementation of our research, we have developed several innovative platforms at TIGS:

i. ***Technology Platforms and Facilities:*** TIGS has multiple technology & innovation platforms that include instrumentation and knowledge expertise, in order to accelerate early transition of research. These include healthcare diagnostics, mRNA and cell-based therapeutics, and genome editing technologies. In addition, we have state-of-the art Insectary and Greenhouse facilities to support our core research. These open institutional platforms and resources enable us to work in a disease-agnostic, adaptive and flexible manner.

ii. ***Technology Implementation:*** TIGS measures its impact by not just developing the solutions but also ensuring they reach the end-user in a cost-effective manner. We have a dedicated technology implementation team that works closely with the scientists and stakeholders to optimize the developed technology for implementation as a product that can fulfil existing gaps and reach society. The technology implementation platform is thus a combination of product development and commercialization domains.

iii. ***Community Engagement and Policy Stewardship:*** TIGS is dedicated to merging scientific breakthroughs with comprehensive community awareness and policy guidance, by creating platforms for knowledge sharing and regulatory aspects to ensure that the benefits of advanced and safe technologies are not ignored. We ensure continuous stakeholder interactions, curate knowledge on relevant topics, and strive for science communication that truly benefits and empowers society.

Our research efforts are amplified by valuable scientific associations established with institutes and researchers across the country. These associations bring together exceptional talent and know-how, thus accelerating our resolve in tackling some of the biggest challenges in human health and agriculture.

Highlights of 2024

TIGS took several major strides in 2024 to reach key goalposts across our research programs.

Implementing wastewater surveillance (WWS): We have built on our expertise in wastewater-based epidemiology (WBE) to create standard operating procedures (SOPs) and guidelines for wastewater sampling that have been shared with our partners in municipal corporations. Approaches targeting multiple pathogens as well as antimicrobial resistance (AMR) have been developed and disseminated to key stakeholders in an effort to establish community WWS across cities. TIGS has partnered with the Indian Council of Medical Research (ICMR) in a program to identify AMR signatures at multiple locations in states across the country.

Advancements in the disease diagnostics arena: The Diagnostics Development platform is a cornerstone of our new pandemic preparedness initiative. We have established capacity to deliver rapid molecular diagnostics, such that detection assays for any new variants or pathogens can be readied in 4-6 weeks. Multiple new assays have been developed this year.

Potential mosquito repellents: Our work on identifying new ecofriendly and effective mosquito repellents derived from natural plant extracts led to promising candidates that are at par with commercial products in efficacy of repelling mosquitos in lab-based assays. A couple of such candidates are at the stage of formulation process to be tested for human application.

mRNA therapeutics: The state-of-the-art mRNA-based platform at TIGS has now achieved capacity to roll out potential mRNA therapies within a timeline of 1-2 years from target disease to patient trial. Therapeutic mRNA candidates for two lysosomal storage disorders have been developed as an alternative to the highly expensive enzyme replacement therapies currently available. These candidates have entered the preclinical validation stage with the goal of reaching patient clinical trials in the next few months.

Indian RGD database: We launched a comprehensively curated database cataloguing RGD information, including affected genes and current research especially in the Indian context. The GenTIGS database is hosted on the TIGS website and is publicly accessible (https://db.tigs.res.in/gentigs/).

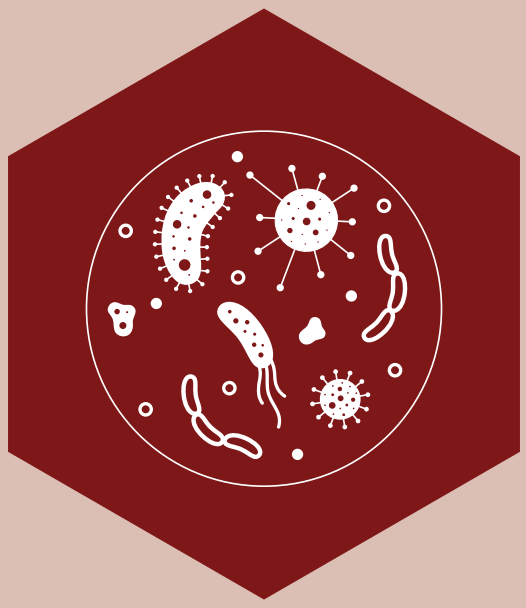
Rice genome editing: The CRISPR/Cas-mediated multiplex genome editing platform at TIGS has been successful in developing two lines resistant to Bacterial Leaf Blight in aerobic and high-yielding rice cultivars. These are in the approval stage for open field trials.

Nutritional profiling: NuTIGS has been created at TIGS as a nutrition assessment facility to measure key nutrients that are relevant to address major nutrition deficiencies in India. The platform has enabled the detection of high iron, zinc, total protein, and low sugar release rates in white rice and low phytic acid in unpolished rice. We plan to expand to vitamin and amino acid quantification and include other food crops.

Knowledge dissemination and community networks: In 2024, TIGS expanded networking with new stakeholders and partners. We held more than 13 workshops and outreach events, including on WWS, AMR and mosquito handling and genetic literacy. The first AMR Research Conference (ARC) was organized this year to bring together stakeholders in AMR surveillance, diagnostics and therapeutics. The 3rd REDRESS Summit, in collaboration with the Organization for Rare Diseases, India, and ICMR, focused on rare genetic diseases.

Research Programs

Infectious Diseases



Infectious Diseases

Arati Ramesh

Farah Ishtiaq

Jay Prakash Shukla

Mansi Malik

Sampath Kumar

Sanjay Lamba

Shivranjani C Moharir

Sonia Sen

The emergence of virulent infectious pathogens (viral, parasitic, or bacterial), and antimicrobial resistance, are serious evolving threats to human and animal health. Lack of comprehensive diagnostic and surveillance strategies compounds the risks, both for individual and community health. At TIGS, 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. 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.

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 recent 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, making disease surveillance an essential component for a strong public health system. We strive to underpin this by using 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.

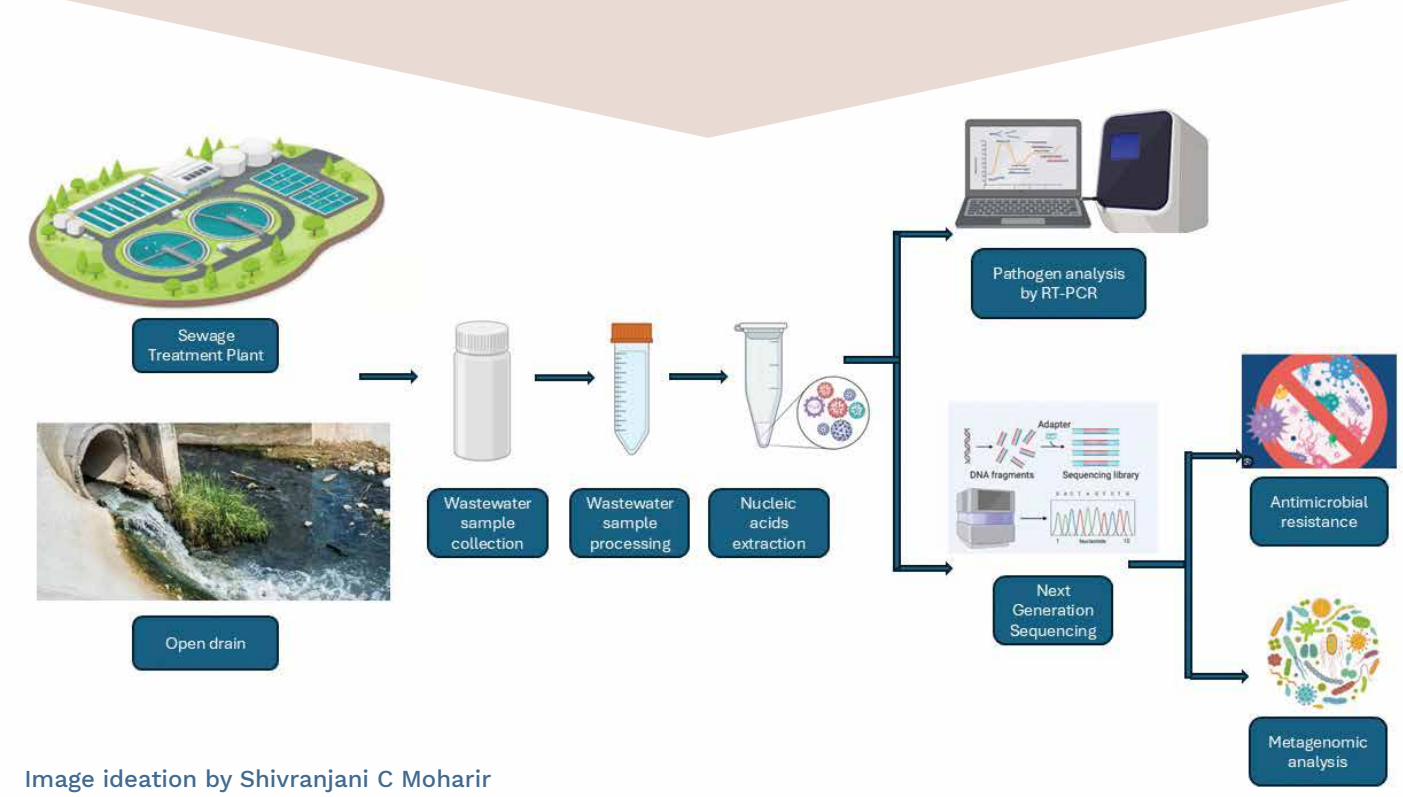


Image ideation by Shivranjani C Moharir

Wastewater-based epidemiology of SARS-CoV-2 and other pathogens in Bengaluru city

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 relied 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 ~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.

Identification of bellwether sewershed sites for a sustainable disease surveillance

As the COVID-19 public health emergency recedes, there is a need for a framework that informs adaptive (representative sampling sites) and sustainable surveillance, which can be integrated into the health surveillance system and response mechanisms such as vaccination, hotspots, risk communication etc at a granular level. Adaptive sampling requires a strategic sampling design that optimizes the value of information and approaches based on community demographics, guiding the interpretation of results. With changing phases of the pandemic, decreased testing, and potential changes in viral shedding characteristics associated with different variants and immunity, it is crucial to have a robust and flexible wastewater surveillance system which can be used for monitoring priority pathogens. We explored this in two ways:

1. Defining STP size category as an indicator of early warning system

We analyzed data from 3,498 wastewater samples collected from December 2021 to January 2024 at 26 centralized sewershed sites in Bengaluru. Four main surges were recorded by both clinical and wastewater genomic data: BA.2.10 surge, BA.2.X surge, XBB surge, and JN.1 surge. The BA.2.10 surge occurred from Week 48, 2021, to Week 9, 2022; the first non-surge period lasted from Week 10, 2022, to Week 19, 2022; the BA.2.X surge spanned Week 20, 2022 to Week 39, 2022; the second non-surge period was from Week 40, 2022, to Week 6, 2023; the XBB surge occurred from Week 7, 2023, to Week 23, 2023; the third non-surge period lasted from Week 24, 2023, to Week 46, 2023; and the JN.1 surge occurred from Week 47, 2023, to Week 6, 2024 (Fig. 1 A and 1 B).

The wastewater data mirrored the clinical data showing a BA.2.10 surge in January 2022 and a small surge in late June 2022. However, from July 2022 to October 2023, the two datasets diverged (Fig.2). Wastewater-derived viral load remained consistent with a large surge driven by the XBB variant in April 2023, followed by a JN.1 surge starting in the last week of December 2023.

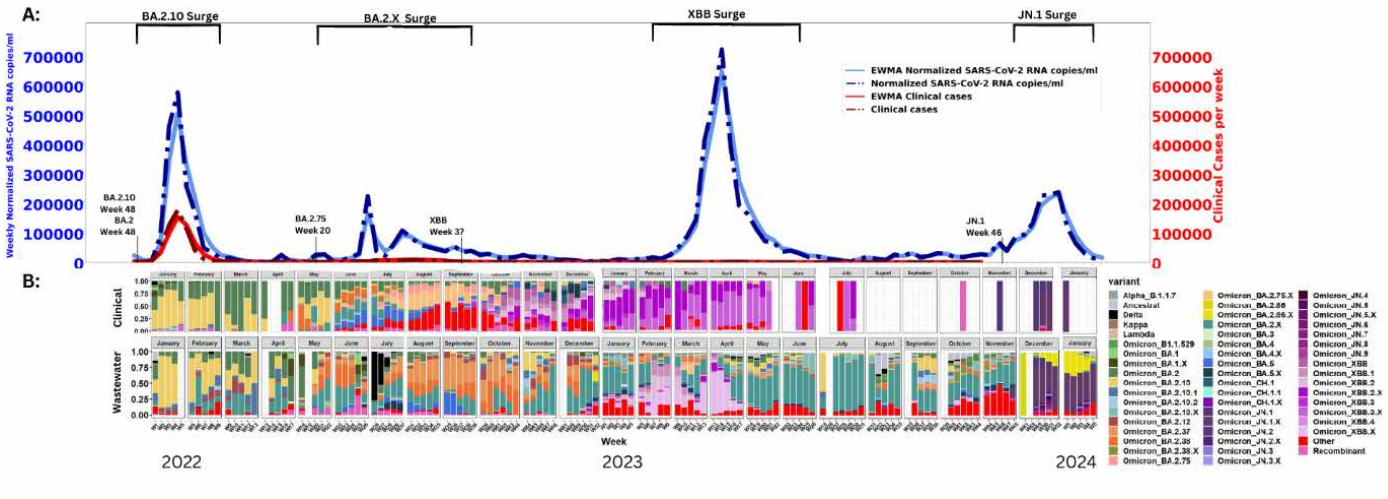


Fig. 1. Time series analysis of EWMA-smoothed (light blue solid trend line) and unsmoothed SARS-CoV-2 wastewater viral load (dark blue hashed trend line) and weekly EWMA-smoothed (maroon solid trend line) and unsmoothed (red hashed trend line) clinical cases for Bengaluru. Horizontal black lines depict the first detection weeks of respective SARS-CoV-2 variants in Bengaluru. (B) Weekly relative abundance of clinically detected and wastewater-recorded SARS-CoV-2 variants.

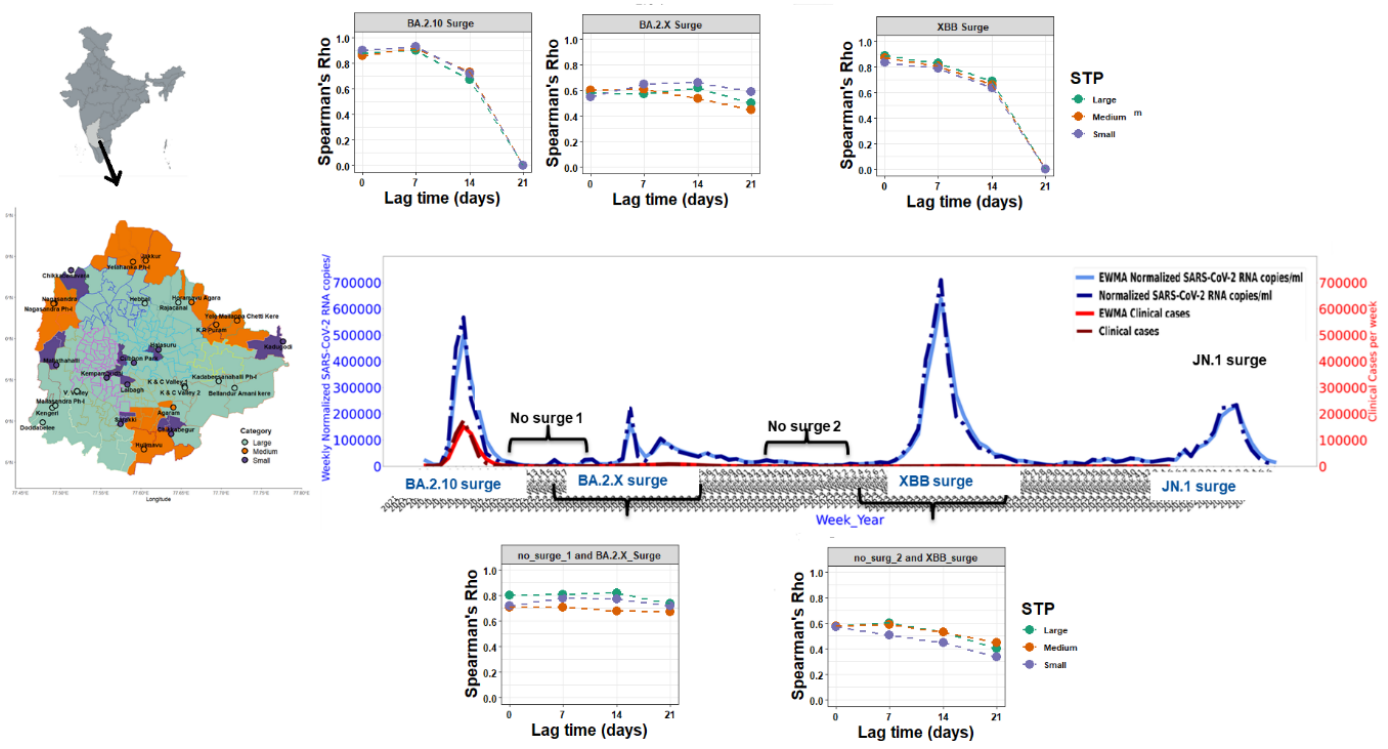


Fig. 2. Time series analysis of EWMA smoothed (light blue trend line) and normalized wastewater viral load (dark blue trend line) along with weekly EWMA smoothed (grey trend line) and unsmoothed (black trend line) clinical cases for Bengaluru. Spearman's Rho correlation between wastewater data and clinical cases reported in Bengaluru was assessed, applying time lags of 0, 7 days, 15 days to 21 days to define surge and non-surge periods.

To examine the lead-time advantage of wastewater data, we compared normalised viral concentrations with clinical case counts. We analyzed correlations between viral load concentrations recorded for each sewershed by size category and city-level case counts. We found that increases in wastewater viral concentrations leading up to the BA.2.10 surge, BA.2.X surge, and XBB surge generally coincided with the timing of rises in city-level case counts (Fig. 2). The strongest correlation between the viral load of the wastewater samples and the number of clinical cases was observed during the BA.2.10 surge at a two-week lag for small (r=0.90, P<0.0001), large (r=0.89, P<0.0001), and medium (r=0.88, P<0.001) size sewershed sites. Restricting the data to periods around the surge periods (that is, excluding periods of low case counts prior to the surge) generally increased the strength of the correlation between wastewater and case data. However, though differences in the strength of correlation varied by size category and pandemic phase. During the BA.2.X surge, the strongest correlation was at a two-week lag for small (r=0.57, P<0.001) and large (r=0.48, P<0.001) size sewershed sites. The BA.2.X surge had varying build time across sewersheds which was reflected in weaker coefficient values and/or limited clinical testing. This was further corroborated by no correlation between wastewater data and clinical cases during the non-surge period 1. When the non-surge period was combined with the BA.2.X surge period, a strong correlation with a two-week lag was observed at small (r=0.79, P<0.001) and large size sewershed sites (r=0.80, P<0.001). A similar pattern was seen during no surge period 2 within a one-week lag after considering both the non-surge and XBB surge periods.

Our analysis suggests that large size STPs may provide early outbreak detection during surge phases of high and low viral loads. Large STPs can capture signals from a broader population segment, facilitating earlier detection of high viral loads. However, our findings also show that small and medium STPs can offer valuable early warnings (1 week in advance). The ability of treatment plants to capture trends earlier depends on the individual process, quality of viral concentrations recorded, area and population covered, and sewage network density.

2. Differentiate between noise versus signal in localised outbreaks in the absence of clinical data

We applied a modified simple algorithm (COVID-SURGE algorithm) to identify 'bellwether' sewershed sites using longitudinal wastewater data on SARS-CoV-2.

We constructed a simple Excel calculator (COVID-SURGE calculator) for user-entered wastewater data that differentiates signal from noise according to the algorithm, with adjustments made to the input format of viral data and a single limit of detection (LOD) value specified by the RT-qPCR kit for three target genes. Additionally, edits were made to the formulas in the Excel calculator, where the re-imputation of LOD values must be done before analyzing datasets. Using wastewater metrics helps select permanent sewershed sites and choose sub-sites that can be scaled up during peak outbreak periods to identify disease hotspots and scaled down during lean periods. Out of the 28 STPs, 11 were identified as bellwether treatment plants, meeting all criteria for consistent and reliable performance (Fig. 3). These bellwether STPs were ranked based on their effectiveness in various analyses. This approach ensures good quality data that captures valid signals amid the noise from wastewater and conserves resources while optimizing public health actions beyond SARS-CoV-2.

In a post-pandemic world, focusing on the best-performing STPs will be essential for obtaining accurate city-level data. This strategy will help conserve resources and improve public health responses by ensuring high-quality data from STPs that can reliably detect valid signals amid the background noise in wastewater.

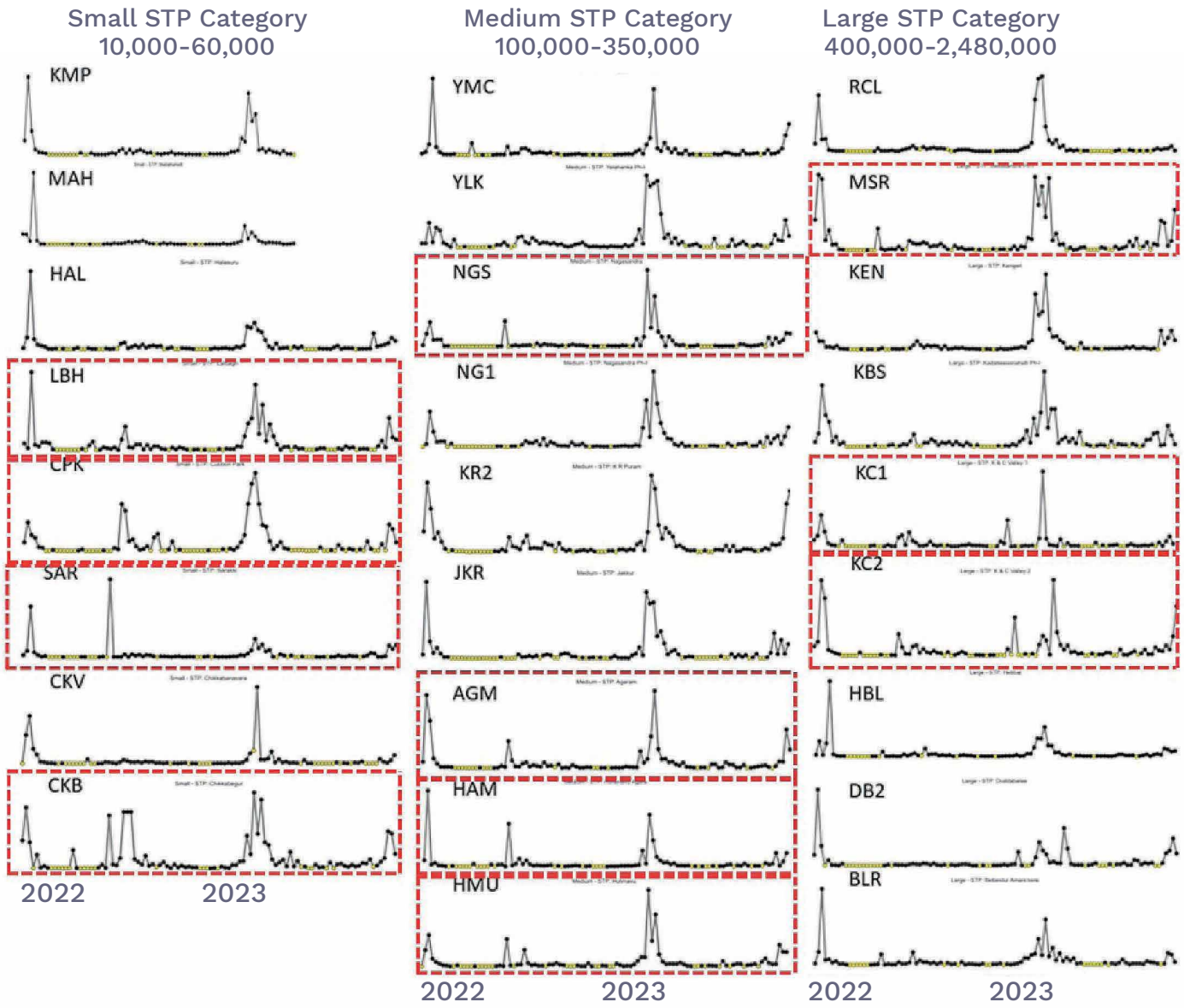


Fig. 3. EWMA of normalised SARS-CoV-2 viral load with corresponding Limit of Detection (LoD; yellow points) plotted weekly for each STP. In the small category, LHB (Lalbagh), SAR (Sarakki), CPK (Cubbon Park), and CKB (Chikkabegur); in the medium category, AGM (Agaram), HAM (Horamavu Agara), NGS (Nagasandra), and HMU (Hulimavu); in the large category, KC1 (K & C Valley 1), KC2 (K & C Valley 2), and MSR (Mailasandra Ph-I) contributes overall city viral trend.

Expansion of ES from SARS-CoV-2 to priority pathogens

As the COVID-19 public health emergency recedes, the existing ES systems can be expanded to identify endemic and re-emerging infections (e.g., cholera, hepatitis, non-polio virus, influenza). It is also important to consider the potential usefulness of ES data in informing public health actions. The actionable intervention aspect of such a community-level surveillance method often hinges on having a well mapped sewage network and the ability to define hotspots for further actions (e.g., vaccination, public awareness programs). The utility of wastewater surveillance goes beyond detecting SARS-CoV-2, the existing ES programs have been used as an early warning of outbreaks for detecting enterically transmitted viruses, (norovirus, astrovirus, rotavirus, adenovirus, Aichi virus, parechovirus, hepatitis A virus [HAV], and hepatitis E) which are shed in large amounts in feces for days or weeks, both before and after the onset of symptoms.

Monitoring hepatitis E in wastewater can identify clinically relevant variants. Wastewater has recently been used to

gather information on circulating respiratory viruses at a localized community level, which is otherwise reliant on clinical records biased towards infected individuals and passive disease surveillance systems. Table below provides a detailed description of molecular methods using adaptable platforms for multi-pathogen detection. Using a combination sensitive and feasible approaches will be required to establish a multi-pathogen surveillance program.

Like SARS-CoV-2, the clinical surveillance of arboviral diseases (dengue, chikungunya, Zika) relies heavily on symptomatic cases and those can be diagnosed accurately to carry arboviral infections. Complementing Zika surveillance with wastewater and mosquito testing has helped mitigate further disease transmission.

	USE CASE				MEASUREMENT GOALS					INTERVENTION				FREQUENCY			SAMPLE TYPE				MOLECULAR TESTING	
Priority Pathogens	Eradication	Elimination or emergence	Burden reduction	Natural History and Ecology	Presence or absence	Time trend	Spatial distribution	Exposure routes	Genomics	Vaccination	Outbreak prepareness	Risk communication	R&D	Weekly	Bi-monthly	Monthly	Inlet	Outlet	Sludge	Satellite sites	Quantitative PCR	Digital Droplet PCR (ddPCR)
Wildlife and Livestock Diseases																						
Avian Influenza		■		■	■	■	■	■	■		■	■			■		■			■	■	■
Mpox				■	■		■	■		■				■			■			■		■
Nipah				■	■		■	■			■	■				■	■			■		
Leptospira				■	■		■	■		■	■	■				■	■			■		
Human Diseases																						
Influenza A&B						■			■	■			■	■			■		■	■	■	
Resp. Syncytial Virus						■			■	■	■		■	■			■			■	■	
Cholera		■	■				■	■			■	■			■		■			■	■	
Hepatitis A&E		■	■				■		■	■		■		■			■			■	■	
Rotavirus							■	■		■	■	■		■			■			■	■	
SARS-CoV-2					■	■	■		■	■	■	■		■			■			■	■	
Dengue, Chikungunya, Zika		■	■	■		■	■	■	■	■			■	■			■		■	■	■	■
Norovirus							■		■		■	■		■			■			■	■	
Human Papiloma Virus (HPV)							■		■			■			■		■			■	■	
Candida auris infection							■	■	■		■	■	■			■	■	■	■	■	■	
Antimicrobial resistance																						
Antimicrobial resistance genes				■	■	■	■	■	■			■				■	■			■		
Microbial diversity				■	■	■	■	■	■			■				■	■			■		
Fungal diversity				■	■	■	■	■	■										■	■		
Emerging contaminants																						
Antibiotics				■	■	■	■	■			■	■				■	■	■	■	■		
Antivirals				■	■	■	■	■			■	■				■	■	■	■	■		
Antimalarials				■	■	■	■	■			■	■				■	■	■	■	■		
Acetaminophen				■	■	■	■	■			■	■				■	■	■	■	■		
Caffeine				■	■	■	■	■			■	■				■	■	■	■	■		
Disinfectants				■	■	■	■	■			■	■				■	■	■	■	■		
Heavy Metals			■		■		■	■				■	■			■	■	■	■	■		

Sample collection frequency, sample type and intervention plan for each pathogen, molecular methods

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

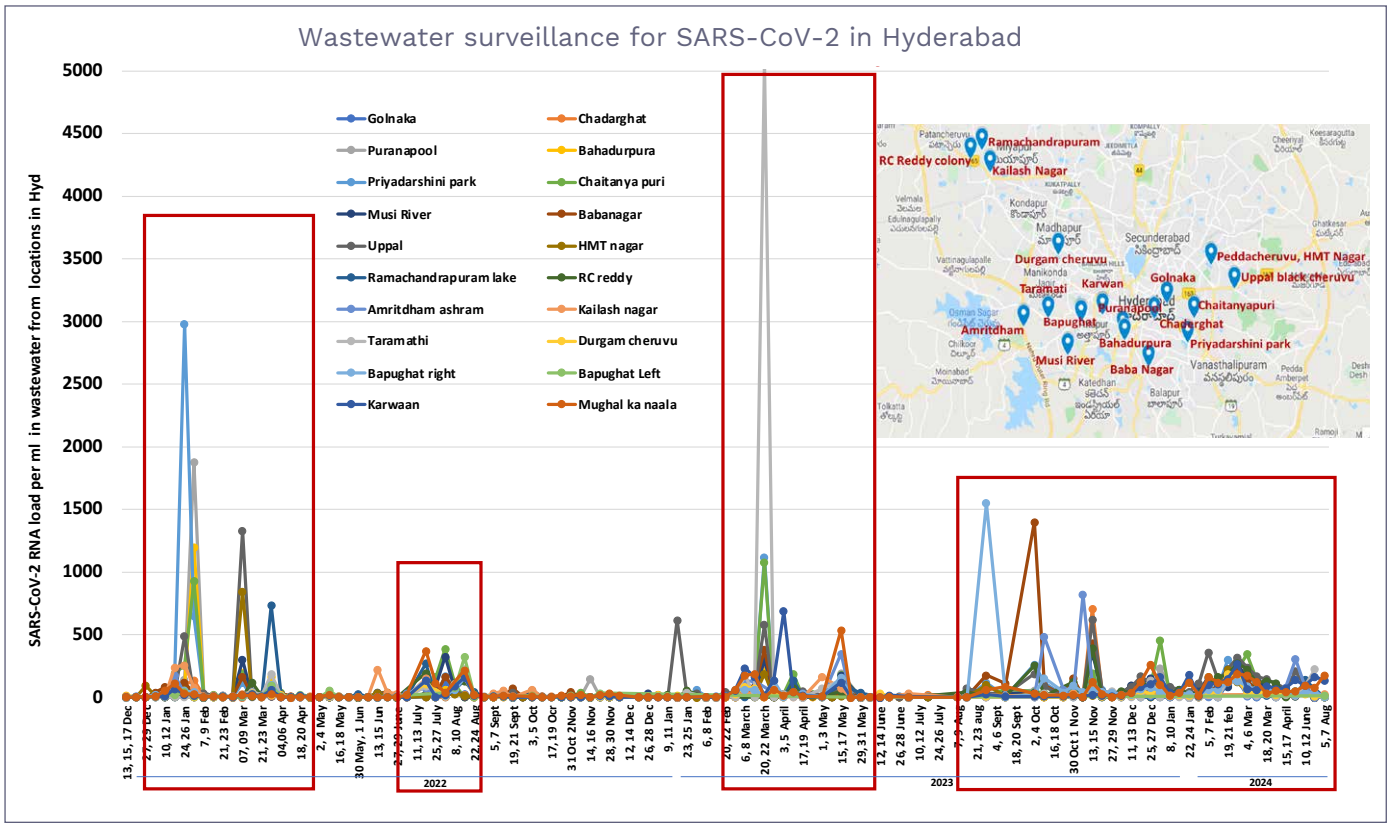
Shivranjani C Moharir

[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 three 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

EpiAlertR: Early Warning System for Infectious Diseases

Sanjay Lamba

The temporal data generated by wastewater surveillance for SARS-CoV-2 from multiple cities was used by TIGS for modeling the viral load and developing an early warning system for infection trends. Being agnostic to the input data source, from sewage treatment plants (STPs) or open drains, the modeling approach has great predictive value for disease tracking across the country, in cities as well as rural towns.

We are now developing a user-friendly package as an early warning system targeting multiple infectious diseases as a valuable tool for advancing real-time monitoring capabilities and ensuring timely responses to potential outbreaks. Conceived as an R-software package, this adaptable tool can be applied to various infectious diseases to predict their potential outbreaks, applying relevant parameters specific to each disease. The package can forecast impending outbreaks in advance by leveraging factors such as historical data on positive cases, viral load findings, and infection rates. This undertaking plays a crucial role in the effective implementation of public health measures, minimizing the adverse impact of outbreaks.

Data Cleaning and Processing:

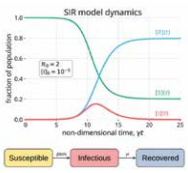
- **Handling Missing Values**
  - Imputation - Mean, Median and Mode
  - Interpolation - Backward and Forward
  - K - Nearest Neighbours (KNN)
- Logarithmic **Transformation** - for improving data linearity
- Karl Pearson's **Correlation** - determining linear relationship

Predictive Models:

- **Linear Module (LM)**
- **Bayesian Regression** - Incorporates prior distribution to estimate a posterior
- **XGBoost** - Extreme gradient boosting using multiple decision trees
- **LSTM** - Long Short Term Memory is a Recurrent Neural Network (RNN) for sequential data

Early Warning System:

- **Estimate Lag** - Estimating lag between time series
- **EWMA** - Early warning sings above UCL/Red alert
- **Change Point Analysis** - Validating the time lag, finding the false alarms
- **ARIMA Model** - Forecasting future trend



Epidemiological Model:

- **SIR Model**
  - Parameter estimation using data with Monte Carlo or likelihood function
- Basic Reproduction Number (R_0)

Overview of Methods in R - software package: Data Cleaning and Processing, Predictive Models, Early Warning System and Epidemiological Modeling.

Features:

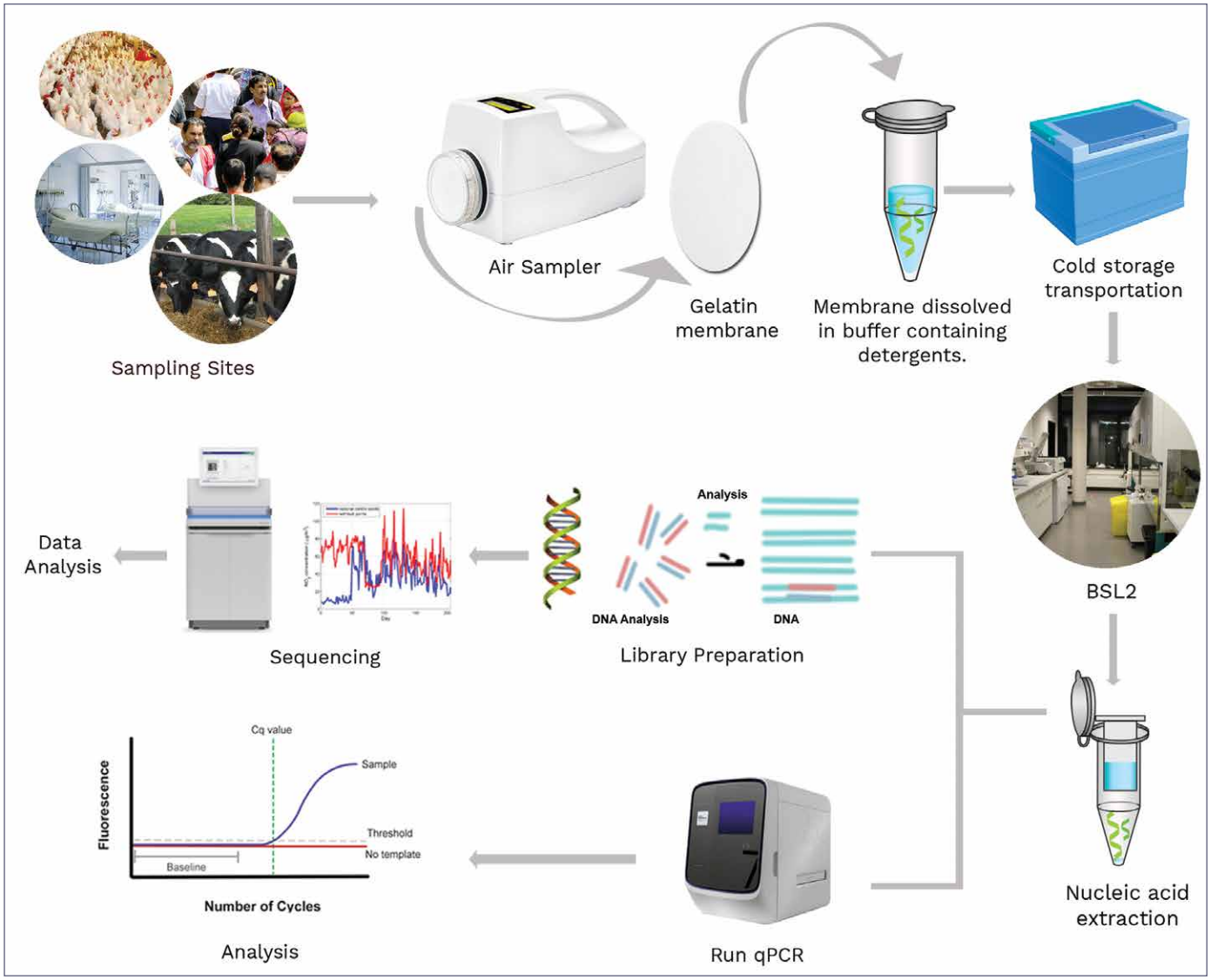
- Packages have been tested and validated for SARS-CoV2 detection (Sewage Treatment Plants and Open Drains), and Chickenpox.
- Package can be used for various infectious diseases, adjusting parameters relevant to the target disease.

Air surveillance study to identify pathogens in different environmental niches

Shivranjani C 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 analysing air samples from diverse environmental settings, including hospitals, zoos, densely populated areas, and sparsely populated regions. We have collaborated with Government and private hospitals in Kerala, Bangalore and Hyderabad and have analysed the bacterial profile in diverse hospital settings, public places, open air places, closed rooms, beaches, poultries and cattle sheds.



A pictorial representation of the protocol for air surveillance

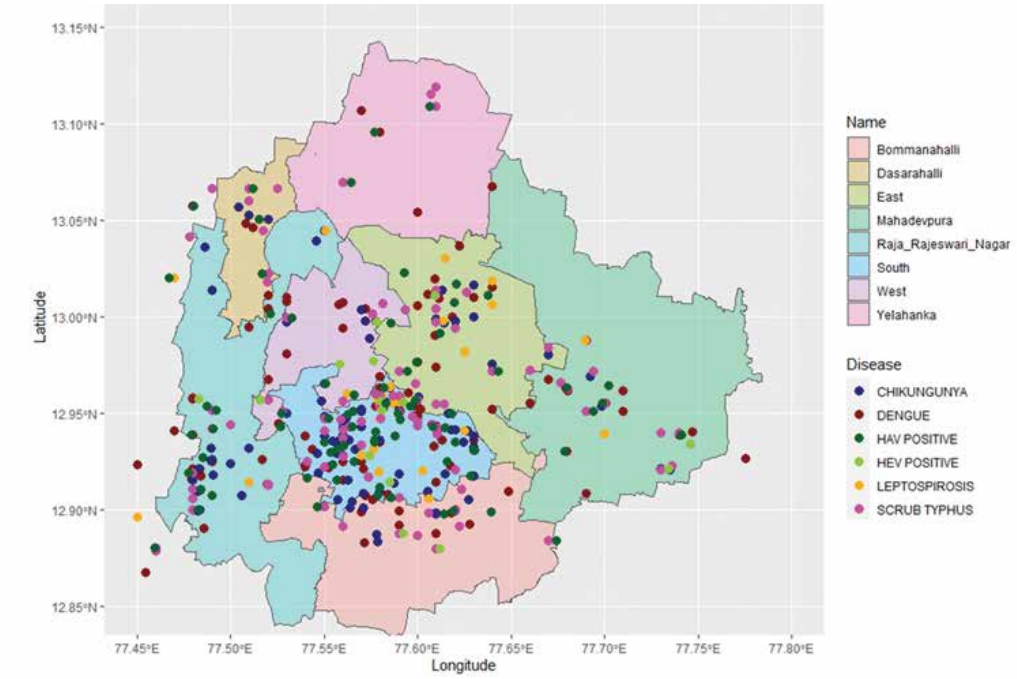
Molecular detection and screening of pathogens and associated biomarkers in clinical samples

Mansi Malik

[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 km2 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.



Prevalence of various infectious diseases in urban Bengaluru

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.

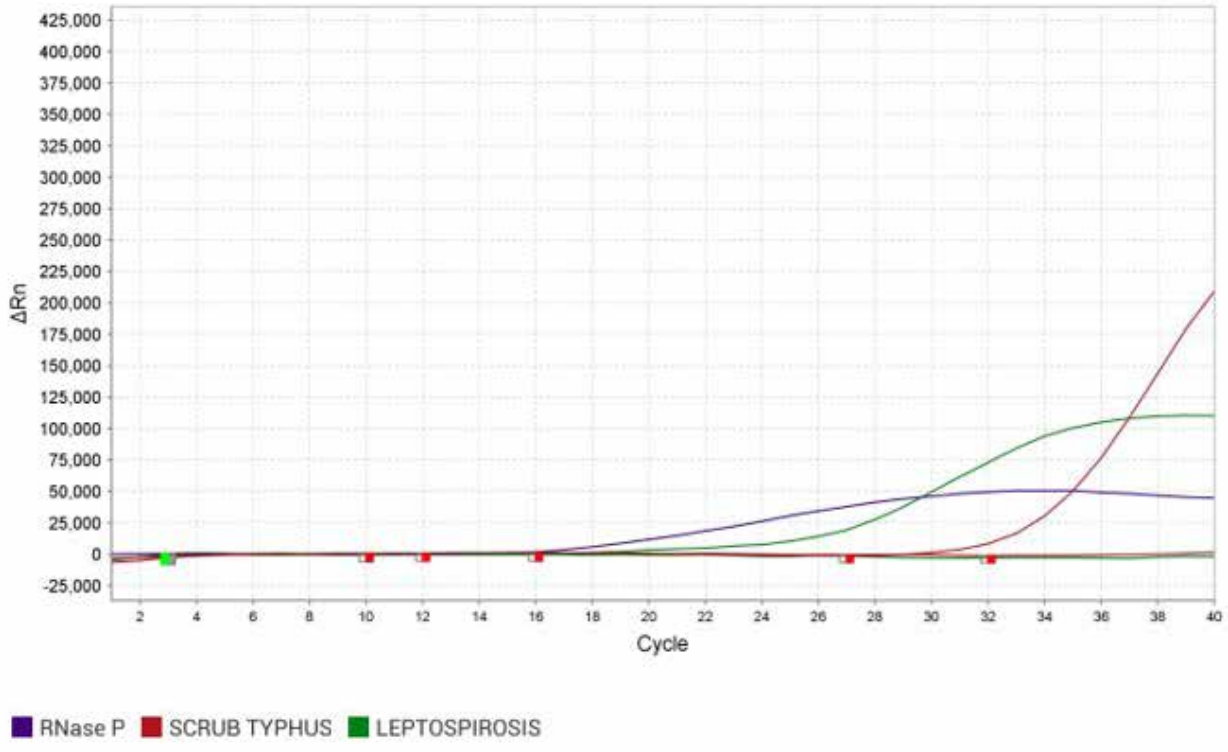
We have expanded our collaborations with having Bangalore Baptist hospital,Aster CMI hospital, Anand neuberg laboratories, AIIMS-Bhopal and Central University of Tamil Nadu,Thiruvarur.

Approximately 2500 clinical samples have been screened until December 2024 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.

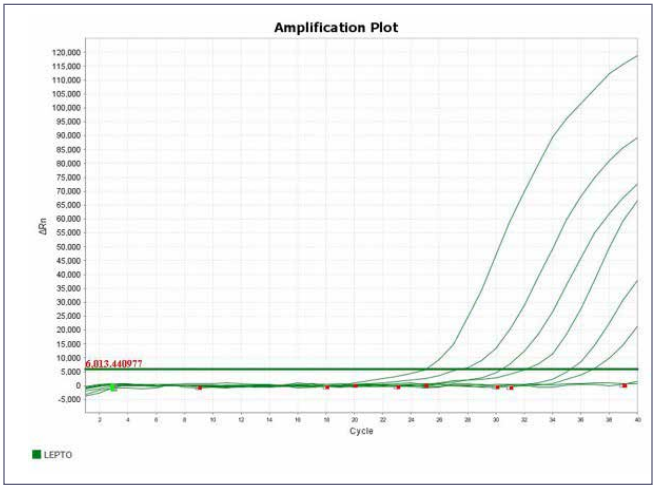
We have developed six multiplex molecular assays based on qRT-PCR to facilitate rapid, accurate and low-cost detection of these infections from patient samples. We have filed provisional patents as well as final patent applications for some of these assays.

We also have transferred two of our inhouse assays to a diagnostic company partner.

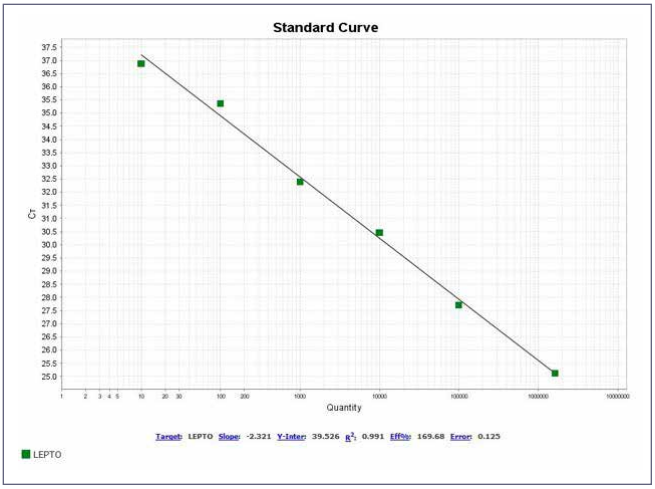
Amplification Plot



Leptospirosis Quantification

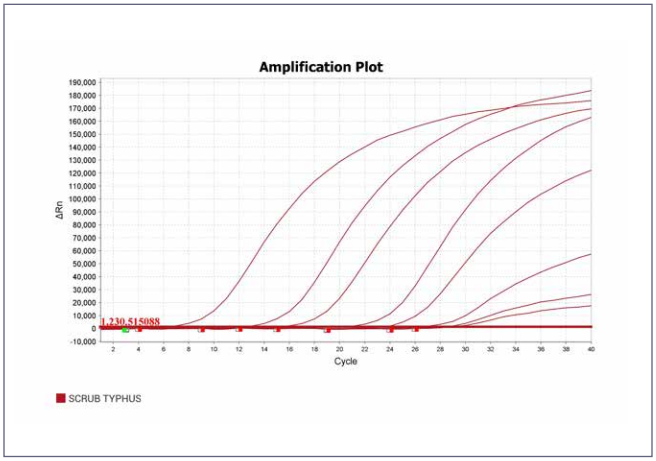


A



B

Scrub Typhus Quantification



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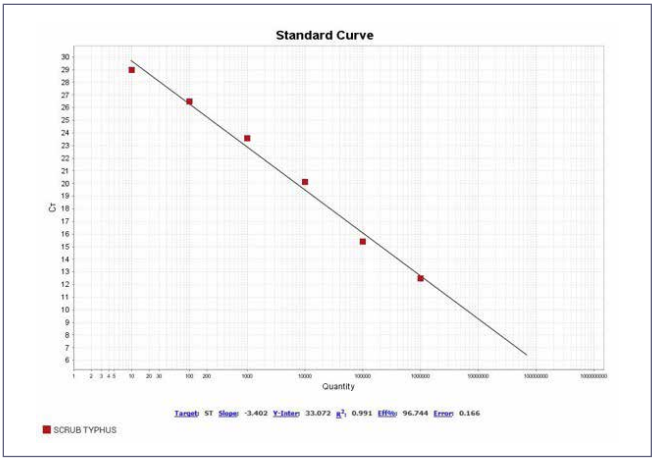
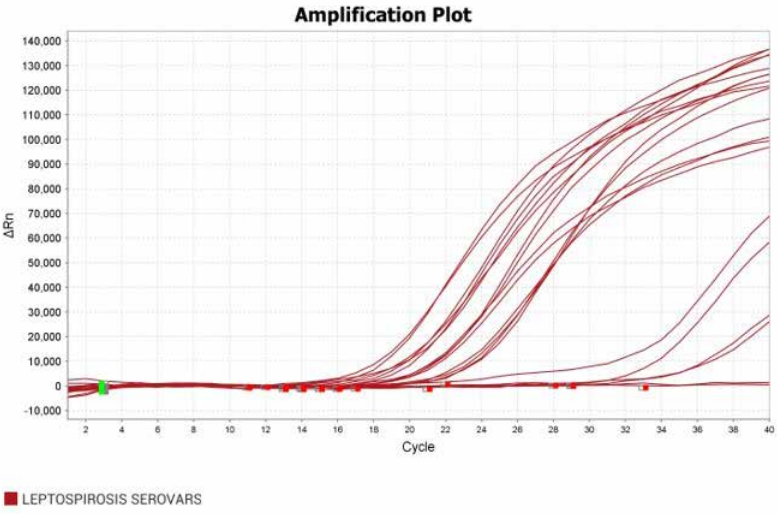


D

Leptospirosis specificity assay with 25 different serovars



Surveillance of vectors, vector-borne diseases, and various pathogens from the Cauvery delta districts of Tamil Nadu

Mansi Malik

(In collaboration with Central University of Tamil Nadu, Thiruvarur)

The Cauvery Delta district of Tamil Nadu is an agriculturally rich region that faces significant public health challenges due to the presence of vector-borne diseases (VBDs). The region's climate, heavy rainfall during the monsoon season, and agricultural practices create ideal conditions for the breeding of vectors such as mosquitoes, mites, and ticks. Surveillance and epidemiological studies of these diseases are crucial to monitor their spread, detect outbreaks, and implement timely control measures.

The surveillance and epidemiology comprise various methods to monitor mosquito vectors, rodent populations, clinical surveillance, environmental and geospatial surveillance, and insecticide resistance. Vector control programs use traps, larval collection, and identifying breeding sites in urban and rural areas. Mite surveillance involves trapping and testing mites to determine their role in disease transmission. Clinical surveillance involves case reporting, epidemiological investigations, and diagnostic support. Environmental and geospatial surveillance uses GIS to map the spatial distribution of vector populations and human disease cases, identifying "hot spots" for vector breeding and human infection. Resistance to insecticides is also monitored to reduce the effectiveness of control measures. Epidemiological studies focus on understanding the patterns and trends of vector-borne diseases, identifying risk factors, and evaluating the effectiveness of control programs. Seasonality, geographic distribution, agricultural practices, poor sanitation, and human behaviour are key factors in vector-borne diseases in the Cauvery Delta district of Tamil Nadu.

We, in collaboration with the Central University of Tamil Nadu, Thiruvarur are working on mosquito, mite and clinical surveillance with the following objectives:

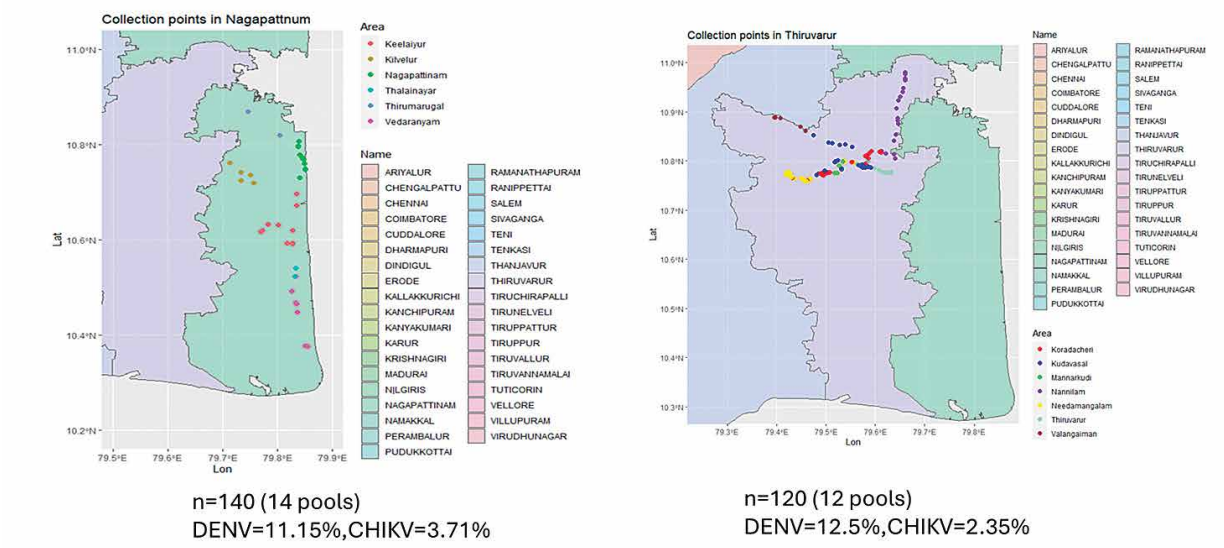
- To detect and analyse the prevalence of pathogens responsible for infectious vector-borne diseases (Scrub typhus and genotypes, Dengue, Malaria, Chikungunya, Leptospirosis) from both entomologically identified vectors such as mosquitoes, mites and ticks and clinical samples using molecular screening methods.
- To correlate the findings of vector surveillance with clinical surveillance to estimate disease burden and hotspots across delta districts of Tamil Nadu.

Field collection of mosquitoes in and around Thiruvarur

Mosquito trap at CUTN, Thiruvarur

Larval and adult mosquito surveillance at Thiruvarur

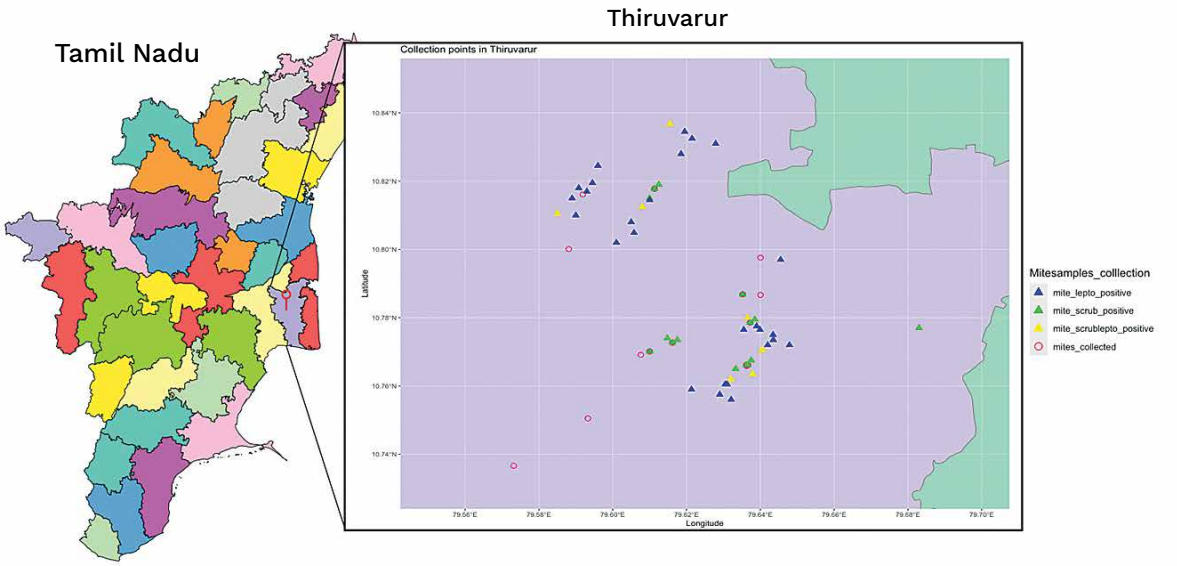
Setting rodent traps for mite surveillance across Thiruvarur



n=140 (14 pools)
DENV=11.15%,CHIKV=3.71%

n=120 (12 pools)
DENV=12.5%,CHIKV=2.35%

Maps of Nagapattinam and Thiruvarur district showing the blocks and respective locations of larvae collection



Mapping of Mites collected across Thiruvarur district for detecting Scrub-Typhus

Antimicrobial Resistance

Antimicrobial Resistance (AMR) poses a significant challenge to global health, characterized by disease-causing microbes' increasing resistance to antimicrobial drugs designed to eliminate them. This phenomenon is particularly alarming as it encompasses bacterial, viral, and fungal pathogens, with the World Health Organization (WHO) identifying AMR as one of the most pressing health challenges worldwide. India, with its excessive and unregulated antibiotic use in humans and livestock, stands as a critical hotspot for the surge in antibiotic resistance. 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 health. Antibiotic misue in humans, livestock and industry is a key contributor to rising resistance rates. There is growing concern that AMR 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. Given this predicament, we are developing a multi-pronged approach enabling surveillance for AMR from humans, animals, and their shared environmental sources in an integrated One Health approach, as well as devising novel ways to diagnose resistant strains and combat them with new therapeutic approaches.

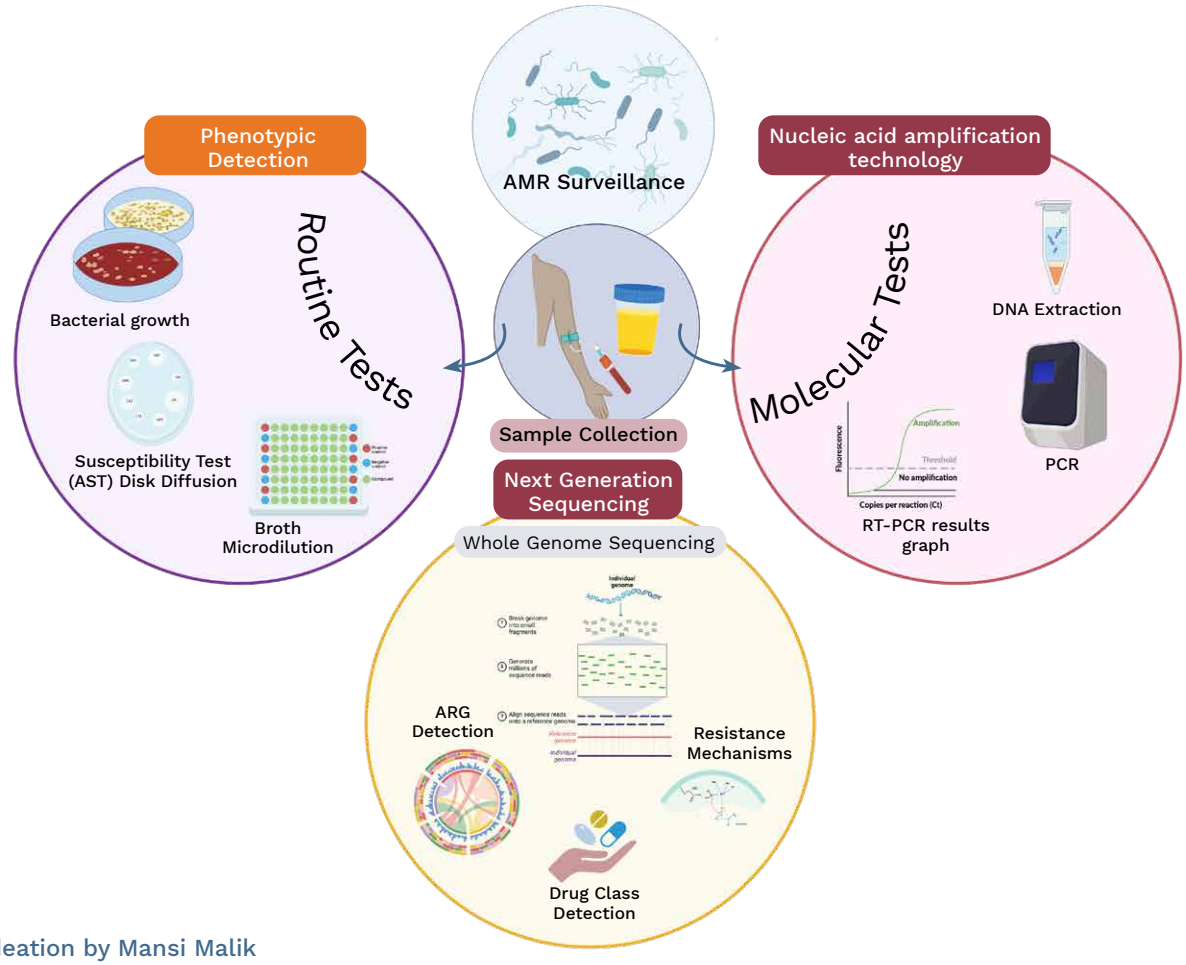


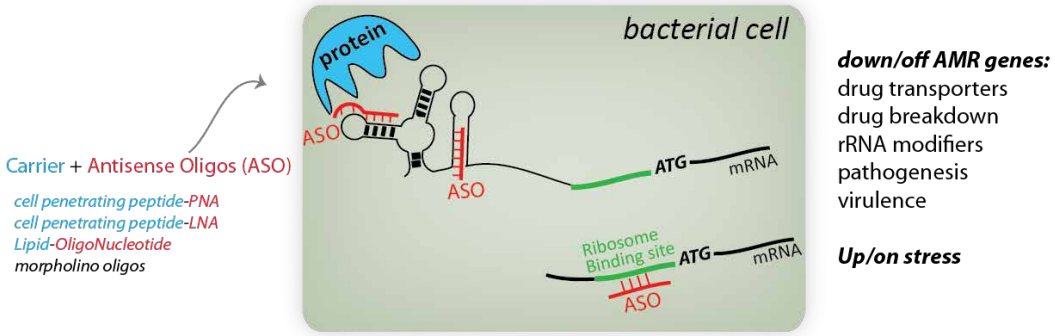
Image ideation by Mansi Malik

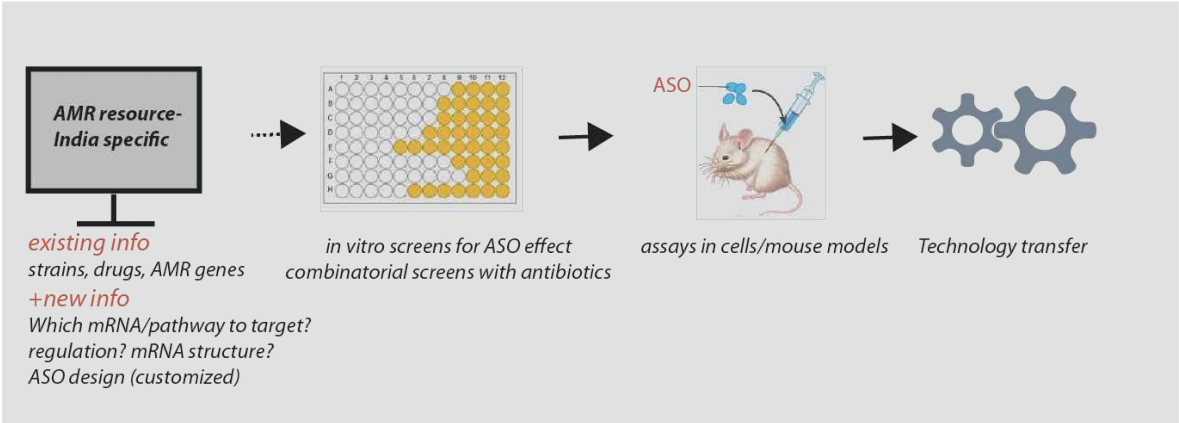
Developing novel therapeutics to target infectious diseases, with a focus on AMR

Arati Ramesh

Disease-causing microbes (bacteria, fungi, and viruses) are becoming 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).

We are using ASOs that are derived by covalently linking cell-penetrating peptides with peptide nucleic acids. These ASOs are designed to bind to the ribosome binding site of different mRNAs of choice and work by blocking translation of essential proteins in the microbe. We are evaluating the effects of these therapeutic ASOs on three of the six ESKAPE pathogens that are of utmost priority in the Indian AMR context. Initial testing of a medium throughput ASO library against UTI-causing bacteria has resulted in a few candidate anti-microbial ASOs which we are currently characterizing for cell penetration, toxicity etc. We find specific pathways such as sugar metabolism, lipopolysaccharide biosynthesis and In *Staphylococcus aureus*, a common cause of respiratory infections, skin infections, and abscesses we have designed and developed an anti-sense oligo that prevents synthesis of an antibiotic resistance gene that is responsible for macrolide resistance. The ASO shows promising results in re-sensitizing macrolide resistant S. aureus to macrolide drugs.





Environmental Surveillance of AMR in the context of water resuse

Farah Ishtiaq

Background

In India, obtaining representative data on AMR for healthy human and animal populations is challenging. Until 2010, India was the largest consumer of antibiotics, with antibiotics easily accessible without a prescription. In low-resource settings, urban sewage, particularly is a major source for the dissemination of ARGs in various environments. Sewage treatment plants (STPs) are critical environments where high microbial density and diverse ARGs are exposed to selective agents such as antibiotics, disinfectants, and heavy metals, presenting great ecological opportunities, as well as niche availability for the transmission of ARGs (horizontal gene transfer) among pathogenic and non-pathogenic bacteria (e.g., waterborne (Vibrio cholera, Legionella), enteric (Escherichia-Shigella) or environmental (Pseudomonas) bacteria that are prone to multidrug resistances. ES is an effective tool for collecting reliable data to assess the spatiotemporal patterns of ARGs diversity at the community level.

Climate change and health are inextricably linked with urban wastewater. Water scarcity and reduced availability of agricultural water have spurred increased interest in the use of treated water for irrigation, groundwater charging, urban landscaping and for industrial use. There is a concern that antibiotic resistance genes (ARGs) persist in recycled irrigation water which could potentially contribute to the growing overall public health challenge of increasing rates of antibiotic-resistant bacterial infections. However, there is limited monitoring of treated wastewater parameters and its impact on ecosystem health.

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. Each STP follows water treatment technology depending on the quality of raw sewage to make the treated water reusable.

Our team conducted a longitudinal study across 26 STPs in Bengaluru to understand diversity and abundance of ARGs and their association with bacterial diversity in wastewater. The study revealed that there is a shift in microbial diversity and the antibiotic resistome from the inlet to the outlet of a treatment plant (Fig. 1 A-B). The conventional STPs effectively eliminated a significant number of bacterial cells, along with their associated resistance genes.

In general, there were more complex and dense correlations between ARG–ARG, ARG–bacteria and bacteria-bacteria in inlet samples. In contrast, outlet samples showed stronger and positive correlations between ARG-ARG pairs and bacterial assemblages, with very few interactions between ARG-bacteria pairs (Fig. 1 C). WBE and treated WBE is a continuum. Therefore, for a complete understanding enables both health practitioners and wastewater use practitioner to understand and mitigate potential risks.

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, in Kolar district of Karnataka, one of the worst affected districts in terms of drought and climate change, the use of 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 also 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, we have been analyzing treated and non-treated urban sewage samples 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.

Our findings aid in the quantification of genes from both culturable and nonculturable taxa. We have so far been working with the Bengaluru Water Supply and Sewerage Board (BWSSB) to improve water treatment

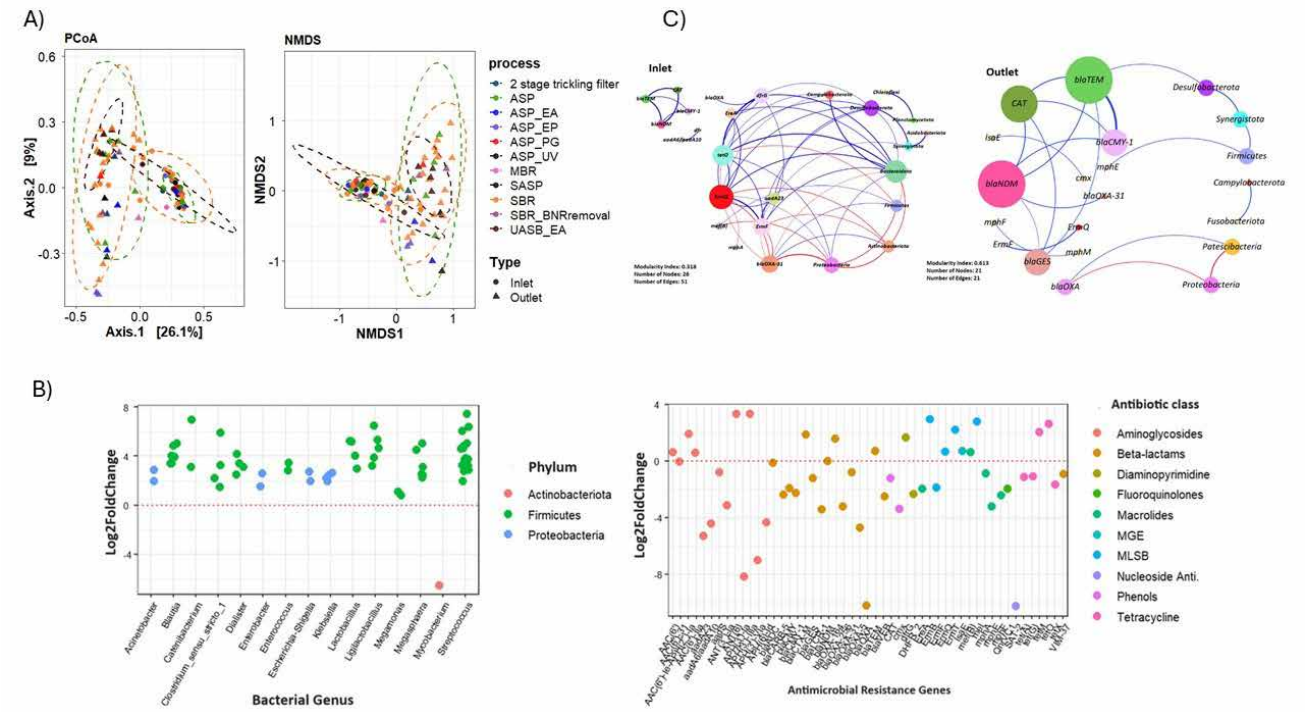


FIgure 1 A: ß-diversity vizualization by sample type using principal coordinate analysis (PCoA) based on unweighted UniFrac distance method; Nonmetric multi-dimensional scaling (NMDS) plots of Bray-Curtis showing separation between inlet and outlet communities; however, there is no effect of STP processing method; 4B: Differential abundance of AMR and microbial communities from inlet to outlet samples; 4C: Co-occurence meta-network showing the strong correlation between ARG-ARG, ARG-baterial phyla, and bacterial phyla-bacterial phyla in the inlet compared to the outlet.

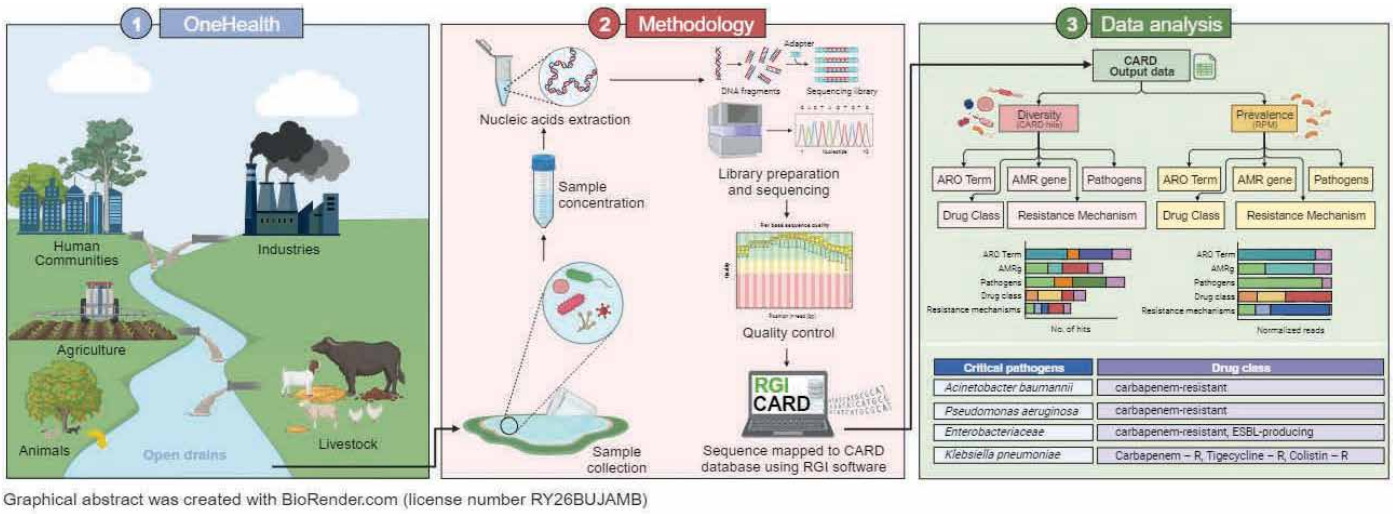
mechanisms of four key STPs which supply treated water for agriculture and groundwater recharging in peri-urban areas. By extending this study to Bengaluru peri-urban areas (e.g., Kollar, Chikkaballapura, Tumkuru and Kollar), we are profiling ARGs, bacterial, fungal diversity to evaluate the health impact of treated water in the areas. These findings will assist in the development of policies and strategies to address water quality issues.

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

Shivranjani C Moharir

We work on understanding the antimicrobial resistance landscape in the city through wastewater-based epidemiology. Samples are collected once a month, from the 18 locations and analysed for the resistant pathogens, the antimicrobial resistant genes, the resistant drug classes, and mechanisms conferring resistance, through metagenomics approach.

Recently, to understand the contribution of the open drain associated ecosystems towards AMR, we investigated the antimicrobial resistance landscape of an Indian metropolitan city- Hyderabad by shotgun metagenomics sequencing of open drains wastewater samples from the city (Madhukar et. al., Environmental Research, 2024). Hyderabad has a population of around 10 million, as of 2023. The city generates approximately 6246 million litres of sewage daily, of which around 2922 million litres is treated through STPs and the remaining volume is discharged in to the open drainage system. We analysed 17 sampling sites that received untreated sewage water from households, industries, and farming practices in the city. The results of the study provided a panoramic understanding of the abundance and diversity of antimicrobial resistance genes (ARGs), pathogens and resistant drug classes across the city. The predominant resistance mechanisms adopted by the pathogens against the antibiotics were also explored. The data suggested that in January 2022, macrolide class of antibiotics contributed the highest resistance of 40.1%, followed by aminoglycoside- 24.4%, tetracycline- 11.3% and lincosamide- 6.7%. The 'mutations in the 23S rRNA gene conferring resistance to macrolide antibiotics' were the major contributor of resistance with a prevalence of 39.7%, followed by '16s rRNA with mutation conferring resistance to aminoglycoside antibiotics'- 22.2%, '16S rRNA with mutation conferring resistance to tetracycline derivatives'- 9.2%, and '23S rRNA with mutation conferring resistance to lincosamide antibiotics'- 6.7%. The most prevalent antimicrobial resistance gene (ARG) 'mutations in the 23S rRNA gene conferring resistance to macrolide antibiotics' was present in multiple pathogens including *Escherichia coli, Campylobacter jejuni, Acinetobacter baumannii, Streptococcus pneumoniae, Pseudomonas aeruginosa, Neisseria gonorrhoeae, Klebsiella pneumoniae* and *Helicobacter pylori*. Most of the pathogens from the WHO Bacterial Priority Pathogen list were seen in the samples, as depicted in the following figure.



Graphical abstract was created with BioRender.com (license number RY26BUJAMB)

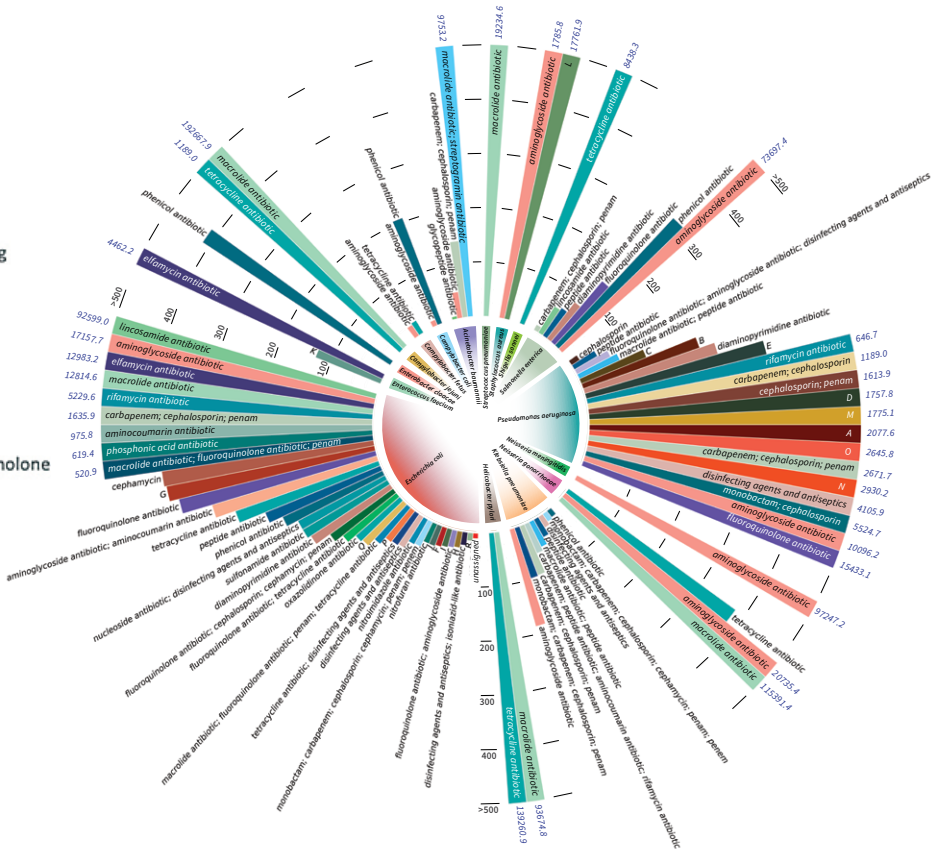
Graphical abstract for surveillance of AMR through wastewater based epidemiology

WHO priority pathogens list for R&D of new antibiotics

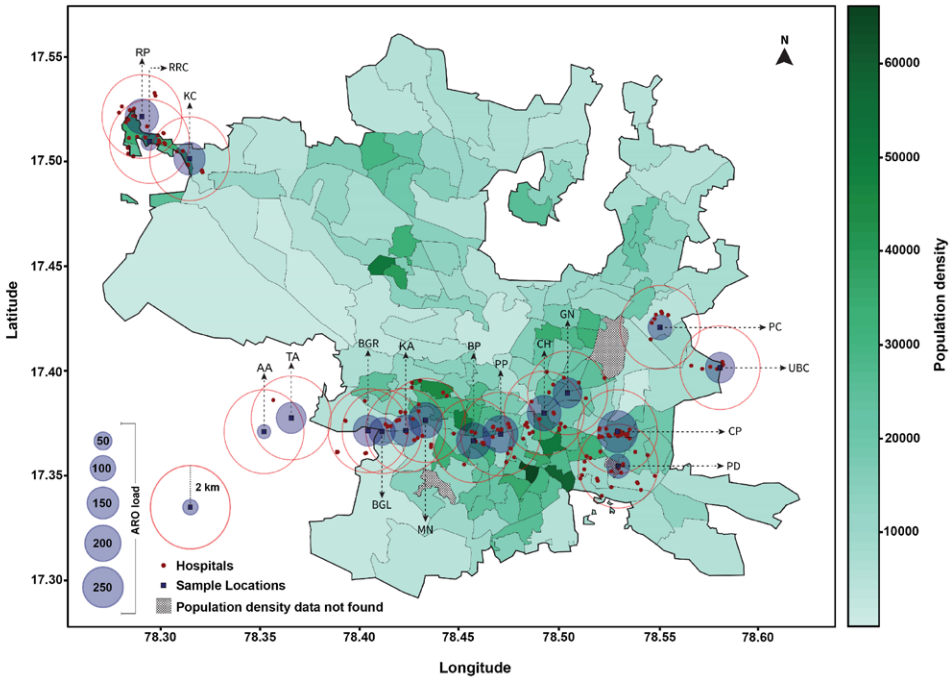
Priority 1: CRITICAL
- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

Priority 2: HIGH
- *Enterococcus faecium*, vancomycin-resistant
- *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant
- *Helicobacter pylori*, clarithromycin-resistant
- *Campylobacter* spp., fluoroquinolone-resistant
- *Salmonellae*, fluoroquinolone-resistant
- *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone resistant

Priority 3: MEDIUM
- *Streptococcus pneumoniae*, penicillin-non-susceptible
- *Haemophilus influenzae*, ampicillin-resistant
- *Shigella* spp., fluoroquinolone-resistant



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



Antimicrobial resistance landscape in a metropolitan city context using open drain wastewater-based metagenomic analysis

Ward-wise population density map of the city showing the antimicrobial resistance ontology (ARO) load at the 17 sampling locations. The blue squares indicate the geographical co-ordinates of the 17 wastewater sampling sites. The translucent blue circles around the sites indicate the ARO loads at the respective sites. The red dots indicate the geographical co-ordinates of the hospitals in the 2 kilometres radius of the sites. The red lined circles indicate the 2 kilometres radius around the sampling sites.

Surveillance of Antimicrobial resistant pathogens and antimicrobial resistance genes from clinical samples

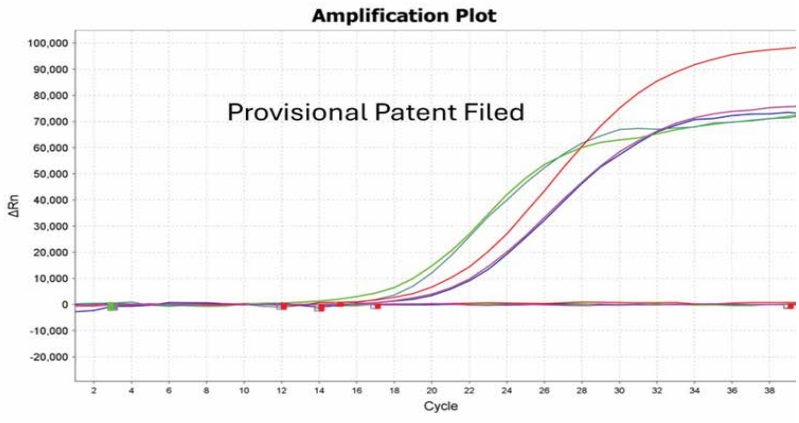
Mansi Malik

Antimicrobial Resistance (AMR) is a significant global health threat, and its surveillance is crucial for understanding, controlling, and mitigating its spread. AMR surveillance involves tracking resistance patterns in human, animal, and environmental sources, providing vital information to guide policy decisions, clinical practices, and public health interventions. It helps in early detection and monitoring of AMR trends, guiding treatment decisions, reducing misuse and overuse of antibiotics, shaping public health policies, and mapping the spread of resistance. By identifying resistance hotspots, surveillance can help in targeting interventions, such as stricter infection control practices in hospitals or more focused public health campaigns. By utilizing AMR surveillance, healthcare providers can select more effective treatments and avoid unnecessary prescriptions, reducing the risk of further resistance development.

Phenotypic methods for detecting AMR pathogens involve growing pathogens in the laboratory and assessing their resistance or susceptibility to antibiotics based on observable characteristics. These methods include Disk Diffusion Test, Broth Microdilution, and E-test. Disk Diffusion Test measures the zone of inhibition around antibiotic-impregnated paper disks, while Broth Microdilution determines the Minimum Inhibitory Concentration (MIC). E-test combines elements of disk diffusion and broth dilution but requires specialized equipment and expertise.

Molecular methods focus on the genetic basis of AMR and can detect specific resistance genes or mutations that confer resistance to antibiotics. PCR (Polymerase Chain Reaction) amplifies specific DNA sequences of the target resistance genes, allowing for rapid identification of pathogens carrying resistance genes. qPCR (Quantitative PCR or Real-Time PCR) quantifies the amount of DNA present in a sample, providing more sensitivity and quantitative data. Whole Genome Sequencing (WGS) provides a comprehensive analysis of the entire genetic makeup of a pathogen, allowing for the identification of all resistance genes and mutations contributing to AMR.

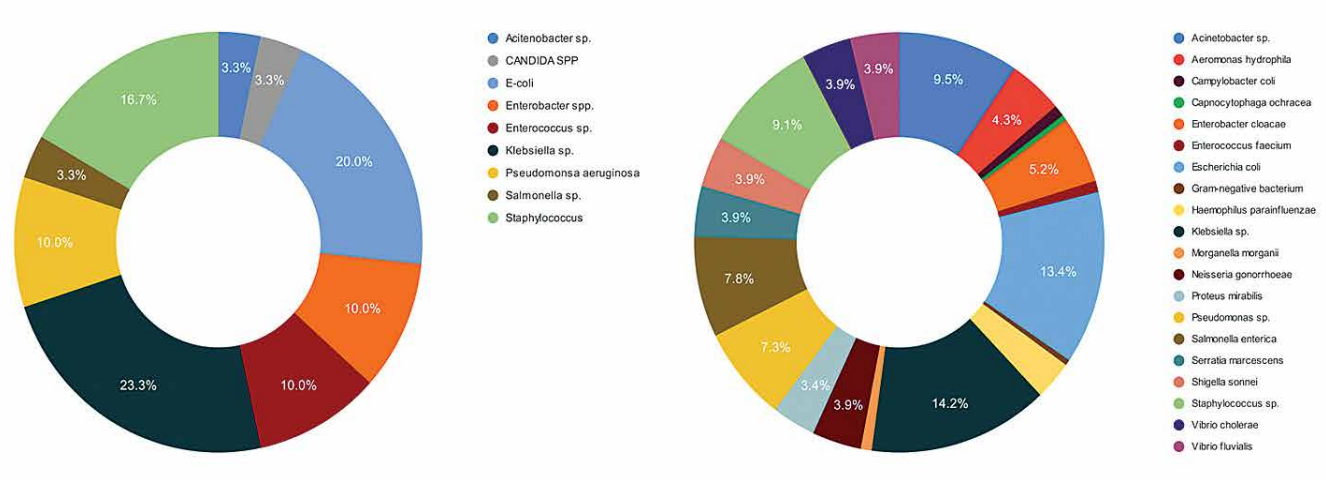
We have begun efforts to investigate the prevalence of antimicrobial resistance (AMR) by identifying pathogens, key biomarkers, and antimicrobial resistant genes (ARGs) in clinical samples using molecular tools.We are developing qRT-PCR-based assays for rapid, accurate, and cost-effective detection. Additionally, we will employ next-generation sequencing (NGS) techniques to gain deeper insights into the evolving AMR landscape in the city.



1. **Fungi (WHO+ICMR+DBT priority fungal strains)**
2. **Viruses (DENV)**
3. **Bacteria (31 WHO+ICMR+DBT Priority bacterium)**
4. **Plasmodium (5 plasmodium species)**

Pathogen	Limit of Detection (LoD)
Fungi	10 copies per microliter
Virus	1-10 copies per microliter
Bacteria	1-10 copies per microliter
Plasmodium	1 copy per microliter

Fever panel developed at TIGS to identify pathogen from clinical samples



Representation of pathogen detection by routine culture methods in comparison to whole genome sequencing

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.

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. However, the escalating resistance of mosquitoes to conventional insecticides necessitates the exploration of novel, ecologically responsible vector control strategies. Additionally, the rapid changes in climatic conditions underscores the urgent need for a comprehensive understanding of mosquito behavior, biology, and ecology to devise effective control measures.

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.

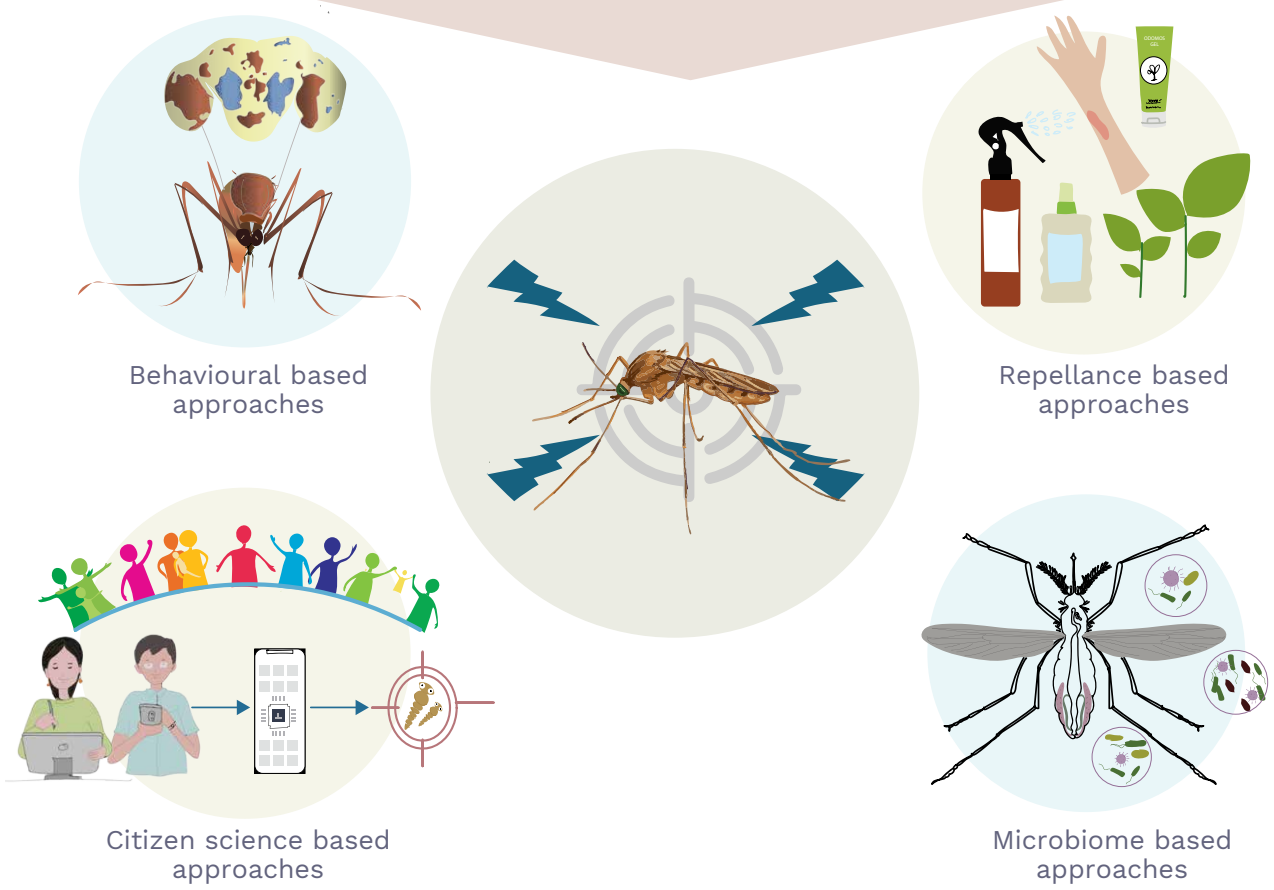


Image ideation by Sampath Kumar and Soumya M

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 disease control include insecticide spraying, insecticide-impregnated nets, and chemical mosquito repellents. Escalating resistance to available insecticides demands novel approaches for vector control. Most 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 diverse cultures. We will use dual choice olfactometer, chemical fractionation, cream formulation, membrane feeding, and a human arm-in-cage assay to find better, safer, and eco-friendly mosquito repellents.

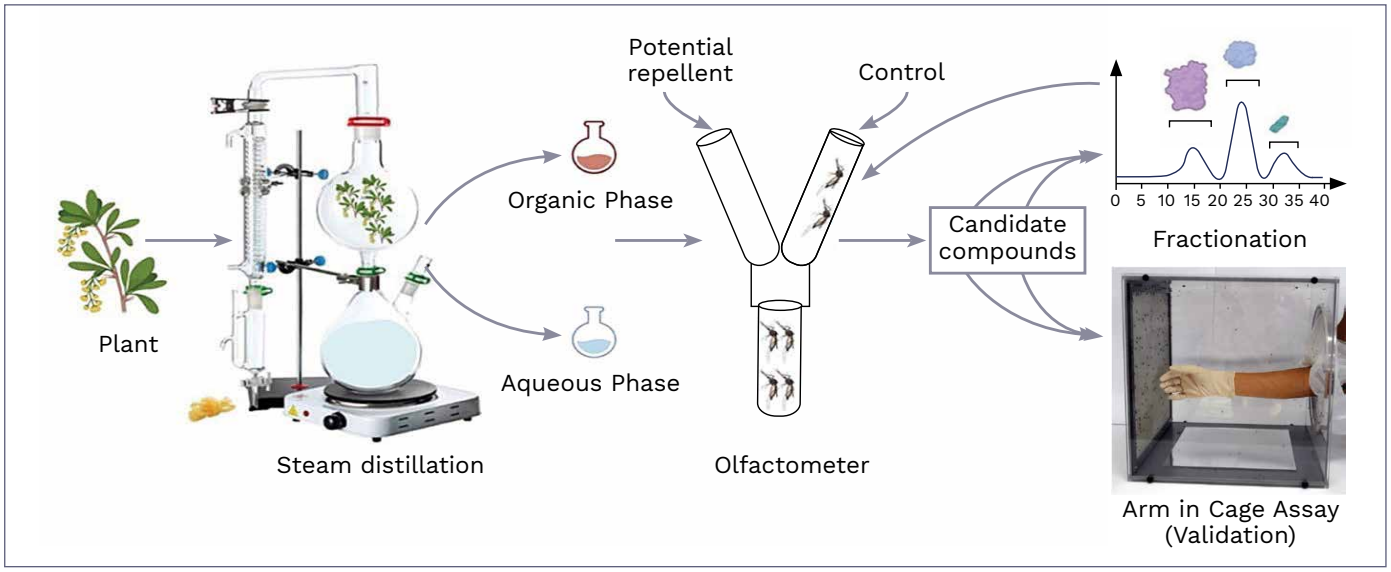


Fig. 1. Stepwise outline: Following plant identification, steam distillation will be performed to extract plant essential oil and test for mosquito behavior activity in the dual choice olfactometer. Potential candidates will be subjected to chemical fractionation for separation at the molecular level and subjected to re-testing. Finally, the cream formulation will be validated on a human Arm in a cage assay to assess the protection time against mosquito biting.

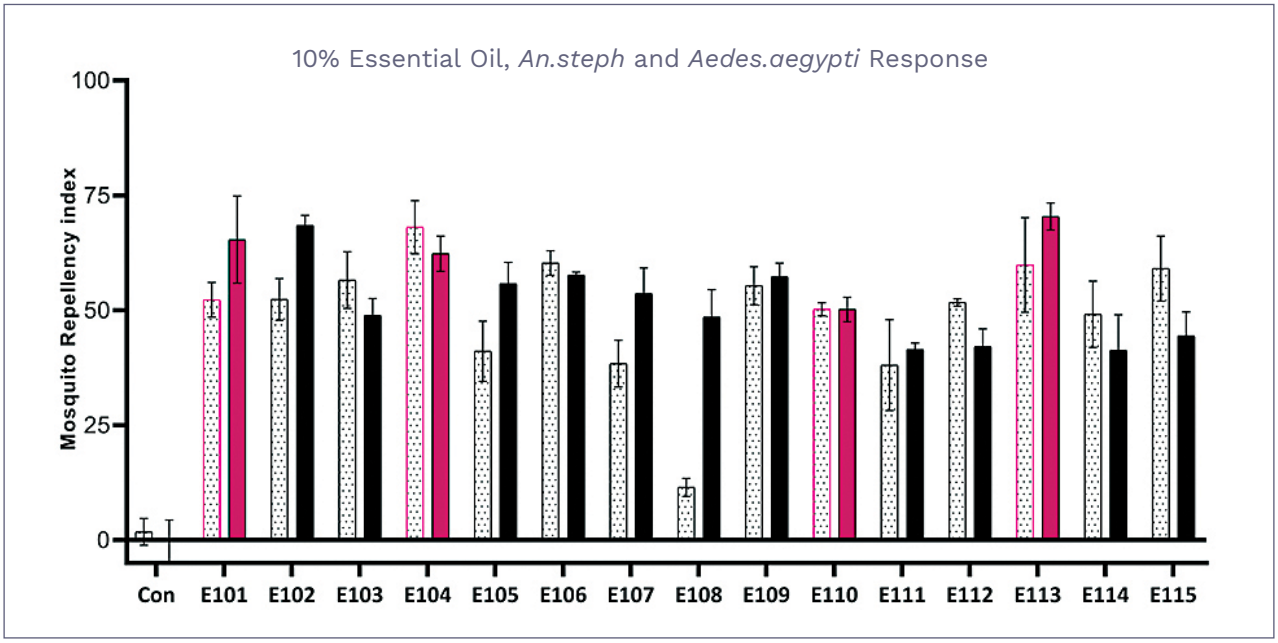
Designing and making of dual choice olfactometer (Y maze)

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, descision 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.



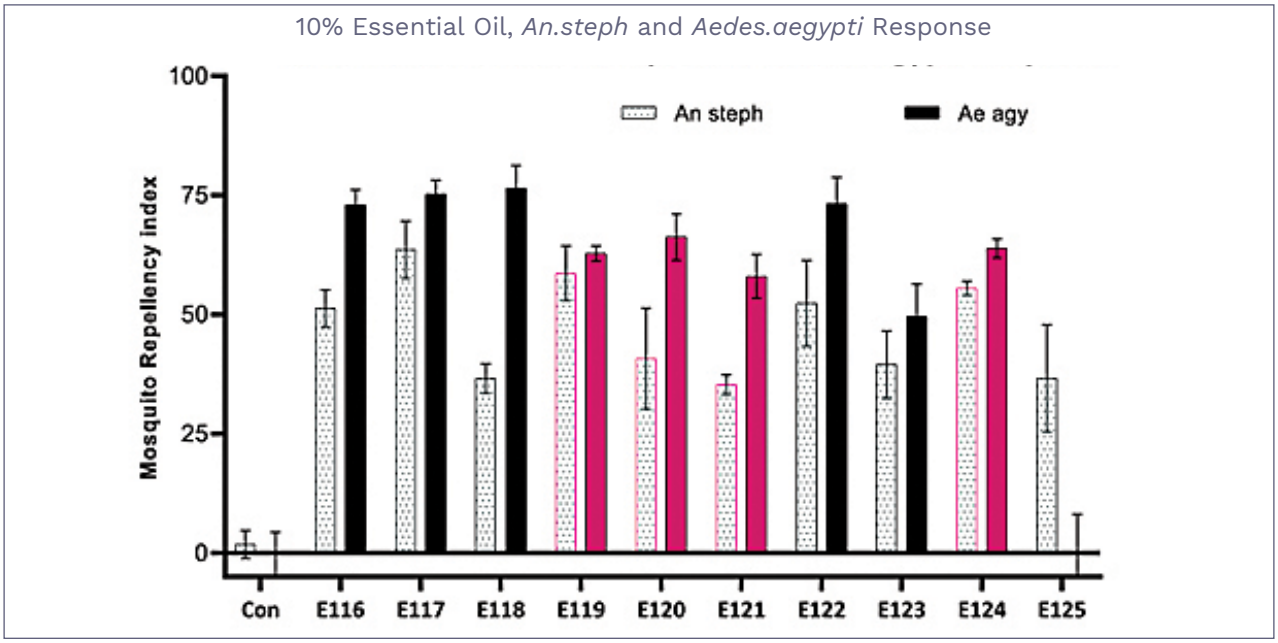


Fig.2 Graph showing mosquito response to various plant essential oils. The Y-axis represents the repellency index of the different plant essential oils (10% plant essential oil diluted with 70% ethanol). The X-axis shows different plant essential oils from E101 to E125. 70% Ethanol was used as a control. The dotted grey bar represents Anopheles stephensi, and the black bar represents Aedes aegypti response towards various plant essential oils. Colored bars (E101, E104, E110, E113, E119, E120, E121 and E124 and the novel finds of the project.

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. Plant essential oil E101, E104, E110, E113, E119, E120, E121 and E124 are the novel finding of the project. 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.

Novel plant essential oil comparison with Citronellal

We have explored the active ingredients of various mosquito repellent products in the market and found that most natural mosquito repellents contain citronellal. Next, we compared our novel plant essential oils with different dilutions of the citronellal; and observed that our novel plant essential oils are at par with a 10% dilution of the citronellal in the mosquito repellency index (Fig.3).

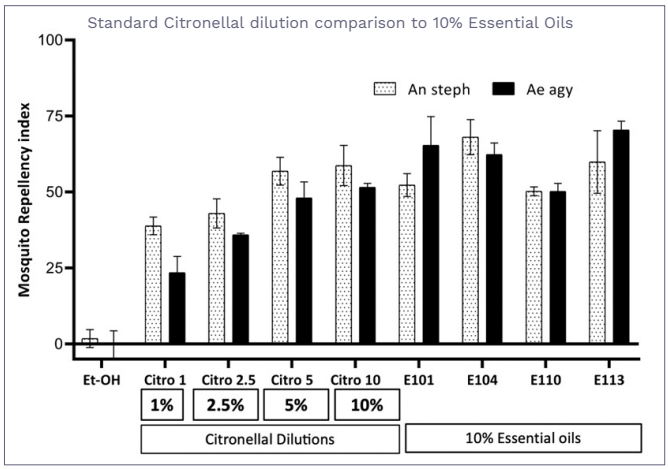


Fig. 3. Graph showing mosquito response to different citronellal dilutions (1, 2.5, 5, 10%) and 10% novel plant essential oils (E101, E104, E110, and E113,). On the Y-axis we plotted the mosquito repellency index of the different plant essential oils (10% plant essential oil diluted with 70% ethanol). 70% Ethanol was used as a control. The dotted grey bar represents Anopheles stephensi, and the black bar represents Aedes aegypti response towards various plant essential oils.

Different essential oil combinations and product formulations

Different plants produce diverse secondary metabolites. In the initial screen, we included plants with diverse chemical profiles and repellent potential. Combining different plant essential oils could be synergistic when repelling mosquitoes. We have combined three essential oils, E101, E104, and E113, and observed that mixing these essential oils strengthens the repellent property against *Anopheles stephensi* (Fig 4). We have decided to develop Two types of products, one with E104 (10% essential oil) and the second with a mix of three essential oils, E101, E104, and E113 (3.33% each).

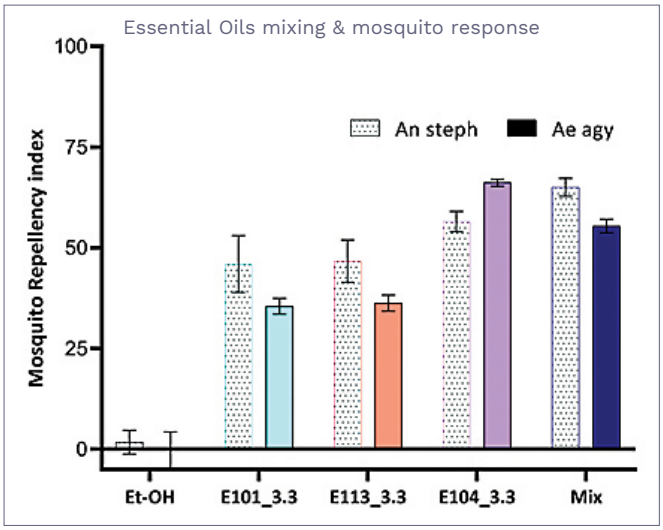


Fig. 4. Graph showing mosquito response to different novel plant essential oils (E101, E113, and E104, 3.33% each). Mixed essential oil E101, E113, and E104, 3.33% each (total 10 %). Y-axis showing mosquito repellency index. 70% Ethanol was used as a control. The dotted grey bar represents Anopheles stephensi, and the black bar represents Aedes aegypti response towards various plant essential oils.

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. Two types of products with cream formulation and testing on human volunteers would further pave the way to control mosquitoes and mosquito-borne diseases.

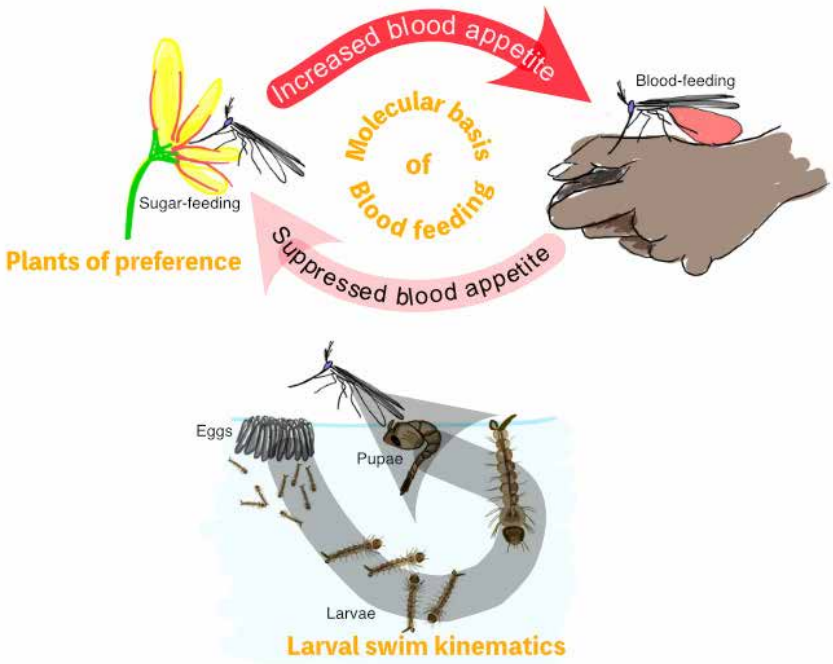
Uncovering the molecular underpinnings of blood-feeding behaviour in *Anopheles stephensi*

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 such as malaria, dengue, and chikungunya. Interfering with the molecules that drive this change in dietary preference will be an effective way of abrogating blood-feeding behaviour and therefore disease transmission.

Many behavioural studies report that *Aedes aegypti* females need to mate to develop an appetite for blood. Once blood-fed, however, they suppress this appetite until their eggs are laid. In contrast, we find that virgin female *Anopheles stephensi* – the major vector for malaria in urban India – have a robust blood appetite that is sustained even after blood-meals. This has implications for vector control strategies that seek to interfere with mating to curb vector-borne diseases. While such strategies may be effective for *Aedes* species, they will likely increase disease transmission through *Anopheles* species.

Mated female *An. stephensi*, however, do modulate their blood appetite. From being uninterested in blood-meals when they emerge, they become highly motivated to take them three days later (this initial ramp-up of blood appetite is regardless of mating status). Blood-feeding is then dramatically suppressed until the mated female lays her developed eggs. This suggests that the internal state of the female influences her dietary choices. We have looked at gene expression changes in the brain across these behavioural states to identify candidates that might promote or suppress blood-feeding. Knock-down experiments implicate two molecules that synergistically act in promoting blood-feeding and expression pattern analyses suggest that they act in different cell types in the brain. These will be useful targets for developing small-molecule interventions for blood-feeding.



Summary of feeding behaviour in Anopheles stephensi

Inducing refractoriness to Plasmodium infection through *Wolbachia* transinfections

Sampath Kumar

Vector-borne diseases, particularly malaria, dengue, and chikungunya, pose significant public health challenges globally, with India being a major contributor to the malaria burden in Southeast Asia. This project aims to leverage the natural endosymbiont *Wolbachia* to develop innovative strategies for vector control.

The rationale for *Wolbachia*-Based Strategies relies on its

a. **Effectiveness Against Multiple Diseases:** *Wolbachia* has demonstrated the ability to induce refractoriness to various pathogens, including Plasmodium, the causative agent of malaria, and viruses responsible for dengue and chikungunya. By manipulating mosquito populations to carry *Wolbachia*, we can potentially reduce the transmission rates of these diseases, thereby improving public health outcomes.

b. **Natural and Sustainable Approach:** Unlike genetic modification techniques, *Wolbachia*-based strategies utilize naturally occurring endosymbionts. This reduces the ethical and ecological concerns associated with genetically modified organisms (GMOs). The use of *Wolbachia* is seen as a more sustainable approach to vector control, as it does not rely on chemical insecticides, which can lead to resistance in mosquito populations.

c. **Dual Strategies of Population Control:** *Wolbachia* can be employed for both population suppression and replacement strategies. Population suppression involves reducing the number of disease-carrying mosquitoes, while population replacement focuses on introducing *Wolbachia*-infected mosquitoes that are less capable of transmitting pathogens. This dual approach enhances the flexibility and effectiveness of vector control programs.

(d) Independence from Pathogen Evolution: *Wolbachia*-based strategies are less susceptible to the evolutionary adaptations of pathogens compared to traditional methods. As *Wolbachia* affects the reproductive capabilities of mosquitoes, it can provide a long-term solution to vector control without being directly targeted by the evolving pathogens.

(e) Promising Preliminary Results: Previous studies across the world have shown that certain *Wolbachia* strains, such as wAlbA, wAlbB, wMel can induce high levels of cytoplasmic incompatibility and maternal transmission, leading to the successful establishment of *Wolbachia* in mosquito populations. These findings provide a strong foundation for further research and application in vector control.

In the project will are focusing on isolating diverse *Wolbachia* strains from various insect sources and evaluating their potential for transinfecting *Anopheles stephensi* mosquitoes. The project has the following phases:

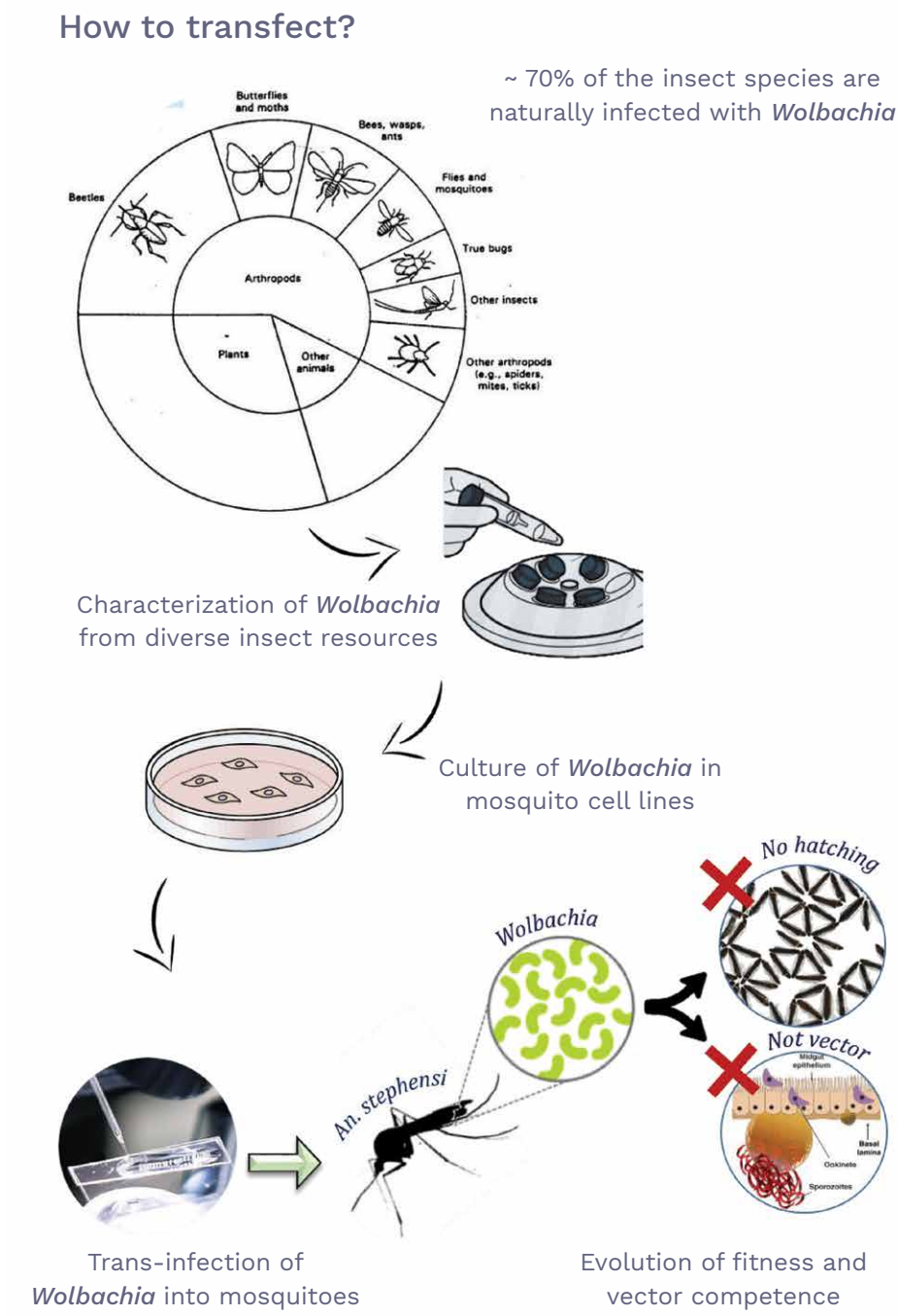
» **Isolation and Culture of *Wolbachia* Strains:** The first objective is to identify and culture a diverse range of *Wolbachia* strains from multiple insect species.

» **Infection Protocol Optimization:** Optimize infection protocols for *Anopheles stephensi* through embryonic and maternal microinjection techniques.

» **Evaluation of Fitness and Reproductive Characteristics:** Assess the fitness and reproductive characteristics of the infected *Anopheles* mosquitoes.

» **Assessment of Plasmodium-Blocking Ability:** Evaluate the ability of the infected mosquitoes to block Plasmodium transmission.

The project represents a significant step forward in adding another important weapon in the multipronged fight against vector-borne diseases. By harnessing the potential of *Wolbachia*, we aim to develop effective, sustainable, and ethically sound strategies for controlling mosquito populations and reducing disease transmission. The multi-disciplinary approach, combining insights from molecular biology, genomics,



and public health, positions this project as a critical initiative in addressing the pressing challenges posed by malaria and other vector-borne diseases in India and beyond.

So far, *Wolbachia* has been isolated and characterized in 14 insect species obtained from the National Bureau for Agriculturally Important Insect Resources. Among these, two strains exhibit male-killing traits, while one strain shows a cytoplasmic incompatibility phenotype in its native host. The An. stephensi (Mos43) cell lines have been revived, and transfection protocols are being standardized. Additionally, adult and embryonic manipulations for transfecting *Wolbachia* from various insect sources have been initiated

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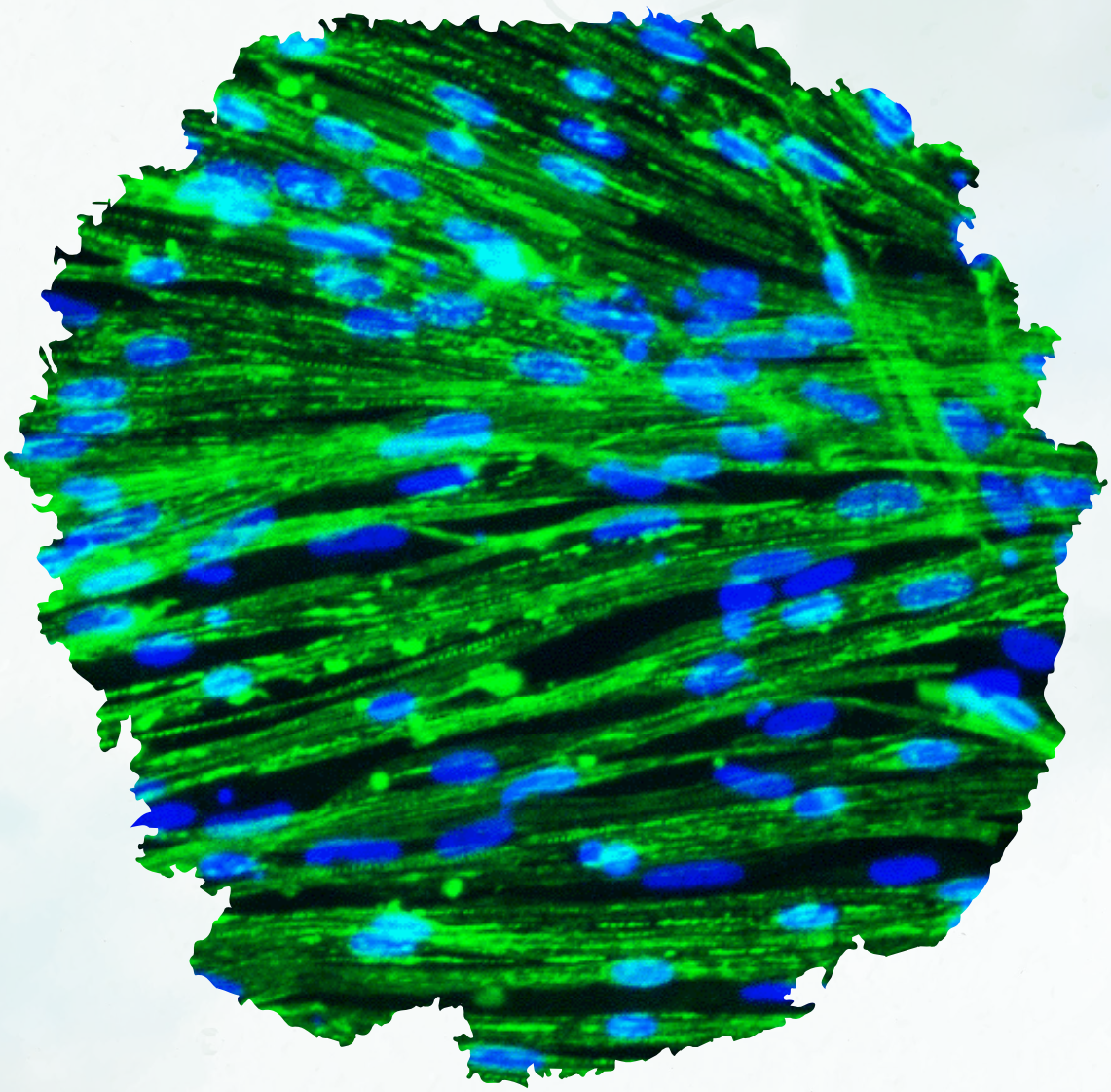

Rare Genetic Disorders

Rare Genetic Disorders

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Rare diseases are conditions that are infrequent in occurrence, affecting fewer than 1 in 1000 individuals as defined by the World Health Organization, but cumulatively impacting over 400 million people worldwide. 80% of these disorders have a genetic cause associated with mutations in specific genes that lead to distinct and often uncommon medical manifestations, known as rare genetic disorders (RGDs).

5000-8000 RGDs have been identified across the world, 450 of which have been reported in India. Given India's population of over 1.4 billion people, estimates suggest ~70-90 million individuals are affected by RGDs. Approximately two-thirds of these disorders impose life-limiting challenges, with around 70% emerging in childhood and nearly 30% of affected children failing to reach their fifth birthday. This is a huge burden for the country, and carries large physical, emotional and socio-economic costs for affected families. Compounding factors such as the practice of consanguineous marriages, disparities in access to healthcare services, limited genetic testing, and a lack of early diagnostics, targeted treatments and specialized care further impacts RGD patients.

TIGS has a dedicated program on rare genetic disorders with a focus on developing cost-effective diagnostics and screening methods at population scale to accurately identify carriers and/or patients. In parallel, we are also working on indigenization and disease modeling to enable platforms for the development of low-cost and affordable therapeutic interventions.

Diagnostics and Screening

Rare Genetic Disorders (RGDs) are of low prevalence and individually rare, making it challenging for industry to develop cost-effective diagnostic tools. Yet collectively RGDs affect a considerable number of children in a highly populous country like India. These patients require accurate diagnosis for therapeutic interventions and management to be initiated at the earliest. The diagnosis of RGDs is challenging due to the lack of awareness, the genetic heterogeneity and variety of overlapping symptoms the patients 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. It typically takes ~7 years for patients to know the underlying cause of their symptoms and get a confirmed RGD diagnosis.

At TIGS we work towards developing affordable, rapid, indigenous diagnostic solutions that are accurate and cater to the Indian RGD community by accounting for appropriate ethnicity-based genetic mutations. Our diagnostic assays are designed with population level screening and compatibility with carrier and newborn screening in mind.

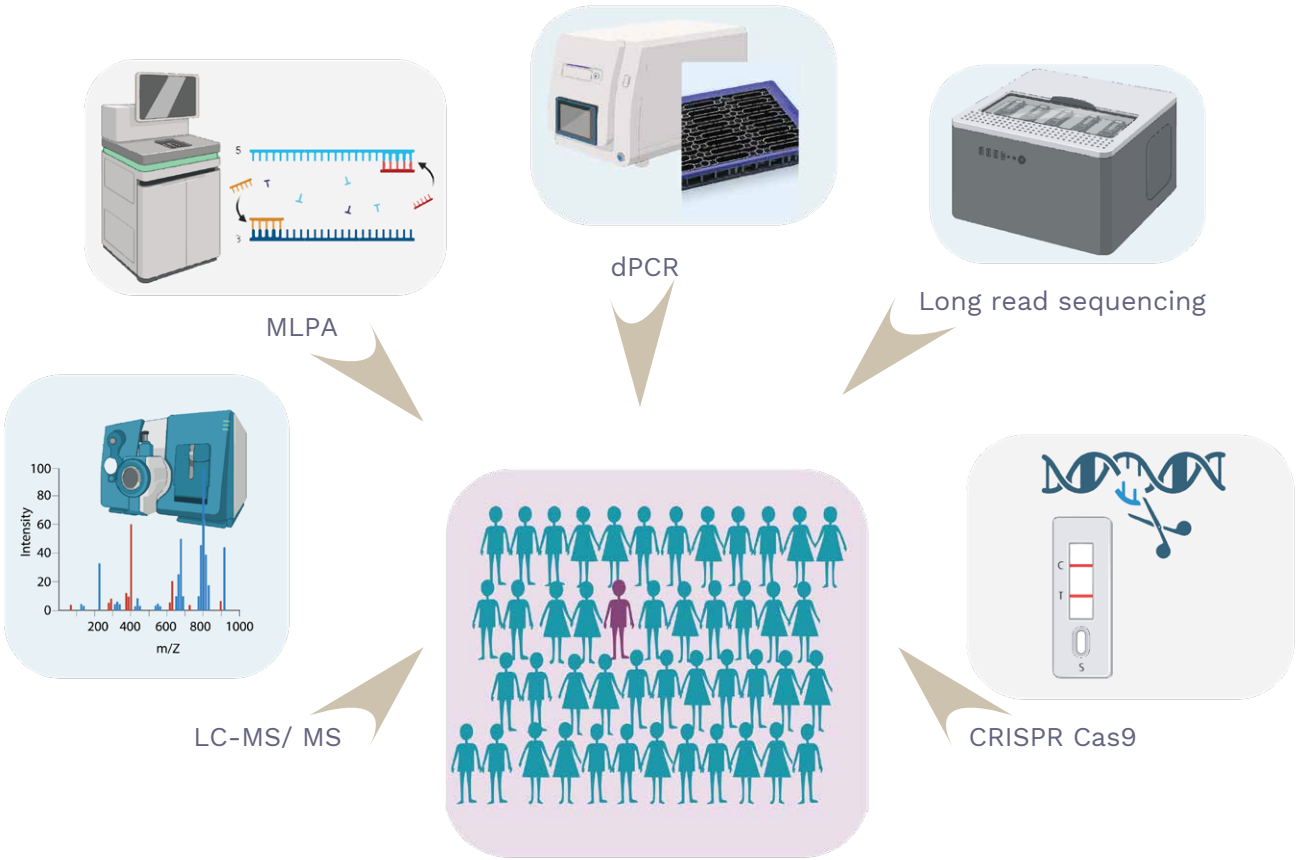


Image ideation by Shivranjani C Moharir

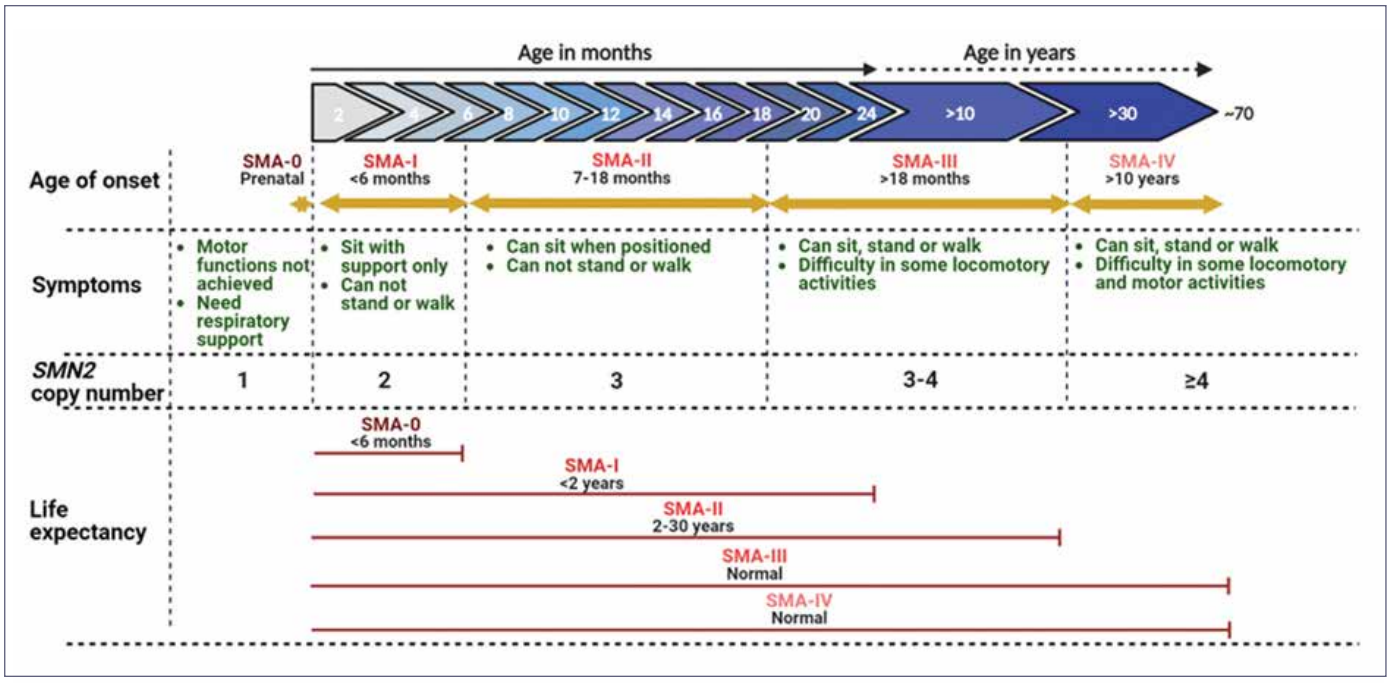
Development of digital PCR-based diagnostic assay for Spinal Muscular Atrophy

Shivranjani C Moharir

[In collaboration with CSIR-CCMB and DBT-CDFD, Hyderabad and CureSMA Foundation of India]

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 developing 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.

The number of *SMN2* copies correlates inversely with the severity of the symptoms. Knowledge of SMN2 copy numbers is crucial for accurate 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. We are establishing 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.



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)

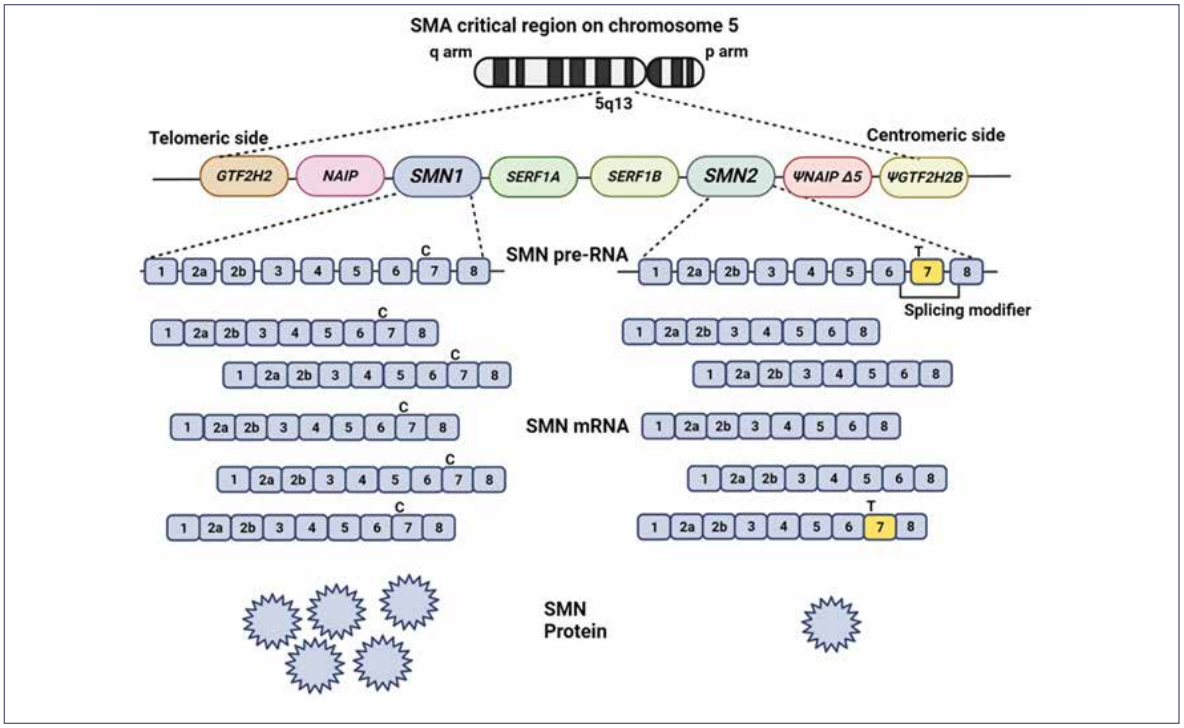


Image showing the SMA critical region on chromosome 5. The SMA critical region on chromosome 5q13 consists of four genes SERF1A, SMN1, NAIP, GTF2H2 and their duplicated copies SERF1B, SMN2, ΨNAIP Δ5 (pseudogene NAIP with exon 5 deletion), and ΨGTF2H2B (GTF2H2 pseudogene). ~95% of SMA patients have a 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)

We have collaborated with the patient advocacy group, CureSMA Foundation of India to understand the implications associated with the disorder and have conducted and participated in conferences and societal events to spread the awareness about the condition and the importance of early diagnosis and screening.

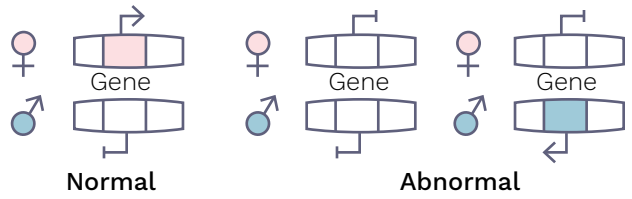
SMArt Con 2024 at Gurugram

Developing cost effective diagnostics and pharmacogenomics driven management protocol for imprinting disorders

Gayatri R Iyer

In collaboration with Kamineni Hospitals, Hyderabad; Jaslok Hospital, Mumbai; Aster Hospital, Bengaluru; JSS Medical College, Mysuru; Karnataka Institute of Endocrinology and Research, Bengaluru; Indian Angelman Foundation and Indian Prader Willi Syndrome Association]

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.



Genomic imprinting illustration. Label Pink denotes maternal allele and blue denotes paternal allele

One such group 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 13 established syndromes and four of these - Prader Willi syndrome (PWS), Angelman syndrome (AS), Beckwith Wiedemann Syndrome (BWS), and Silver Russell Syndrome (SRS) - are in focus currently at TIGS. 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 affected babies. 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 thus the backbone for investigating these syndromes which only a few labs offer at expensive rates.

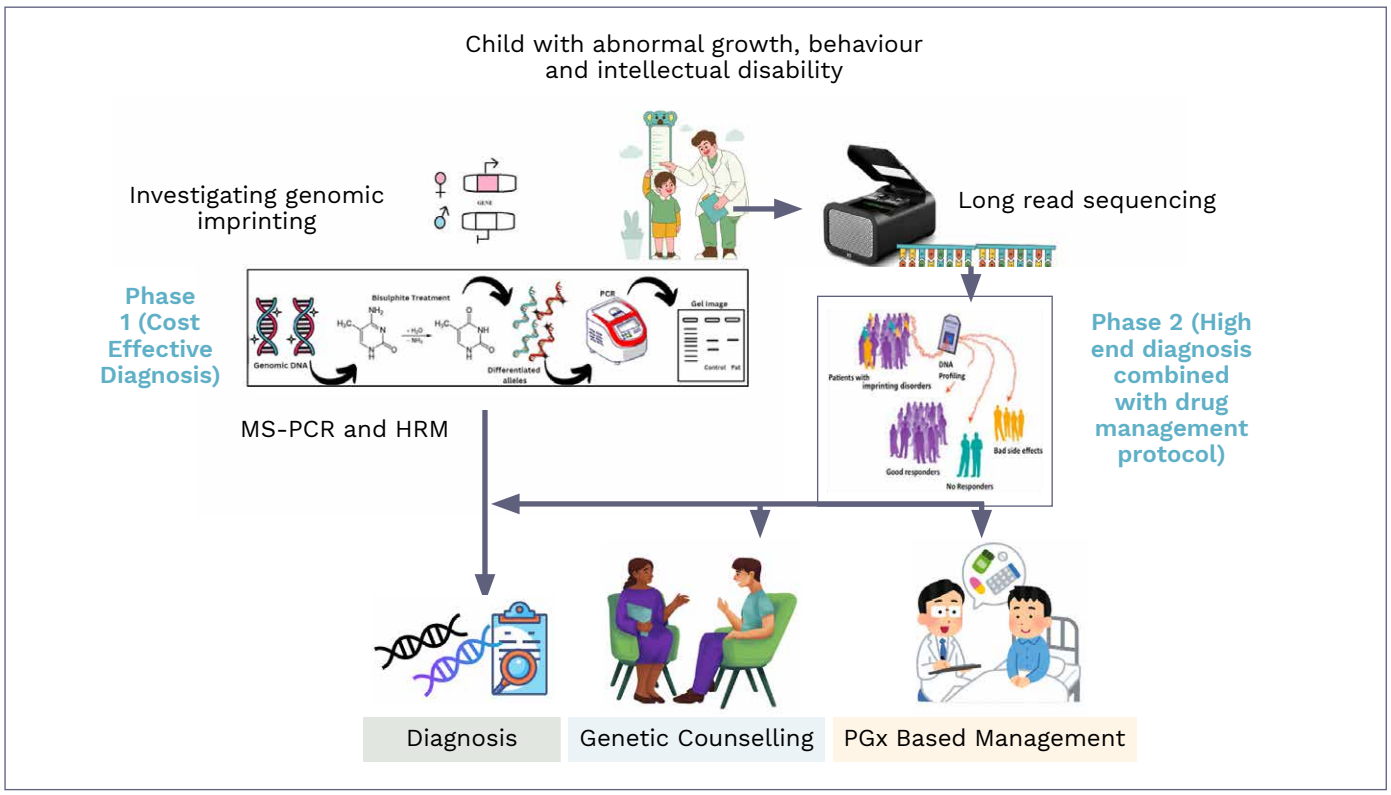
Methylation-specific polymerase chain reaction (MS-PCR) is a simple, rapid and cost-effective modality with robust performance that requires low labor and equipment and can be easily deployed in remote locations. A pilot study of 102 clinically suspected cases mentioned above showed about 28% to be confirmed as one of four known imprinting disorders by a simple methylation-based test indicating that these disorders are not as rare as cited, but require a timely referral and correct diagnostic modality to offer genetic counselling, plan prenatal diagnosis and facilitate appropriate management.

Every individual responds differently to medications because of differences in genetic makeup that affect drug metabolism. Genic polymorphisms govern enzyme activity like absorption, distribution, metabolism, and excretion of drugs. Applying this information in optimizing patient prescription can reduce adverse drug reactions while achieving maximum benefits - a branch of personalised medicine called pharmacogenomics.

PWS & AS individuals require to be on long-term medications from early childhood, which can show side effects like neurosis, aggressive behaviour, anxiety, depression, insomnia which often get misinterpreted as syndromic presentation. Imprinting disorders as a group is more sensitive to psychotropics, requiring lower than typical doses. Performing pharmacogenomic profiling can thus enable clinicians to devise personalized therapies for these patients.

We are working towards a two-phase plan wherein the first stage, MS-PCR based diagnostics will help in qualitative confirmation of an imprinting disorder and in the second phase a long-read sequencing panel for diagnosis as well as pharmacogenomic profiling of individuals suspected to have imprinting disorder will

be applied. This will shorten the time for diagnosis, rule out the need for different diagnostic techniques, inform genotype-phenotype based counselling and surveillance as well as allow drug efficacy to be incorporated into their clinical management. This project is also sanctioned for the DST INSPIRE Faculty grant.



Workflow for genomic imprinting disorders – diagnosis, management and counselling

Molecular investigation of syndromic cleft lip and palate for appropriate management and genetic counselling

Gayatri R Iyer and Saveetha Meganathan

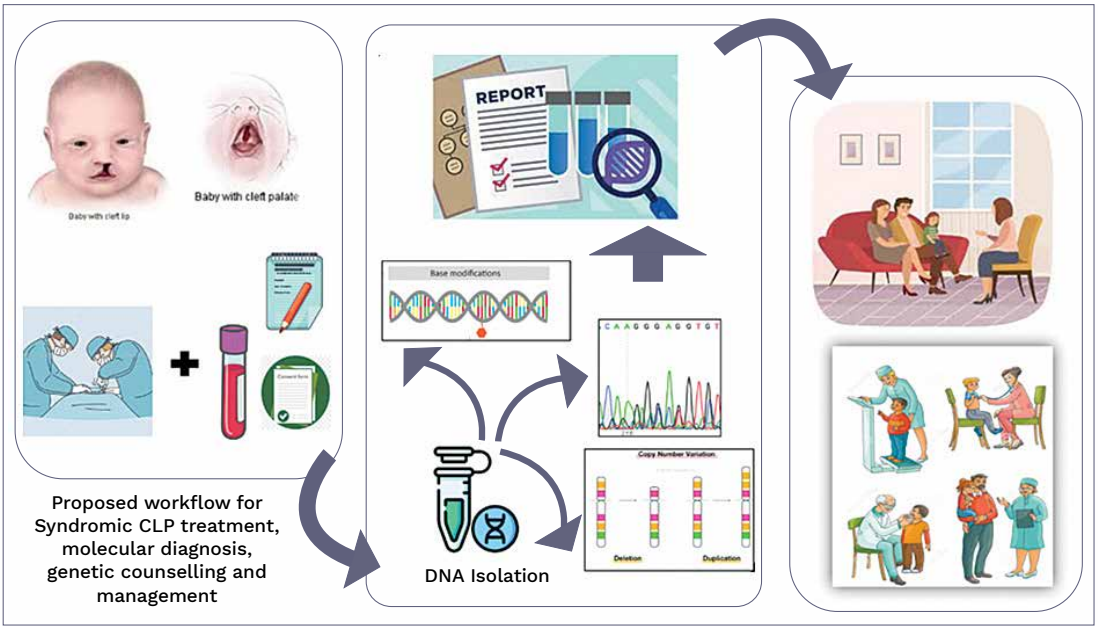
[In collaboration with Kamineni Hospitals, Hyderabad and JSS Medical College, Mysuru]

Orofacial clefts, notably cleft lip (CL) and cleft palate (CP), are the most common craniofacial birth defects in humans and represent a substantial personal and societal burden. Clefts affect approximately 1 in 700 individuals globally. Studies have shown that cleft palate has a relative risk of occurrence which is 15 to 56 times higher among first degree relatives. About 30% of cleft lip and palate cases have a genetic origin with around 154 characterized syndromes which present with additional phenotypic features to cleft lip and palate. In syndromic cases, other systems like skeletal, neurological, and cardiac are additionally involved, affecting growth and development. Clefting is also associated with a higher risk of various cancer types, including breast, brain, and colon cancers.

Cleft syndromes can be associated with chromosomal aberrations which are typically detected by karyotyping or chromosomal microarray, sequence variants that require short read sequencing panels like whole exome or genome sequencing and epimutations that are identified by MS-PCR and MS-MLPA.

Molecular diagnosis of cleft lip and palate can therefore be complex, but it enables early syndrome identification, personalized management and prenatal diagnosis in high-risk pregnancies. India is a resource restricted country where the basic stratification of syndromic and non-syndromic clefts is not uniformly practiced. We propose developing a single assay that will help in molecular diagnosis which will allow proper genetic counselling, syndrome specific management, prediction of recurrence risk and prenatal diagnosis. The assay in addition to being comprehensive and conclusive will also save resources in terms of repeated cross consultations, time, expense and logistics.

To validate the long read sequencing comprehensive assay with clinical samples, genotype-phenotype correlation studies will be performed. In the long run, this study will enable a registry of patients with cleft lip and palate enabling real-time prevalence prediction and aid the development of innovative and cost-effective diagnosis. Both these goals are essential in assisting clinicians in delivering holistic management of syndromes to improve patient outcomes and prevention of syndromic occurrence by facilitating prenatal diagnosis. Additionally, in collaboration with the community engagement team, a model of “Phenotype first” based clinical intervention shall be developed for early screening, stratification for treatment/management and outreach to address the burden of rare genetic disorders in India.



Workflow for syndromic cleft lip and palate syndromes for diagnosis, genetic counselling and management

Development of a diagnostic method for monoamine neurotransmitter rare genetic disorders

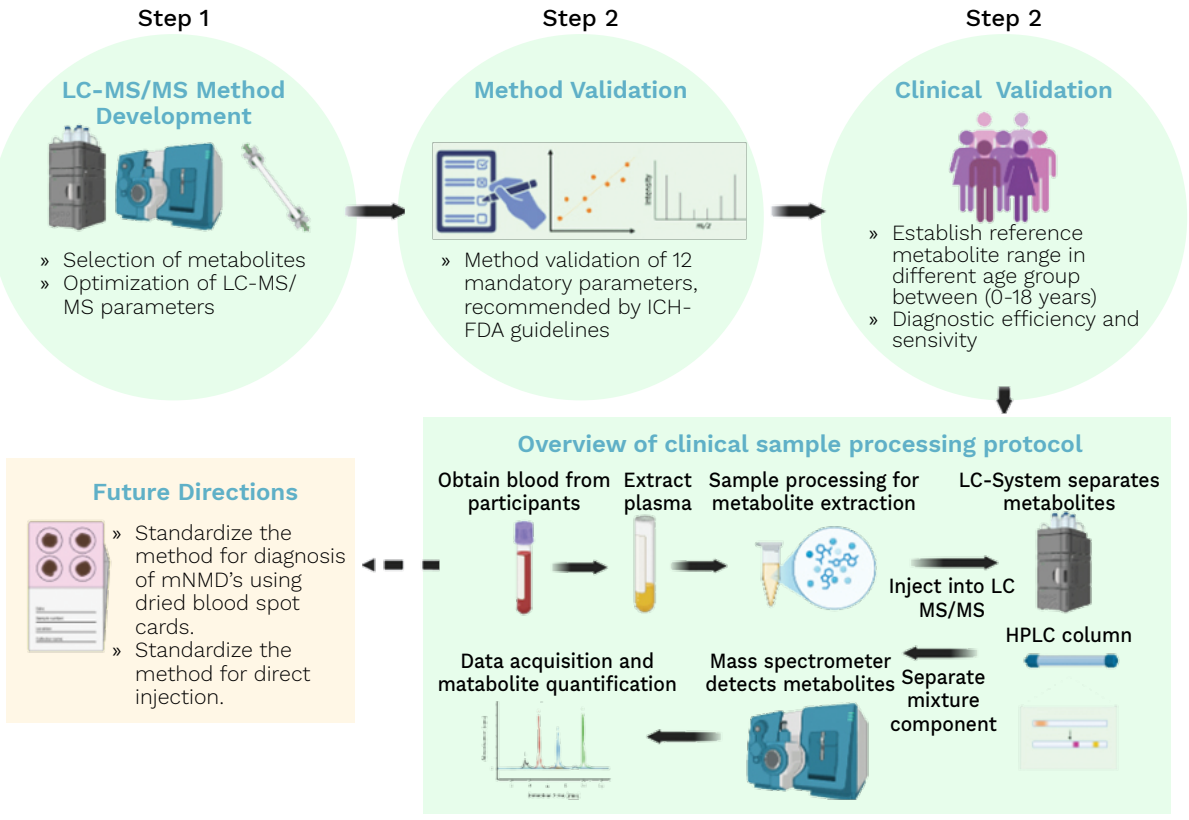
Runa Hamid

[In collaboration with IGICH & Bangalore Neurology and Rehabilitation Centre, Bengaluru]

Monoamine neurotransmitter disorders (mNMDs) are a group of thirteen rare genetic disorders (RGDs) arising due to defective components in the biosynthetic pathways of monoamine neurotransmitters (Dopamine, Serotonin, Epinephrine and Nor-epinephrine). Early diagnosis is crucial for monoamine disorders, as they are metabolic conditions that have the potential to be reversed with therapeutic interventions.

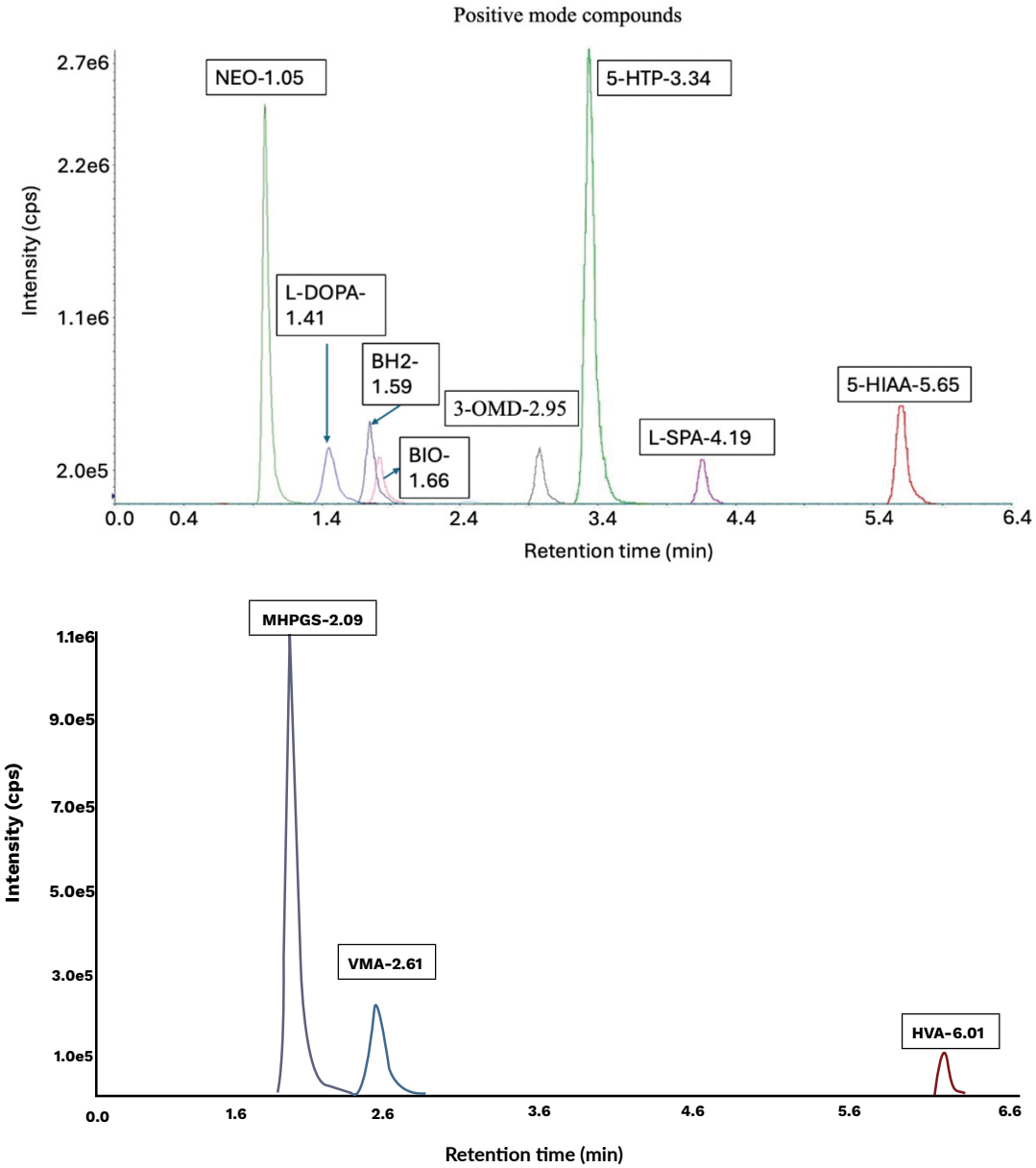
These disorders are generally diagnosed through cerebrospinal fluid (CSF) analysis which is an invasive technique associated with risk of nerve damage, infection and bleeding. The clinical phenotypes largely resemble other neurological disorders, because of which patients are often misdiagnosed or undergo diagnostic delay. There is a lack of comprehensive global epidemiological data on neurotransmitter-related disorders. An estimated occurrence can be inferred from the number of registered patients on the International Working Group on Neurotransmitter Related Disorders (iNTD) website. As of October 2024, there are 562 registered patients from 21 countries across 48 participating centers (*https //intd-online.org/*). However, India is not included in this consortium. Our unpublished literature survey of Indian case-reports suggests that these disorders are present in the Indian population at a similar frequency. Collectively, the rarity, complexity, absence of definitive biomarkers, and progressive nature of these disorders pose a significant challenge for accurate diagnosis.

We are working on a blood based diagnostic test that is quick, minimally invasive, cost-effective and predictive of mNMDs. We have developed a high throughput LC-MS/MS based diagnostic method for monoamine metabolites present in blood and are also optimizing the method for analysis through dried blood spots.



Schematic showing stepwise workflow for diagnosing mNMDs

The Liquid Chromatography-Mass spectrometry (LC-MS/MS) approach is useful because of its ability to simultaneously analyze multiple known metabolites (a process known as targeted analysis) within a specific biological pathway. An LC-MS/MS based method for extraction, separation and simultaneous quantification of 11 metabolites in the plasma have been successfully developed by us. The method has been validated for essential parameters recommended by US FDA guidelines and we are currently at the clinical validation stage. The total ion chromatogram (TIC) in the accompanying figure represents a successful separation of 11 metabolites, displaying the peak intensities of the analyte ions versus their retention time (RT). These measured ion abundances serve as quantitative indicators during LC-MS/MS sample analysis.



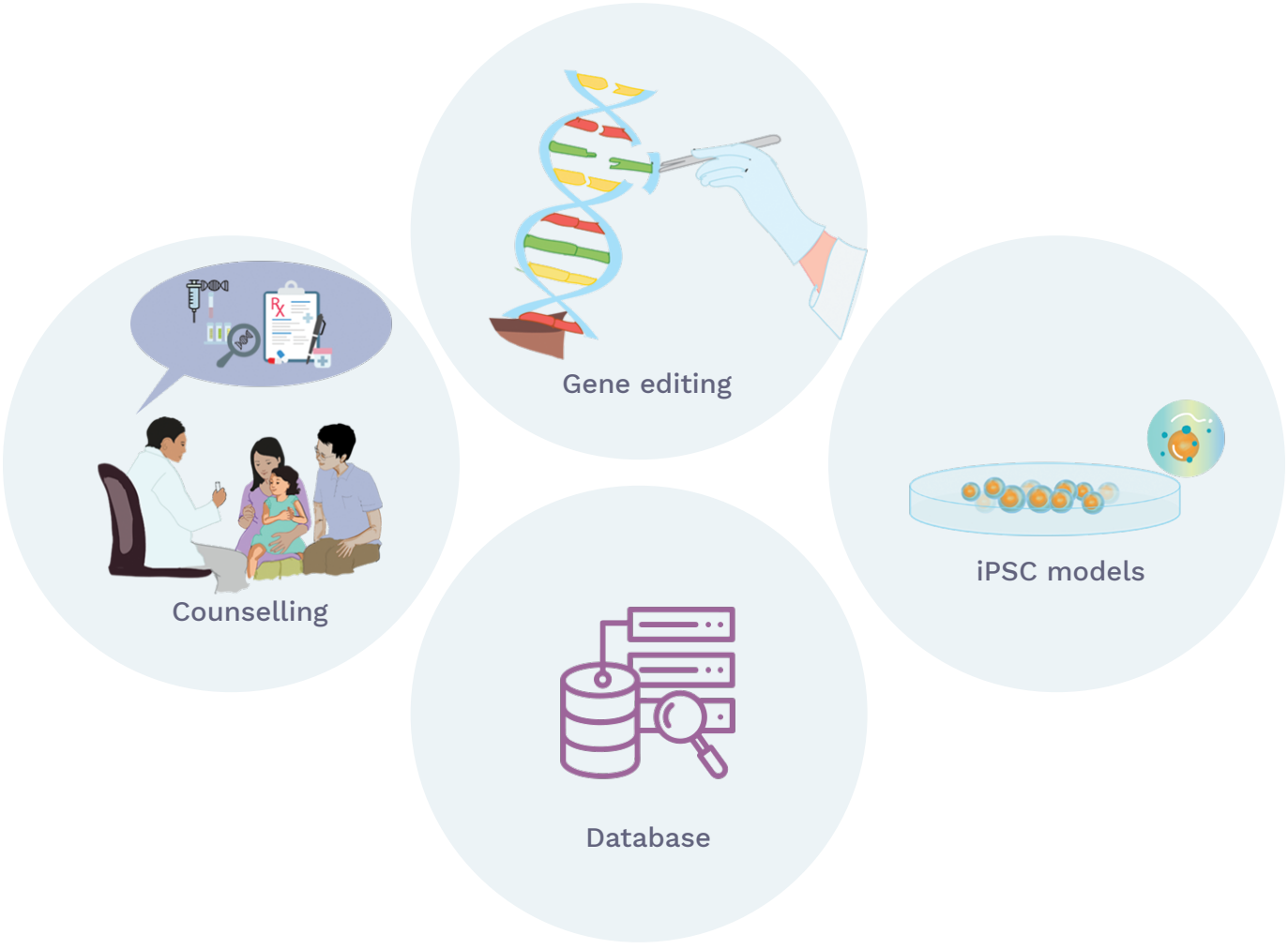
Total ion chromatograms (TIC) for positive (upper panel) and negative mode metabolites (lower panel). x-axis shows retention time of each metabolite whereas y-axis shows total intensities of ions of specific metabolites as indicated on each peak shown. cps=counts per second

In future, we aim to utilize this method of detection using dried blood spots (DBS) on filter paper, that require a small volume of blood (100 ul). Being less invasive, convenient and easy to deploy in low resource settings while maintaining sensitivity, the technology can be implemented in newborn screening programs across the country.

Therapeutics and Novel Interventions

Genetic disorders can account for up to 22% of infant deaths globally. Despite significant efforts to create new therapies, treatment options are available for only about 5% of genetic disorders due to undiscovered etiology or rapid progression to the point of no return. Most of the categorized RGDs are monogenic and occur due to loss-of-function mutations in the disease-causing gene. For a few disorders caused by a loss of protein function, 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 most of the global population, including in India. Urgent focus areas in the field include point-of-care production of therapeutics to reduce cost and/or innovation in R&D for a quick transition from the lab to clinically treating RGD patients.

At TIGS, we develop targeted therapeutic interventions using cutting-edge technologies, including mRNA and stem cell-based therapies and drug repurposing.



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

Vasanth Thamodaran

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.

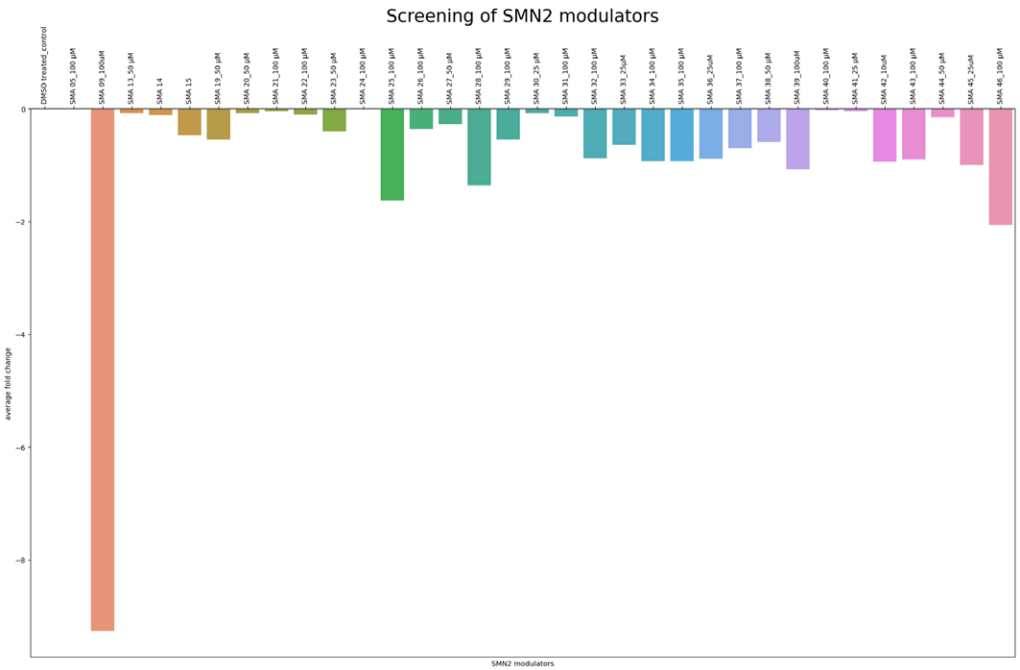
Deleterious mutations in the survival motor neuron 1 (*SMN1*) gene cause a degeneration of motor neurons, leading to muscle weakness and atrophy. SMN2 gene, an isoform of the *SMN1* gene is not able to complement the defect due to the exclusion of exon 7 during splicing, resulting in truncated non-functional 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. We are working with industry partners to identify drug candidates by screening lead compounds using our platform.



A cell-based model to identify SMN2 splicing modulators. HEK293T cells treated with risdiplam showing specific downregulation of the SMN2 short form and the same approach was used for screening 45 potential splicing modulators.

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.

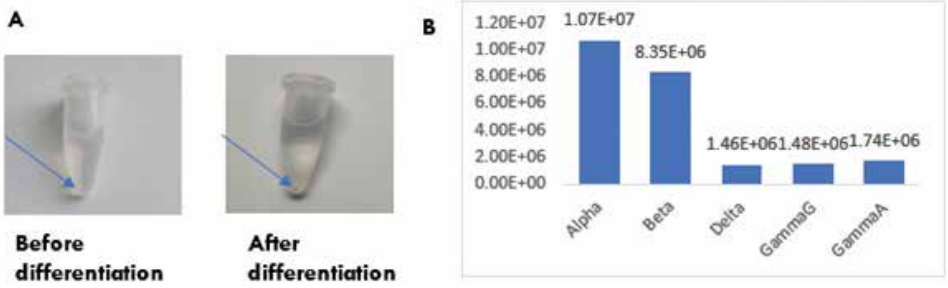
In the Indian context, CRISPR-Cas9 based gene editing approach to treat hemoglobinopathies has been well studied. However, the therapy can cost up to 50 lakhs INR, making this life-saving treatment less accessible. We are working on different components in gene editing-based gene therapy, where identifying alternative strategies that can cut down costs. We have developed an approach to upregulate fetal hemoglobin using CRISPR-Cas12 genome editing by targeting gamma globin expression, as an alternative to Cas9 based gene therapy. This will reduce the disease severity in patients with ***β***-*haemoglobinopathies* and patients with upregulated fetal haemoglobin levels can become transfusion independent. CRISPR-Cas12 genome editing tool relies on a PAM sequence that is longer than the Cas9, thus reducing the levels of off-target effects. Importantly, the smaller size of the guide RNA can reduce the cost of manufacturing, making it a better option compared to the existing Cas9 based gene editing therapies.

Identification of crRNA: The expression of ***γ***-*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 ***γ***-globin activation.

Ex-vivo editing in hematopoietic stem cells (HSCs): We plan on working further with the crRNA that gives the highest activation of ***γ***-*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.

We have developed capacity for the expansion and maintenance of patient-derived stem cells in an undifferentiated state to enable their genetic manipulation. We are currently focusing on hematopoietic stem cells (HSCs) isolated from patients suffering from blood disorders as described above but the protocols developed will be suitable for other stem cells and lineages as well in the future.



Screening of CRISPR-Cas12 gRNAs in an immortalized erythroid cell line. A) Differentiation of immortalized erythroblasts to early red blood cells expressing hemoglobin. B) LC-MS analysis showing different globin chains expressed in the erythroid cells.

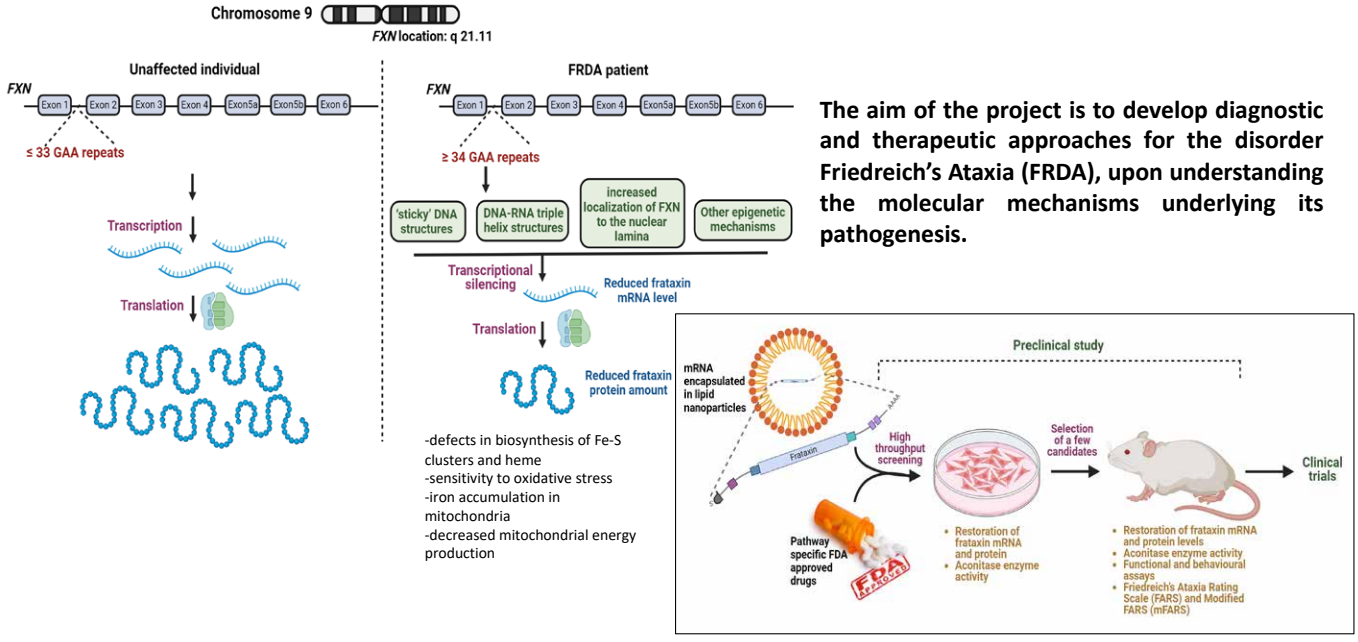
Friedreich's Ataxia: Diagnosis to therapeutics

Shivranjani C Moharir

Friedreich's Ataxia (FRDA) is an autosomal recessive genetic disorder caused due to expansion of poly GAA repeats in the intron 1 of FXN gene leading to its transcriptional repression and deficiency of frataxin protein in the cells. Healthy individuals have less than ~ 32 GAA repeats in *FXN* gene. Among FRDA patients, there is a direct correlation between the number of repeats and gene repression, reduction of frataxin protein and the severity of the disease. While around 96-98% of patients are homozygous for this mutation, the remaining fraction of heterozygous patients have other mutations along with one allele with the repeats. FRDA symptoms include ataxia, unsteady posture, frequent falling, and progressive difficulty in walking due to impaired ability to coordinate voluntary movements, slurred speech, characteristic foot deformities, and an irregular curvature of the spine. It is often associated with cardiomyopathy. The disease onset is usually early adolescence and the patients usually die by 20-40 years of age due to cardiac hypertrophy. As per an Indian cohort study, the expected prevalence in Indian population is 1: 1,00,000, while the global prevalence ranges from 2:100,000-4:100,000 and the carrier frequency is 1:60-1:100.

The molecular mechanisms underlying the pathogenesis of FRDA are still not well understood. The limited awareness and non-specific symptoms often lead to delayed diagnosis. The lack of understanding of the biomarkers associated with the disease and its progression further adds to the complexities. Appropriate therapy can be given only when the disease is correctly diagnosed. This study aims at identifying the molecular markers for FRDA and make an attempt to explore therapeutic interventions.

Development of diagnostic assay and therapeutic interventions for Friedreich's Ataxia (FRDA)



The aim of the project is to develop diagnostic and therapeutic approaches for the disorder Friedreich's Ataxia (FRDA), upon understanding the molecular mechanisms underlying its pathogenesis.

GenTIGS: Advancing research and clinical insights into rare genetic disorders

Iliyas Rashid

Rare Genetic Diseases (RGDs) are uncommon genetic disorders affecting a small portion of the population, lacking adequate diagnostic and therapeutic options. In India, the substantial disease burden associated with rare disorders is heightened by the country's large population. Stemming from gene mutations or function-altering variations, RGDs pose unique challenges due to their infrequency and impactful consequences. RGDs manifest various inheritance patterns, such as dominant or recessive traits, and can be autosomal or sex-linked. Often chronic and severely disabling, these conditions place a significant strain on healthcare systems. The intricate landscape of rare genetic disorders demands a comprehensive understanding of associated genes and variants, presenting a challenging scenario for both researchers and clinicians seeking effective interventions.

The National Policy for Rare Diseases (NPRD), launched by the Ministry of Health and Family Welfare in 2021, aims to address rare diseases through improved prevention, diagnosis, treatment, and financial support. The policy emphasizes accessible healthcare, awareness programs, and reducing the financial burden on patients and families. The UMMID (Unique Methods of Management and Treatment of Inherited Disorders) and NIDAN (National Inherited Diseases Administration) Kendras were established to provide specialized care for inherited genetic disorders. UMMID focuses on genetic counseling, diagnostic testing, and treatment, while NIDAN Kendras offer expert medical care and support for managing genetic conditions. Together, these initiatives aim to enhance healthcare access, raise awareness, and improve outcomes for rare disease patients in India. Collaboration across healthcare institutions, researchers, and policymakers is essential to strengthening these efforts.

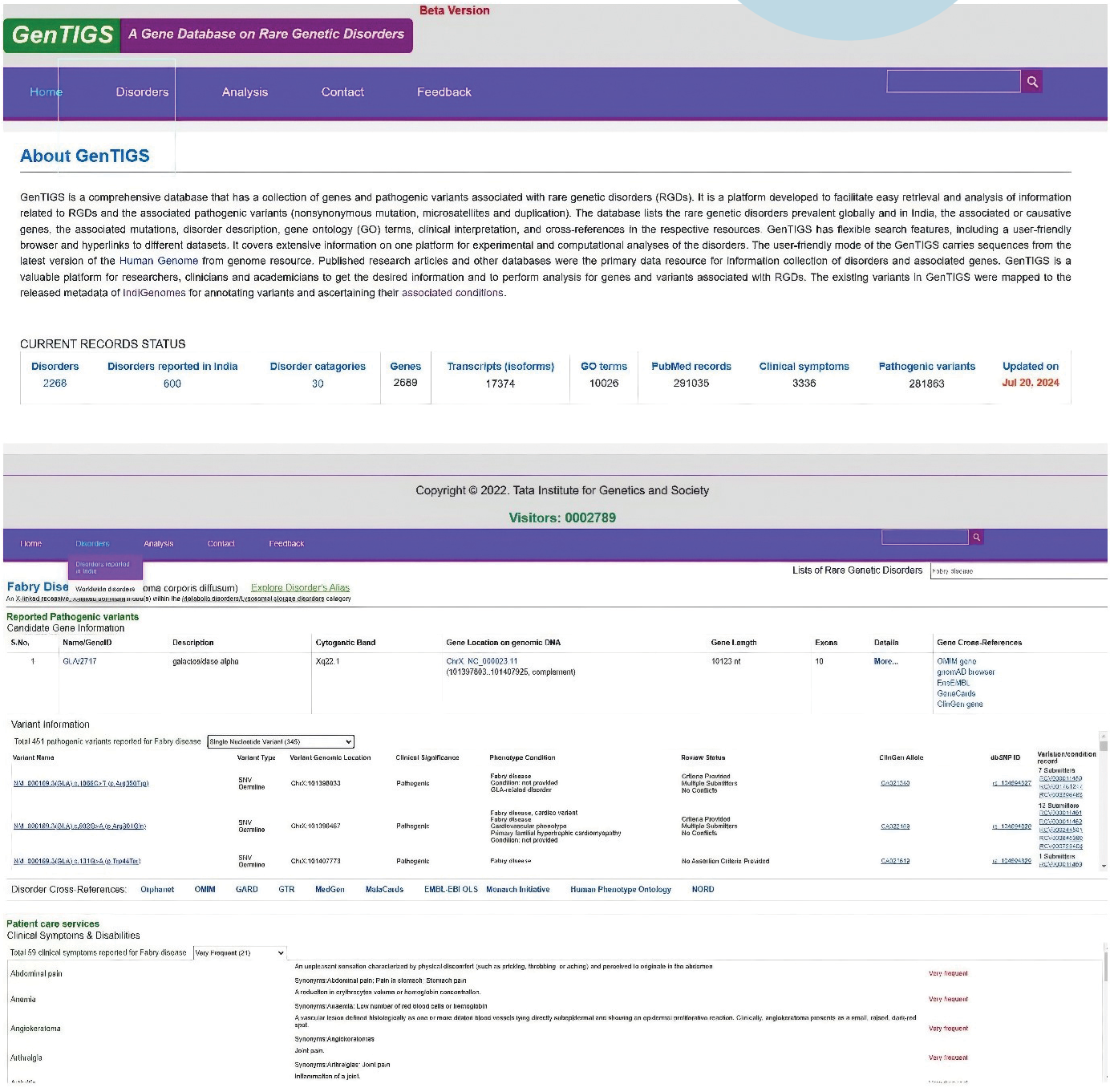
With approximately 70 million people affected by rare diseases in India, the healthcare system is under significant strain, emphasizing the need for efficient data management and research systems. In this context, platforms like GenTIGS aim to fill critical knowledge gaps and improve patient care by consolidating diverse data on a single platform. GenTIGS enhances the understanding of rare genetic disorders by providing key insights on disease prevalence, symptoms, and ongoing research. This centralized platform facilitates collaboration, research, and improves patient care by offering comprehensive information on genetic alterations, clinical symptoms, and disorder prevalence.

GenTIGS is pivotal in advancing the understanding of rare genetic conditions, offering a range of analytical tools and functionalities. It provides critical data on rare genetic disorders globally, with a particular focus on India. By centralizing genetic data and offering a structured approach to information retrieval, GenTIGS supports efficient research and clinical applications, making it a vital resource for understanding complex genetic disorders. This initiative, in conjunction with advancements in genetic sequencing, precision medicine, and patient advocacy, offers a promising path forward for improving diagnosis, treatment, and the overall management of rare genetic diseases in India. GenTIGS also emphasizes the importance of leveraging global resources and research to strengthen the understanding of genetic disorders in India. The platform offers extensive data on genetic mutations, clinical manifestations, and associated genes, contributing to a deeper understanding of the molecular intricacies of these diseases. By consolidating this information, GenTIGS facilitates a more targeted approach to research and clinical care, helping to address the challenges posed by rare genetic conditions. In summary, initiatives like GenTIGS play a crucial role in advancing the research, diagnosis, and treatment of rare genetic disorders, offering hope for improved patient outcomes in India.

The key features include a catalog of rare genetic disorders, ensures efficient retrieval of information on RGDs, their associated genes, variants, and clinical symptoms. This system provides data on 2,268 rare genetic disorders (RGDs) reported globally, along with 2,689 associated genes. It includes 600 RGDs prevalent in India, with details on 3,336 clinical symptoms and 281,863 pathogenic variants linked to these disorders. GenTIGS provides a range of analytical tools and resources for researchers, clinicians, and academicians, facilitating in-depth exploration of genes and variants associated

with rare genetic disorders. Its extensive data and features could drive advancements in genetic medicine by improving understanding, disease intervention, and analysis within the scientific community.

Scan to access GenTIGS



The GenTIGS Data Delivery System offers global and India-specific disorder data, with a summary web page serving as a hub for all relevant data points and detailed information on India-specific disorders.

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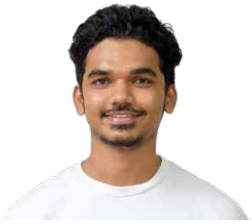

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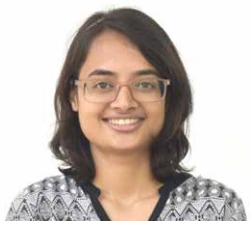

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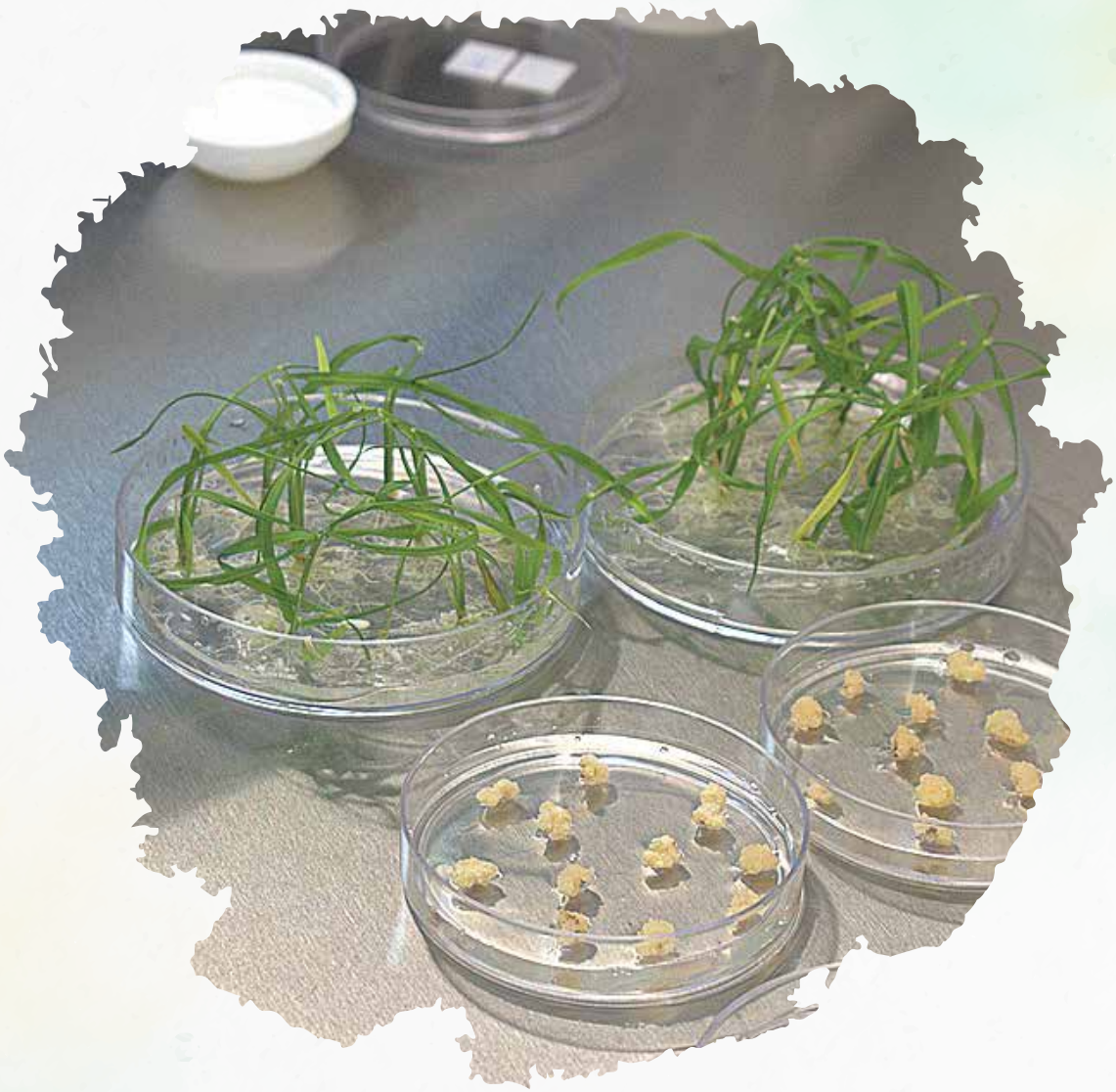


Crop Improvement

Crop Improvement

Kamal K Malukani

Sampath Kumar

V S Sresty Tavva

Ensuring a sustainable and healthy food supply is of utmost importance in a country's priorities. The emergence of invasive pests, novel diseases, and resistance issues presents significant threats to global food production, exacerbated by climate change-induced shifts favoring pest proliferation, and prompting the need for innovative technologies. It is critical for India to tackle challenges such as enhancing nutritional quality of food grains, reducing crop losses due to diseases and pests, and developing crop varieties that are resilient to environmental stresses. We are working towards overcoming these enormous challenges by focusing on cutting-edge technologies and approaches.

Genome Editing

In the face of climate change, deterioration of soil health and an increasing global population, food security and nutrition have become some of the biggest challenges. TIGS Crop improvement program intends to develop crop varieties with enhanced productivity by unification of discrete beneficial traits such as disease and pest resistance and herbicide tolerance in leading rice cultivars. The outcome of the proposed research will provide the leading cultivars in the local geography with an added advantage to survive in the drastic environmental conditions and will eventually minimize the crop yield losses. 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. The new breeding technologies such as genome editing by CRISPR/Cas (Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-associated protein) are being harnessed to achieve sustainability in agriculture by modifying target genes precisely. These tools can be used to create crop varieties with desired features such as disease and pest resistance and tolerance to herbicides within a short period of time 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 obtained through conventional breeding.

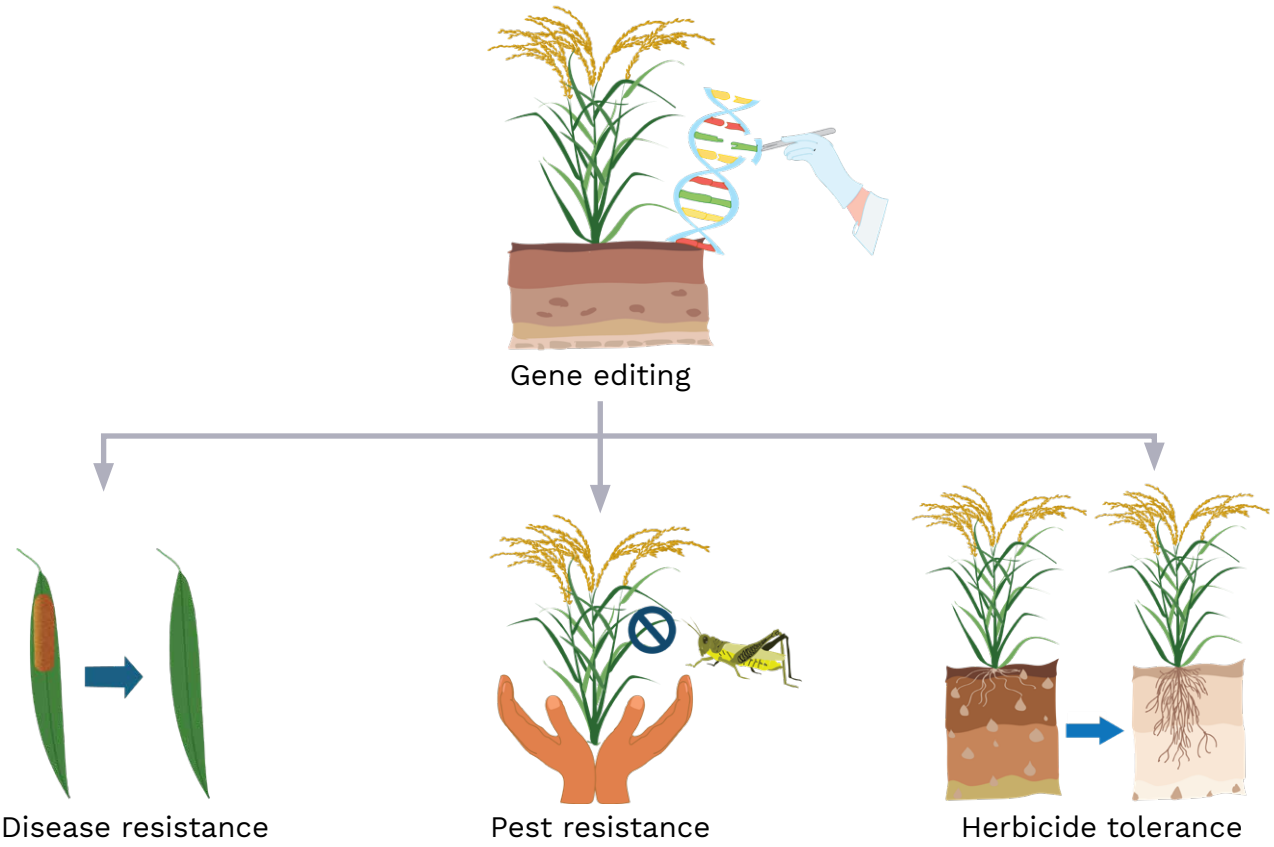


Image ideation by Sampath Kumar

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

V S Sresty Tavva

We have made considerable amount of progress towards developing bacterial and fungal disease resistant rice lines in the background of an aerobic rice cultivar (KMP 175) and a mega variety (MTU 1010). Bacterial leaf blight (BLB) 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. Similarly rice blast is a fungal disease that greatly reduces yield and grain quality in rice. Blast resistant genes are present in less than 10% of the rice varieties and introducing these into leading rice varieties can make a significant impact. Single gene edited rice lines have been developed for each of these desirable traits (BLB and Blast resistance). The selected lines having mutations in the target genes have been subjected to backcrossing to segregate out the transgenic elements.

Generation advancement and segregation of exogenous introduced DNA from selected genome edited lines

To segregate out exogenous DNA, the selected T0 genome edited lines developed for BLB resistance were backcrossed with their wild-type parental genotype (Fig. 1a). Since the construct used to transform rice lines carries a visual selection marker (DsRed) gene, the BC0F1 seed obtained from backcross experiments were screened for the presence or absence of DsRed fluorescence (Fig. 1b). The seeds which were negative for DsRed fluorescence were assumed to be free from exogenous DNA and were selected for advancement. Based on the molecular analysis, the DsRed negative BC0F1 lines carrying intended mutation in heterozygous condition (one allele from T0 mutant line and one allele from wild-type parent) were selected and advanced to BC0F2 generation through selfing. We have germinated BC0F2 seed and performed molecular analysis to identify the lines carrying mutations in homozygous condition. The BC0F2 lines which are negative for DsRed expression and carry intended mutations in homozygous condition were advanced to collect BC0F3 seed. Refer to the backcross breeding scheme presented to understand the process of mutation inheritance across generations (Fig. 1a). The inheritance of mutation from T0 to BC0F3 was studied using Sangers sequence analysis (Fig. 2).

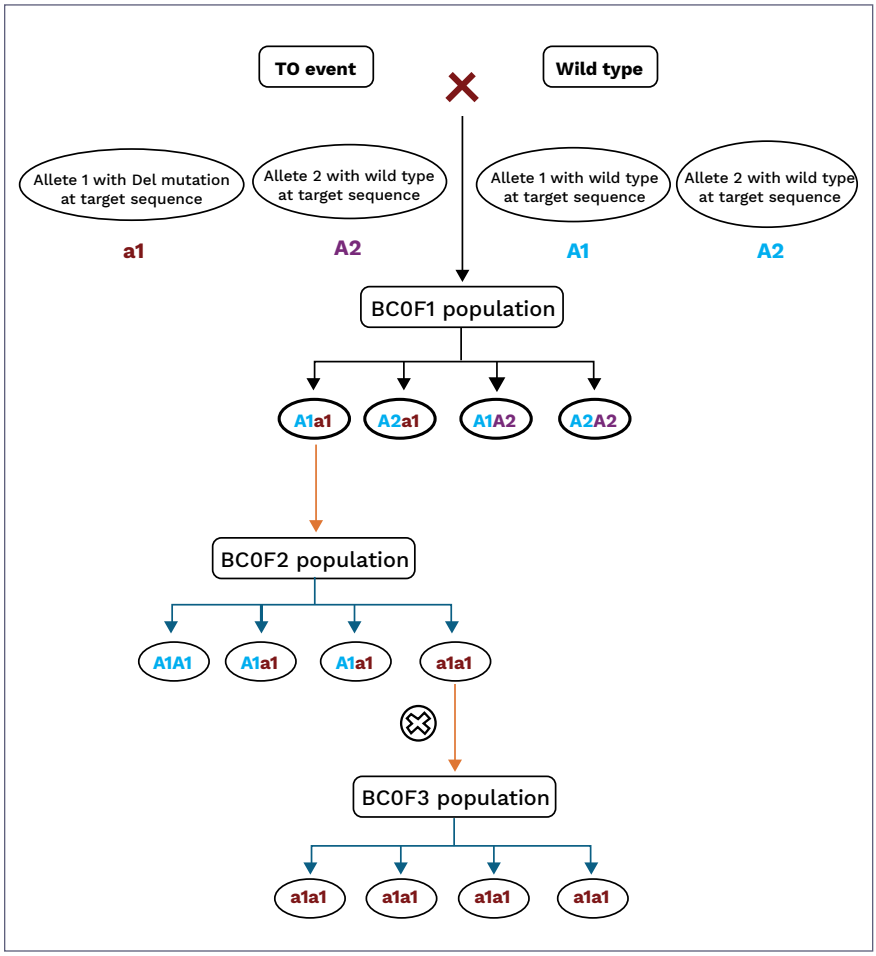


Fig. 1a Schematic representation of backcross breeding employed in this study to segregate out exogenous DNA and to understand the process of mutation inheritance across generations.

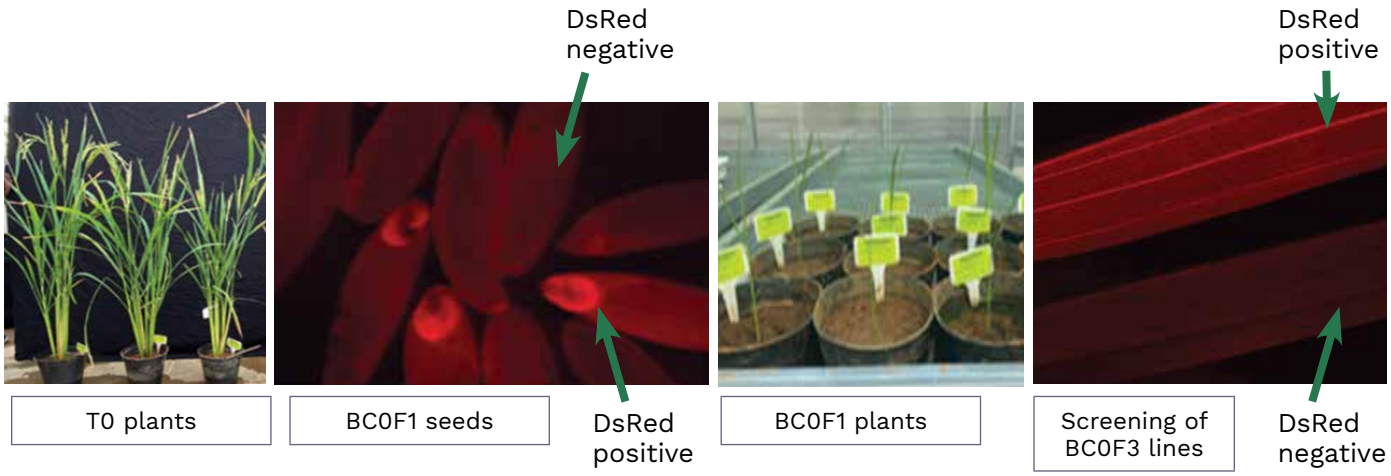


Fig. 1b Generating transgene free edited plants by segregating out the exogenous introduced DNA through backcross breeding

Inheritance of mutation from T0 to BC0F3 generations

Details of the mutations observed in T0 and in subsequent generations:

Three substitutions (marked in red) C to A; C to T and T to C and deletion of 34 bases were observed uniformly across the generations.

A T (-CCCCCTACTGTACACCACCAAAAGTGGAGGGTCT) CTAACTAC

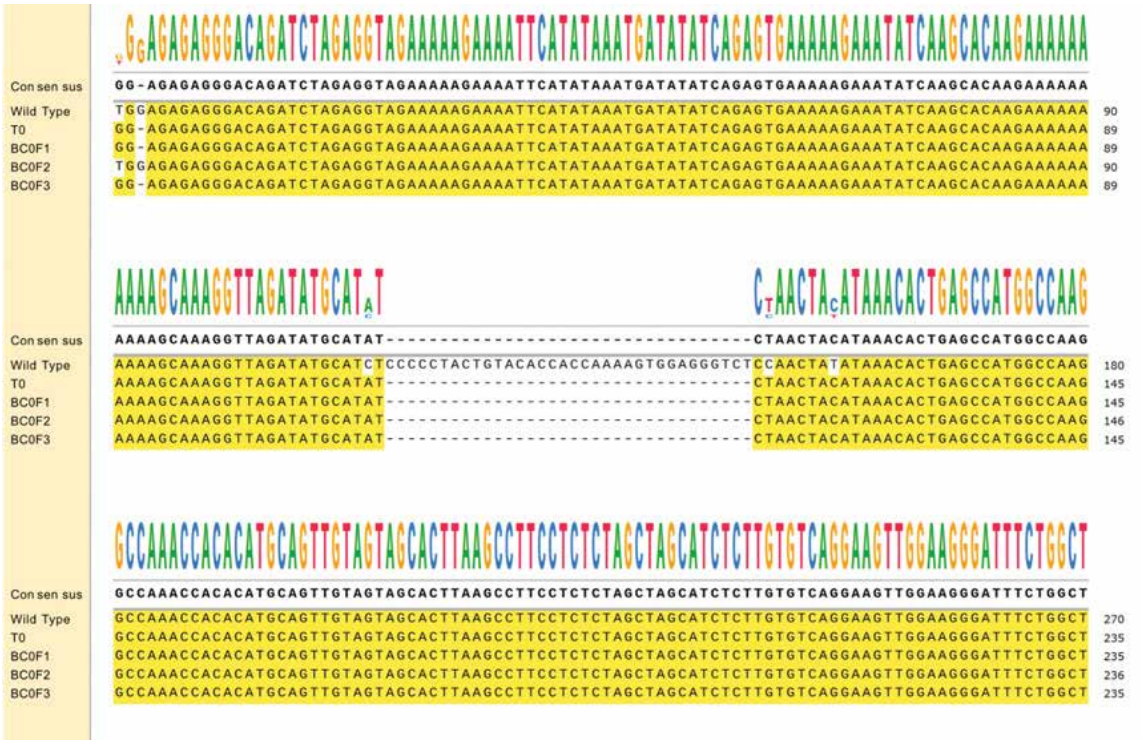


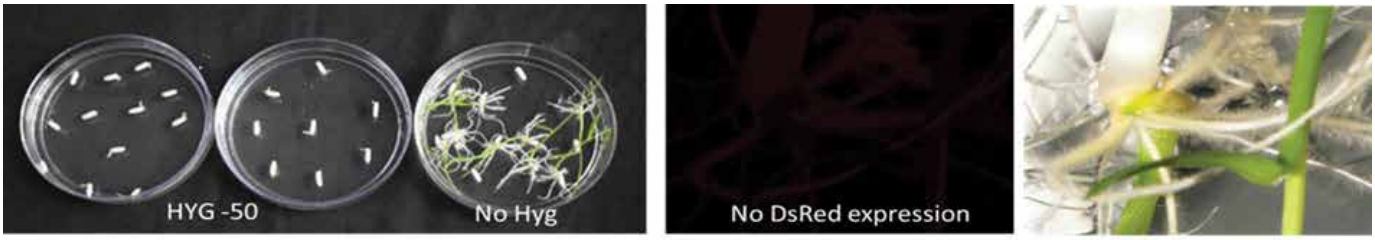
Fig. 2 Multisequence alignment of Sangers sequence data of the edited alleles obtained from T0, BC0F1, BC0F2 and BC0F3 population. The sequence alignment confirms the inheritance of mutations across generations and its zygosity.

Evidence to confirm that the genome edited lines are free from exogenous introduced DNA

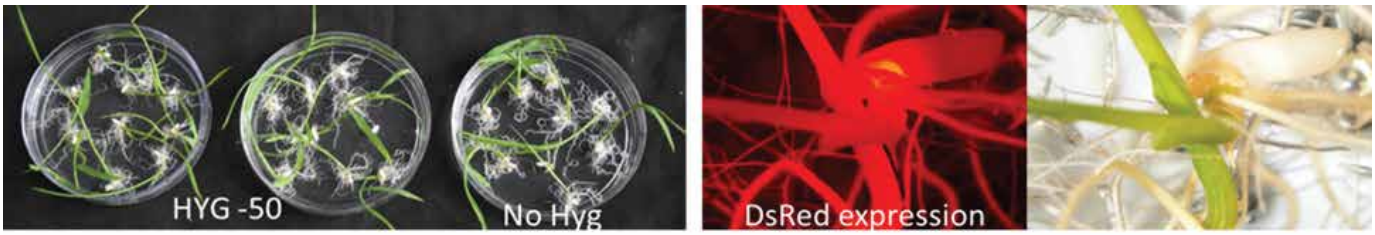
As per the 'SOPs for Regulatory Review of Genome Edited Plants under SDN-1 and SDN-2 Categories, 2022', we have performed two different studies, (i) phenotypic selection and (ii) PCR analysis on the genome edited lines to check for the presence or absence of exogenous introduced DNA.

1. **Phenotypic selection** (sensitivity to herbicide/ antibiotic, or absence of scorable marker)

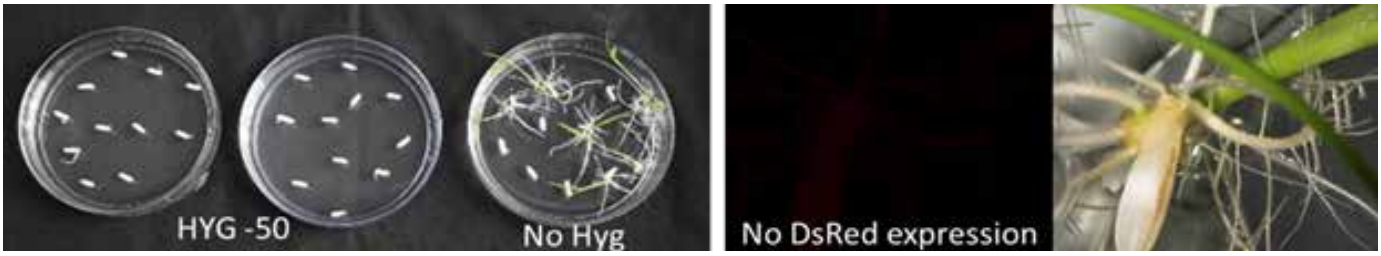
As per the DBT guidelines, the final edited plant lines must be sensitive to the selection reagents such as antibiotics at the concentration used for selecting the plants having exogenous introduced DNA. In the case of a scorable marker (reporter gene), the final edited plant line should be phenotypically negative for the same. To test if the selected lines are free from exogenous introduced DNA, the seeds from the edited line (BC0F3), segregant line harbouring the exogenous introduced DNA (positive control), and the parental genotype used for genome editing (negative control) were germinated on the media supplemented with the same concentration of antibiotic used in the transformation experiments. The construct used to transform rice lines also carry fluorescent marker gene (DsRed); therefore, we have tested both sensitivity to antibiotic and presence or absence of the fluorescence. Based on the data presented below, the selected BC0F3 line was susceptible to antibiotic and didn't show any fluorescence (Fig. 3).



MTU 1010 wildtype parental genotype (negative control)



MTU 1010 segregating line harboring the exogenous introduced DNA (positive control)



Genome edited line (BC0F3)

Selection media **Scorable marker (DsRed)**

Fig. 3. Phenotypic selection of BC0F3 line to test its sensitivity to antibiotic and to check the presence or absence of fluorescent marker gene.

2. PCR analysis of edited lines to check for the presence or absence of exogenous introduced DNA.

To test the presence or absence of any vector plasmid DNA component in the final genome edited line, PCR analysis was performed by using overlapping or nested primers. The primers were designed such that the amplicons (~500 bp) cover full length of the vector DNA used to transform rice lines. While designing primers, we ensured that the intended amplicon should not exceed 500 bp in size and the overlap between consecutive amplicons should be at least 50 bp. We have tested each set of primers using the total genomic DNA isolated from the edited line, wild-type parent plant (negative control) and segregant line harbouring full or part of the exogenous introduced DNA (positive control) for the presence or absence of exogenous DNA. In addition, we have also included another positive control; genomic DNA of the parental genotype spiked with 1/1000th (w/w) of the full-length purified plasmid DNA. Duplex PCR method was employed to amplify both exogenously introduced DNA (~500 bp) and internal control gene, actin (200 bp) in a single reaction. We have observed consistent amplification of internal control gene, actin across all the samples (Fig. 4). We have not detected any amplicons in any of the reactions with primers directed against exogenous introduced DNA for the final genome edited line, whereas clear amplification was observed in all the positive controls (Fig. 4).

Based on the phenotypic selection data and PCR analysis data presented above, its clearly evident that the selected genome edited lines which were advanced to BC0F3 generation are free from exogenously introduced DNA (Fig. 3 and 4).

Development of BPH resistant rice lines: We are in the process of generating genome edited rice lines that confers resistance to brown plant hopper (BPH). Brown planthoppers *(Nilaparvata lugens)* and white-backed planthoppers *(Sogatella furcifera)* are among the most destructive pests on rice. They damage plants by feeding on the phloem sap, depositing eggs in plant tissues and transmitting viruses, leading to decreased yield. Knockout of selected susceptible genes significantly reduce BPH infestation and enhance natural biological control by attracting natural enemies.

Multiplexing: We are in the process of generating multiplex genome edited lines carrying mutations in all the target genes selected to develop bacterial leaf blight, blast and BPH resistance. The selected rice lines that were generated using either BLB, blast or BPH SDN1 constructs were used further to stack BLB, blast and BPH gene edits in a single line.

The data collected from BLB single gene edited rice lines is submitted to IBSC and RCGM to seek committees' approval for field evaluation. Multiple gene edited lines will be ready for field trials in a few months.

We are also in the process of setting up the platform to improve other crops such as millets and pulses through genome editing.

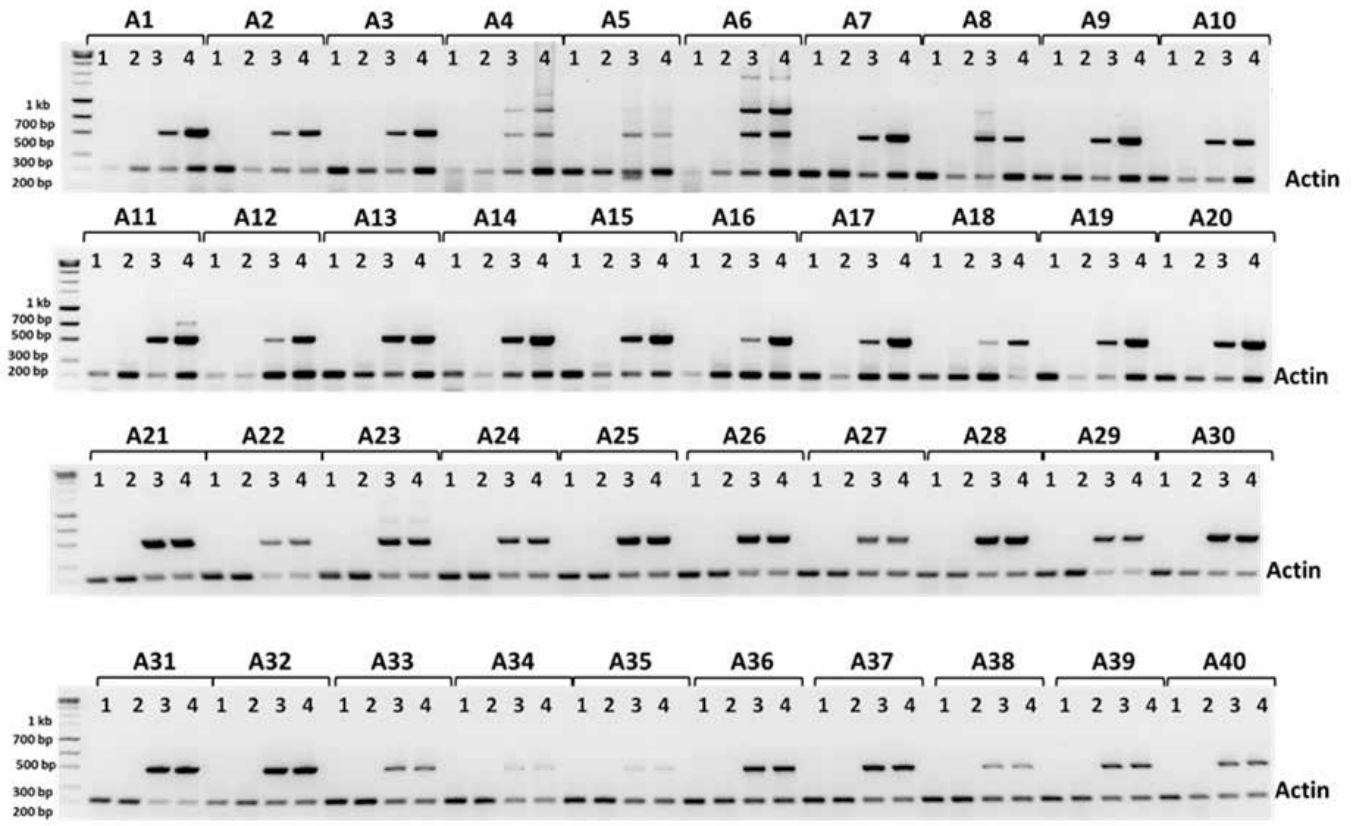


Fig. 4. PCR analysis of edited lines to check for the presence or absence of exogenous introduced DNA. A1 to A40 – PCR amplicons using 40 different sets of primers designed to detect the exogenously introduced DNA (plasmid DNA construct)

1. BC0F3 Edited line
2. Genomic DNA from Wild-type parent (negative control)
3. Segregating line harboring exogenous introduced DNA (positive control)
4. Genomic DNA of the parental genotype spiked with 1/1000th (w/w) of the purified vector DNA (positive control)

Justification for observing additional amplicons:

Amplicon 4 (A4) - The reverse primer has two binding regions. One at CaMV35S promoter (position 1889) yielding amplicon of 499 bp (expected) and another region at the spacer sequence (2283 position) between CaMV35S promoter and guide RNA (gRNA) scaffold yielding a higher amplicon of 824 bp.

Amplicon 6 (A6) - The forward primer has two binding sites. One in the spacer region (position 2208) between CaMV35S promoter and guide RNA (gRNA) scaffold yielding an amplicon of 500 bp (expected) and another region at CaMV35S promoter (position 1883) yielding a higher amplicon of 830 bp.

Mutation Breeding

Food crops, such as rice, have been domesticated for thousands of years and bred over many generations to increase some of their desirable qualities. However, cultivation of specific rice varieties generation over generation for selected traits leads to the loss of other beneficial traits and narrows down the genetic variability over time. Mutation breeding, a technique to induce genetic variation, is a vital strategy in addressing this challenge by developing new crop varieties with enhanced traits. A mutagenized population can become a source of novel traits that might not be present naturally in existing varieties. Considering its century-long application in crop improvement contributing to global food security, there is a pressing need to leverage this approach to address contemporary issues such as nutritional deficiencies and agricultural sustainability.

At TIGS we have developed the ability to perform mutagenesis on a desirable genetic background and screen the mutant lines for beneficial traits of interest. The mutations associated with the beneficial phenotypes can be mapped by next-generation sequencing (NGS) or microsatellite markers to ensure the propagation and distribution of pure lines.

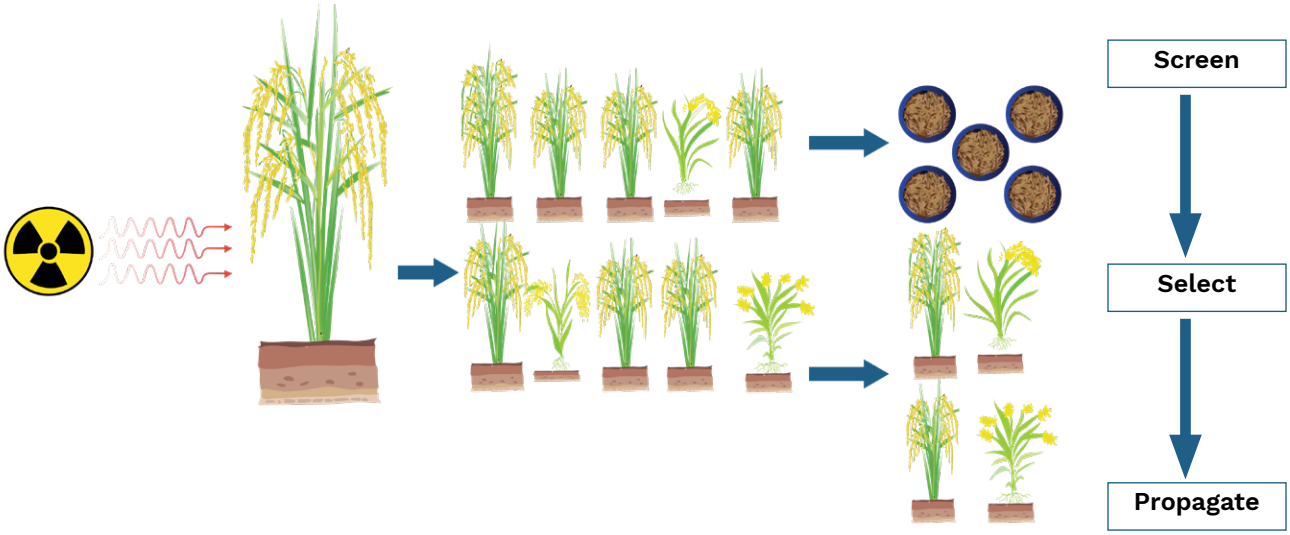


Image ideation by Kamal K Malukani and Sampath Kumar

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

V S Sresty Tavva

Pointed gourd (*Trichosanthes dioica*) also known as parwal, is a dioecious species with male and female flowers observed on separate individual plants. It is mostly cultivated in the eastern and northern parts of India. Though pointed gourd vegetable has several health benefits, the production happens at very low scale due to the plant being dioecious and the pollination has to 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 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 study the flowering pattern and extent of fruit setting. Since Parwal is a perennial and a vine (creeper) plant, detailed analysis can only be done on field grown plants. Therefore, TIGS collaborated with Department of Horticulture, University of Agricultural Sciences, GKVK, Bengaluru to carryout field experiments and to generate and evaluate hermaphrodite parwal plants.

Observations from first year field studies

We have planted mutant parwal lines along with parent control plants in GKVK field and studied their flowering and fruiting pattern. We encountered quite a few issues during the first year of field evaluation of mutant parwal plants. We have observed different sex forms in clones of a single line, suspecting there is an admixture of lines. The clones received may not have originated from a single line. None of the progenies have only hermaphrodite flowers. In hermaphrodite flowers, anthers were below the stigma, showing heterostyled condition that mostly leads to cross pollination. Fruits from hermaphrodite flowers were not of marketable size.

We have performed crosses between hermaphrodite and male plants and collected fruits and seeds. The hybrid seeds as well as open pollinated seeds (flowers were fertilized by bees/moths/wind) were germinated in pots and transplanted to further evaluate the phenotype in the field conditions along with mutant lines. In this year (2024), we have taken up new planting in replicates with proper randomization.

We have evaluated flowering patterns (Fig. 1) and fruit setting in this season by taking all the precautions to control any untoward cross pollination in the field due to natural agents. Appropriate isolation is maintained in the field to avoid any cross pollination between hermaphrodite flowers and male flowers from wild-type plants. The measures are also in place to control root rot and fusarium wilt infestation, which damaged the plants in the last season.

Observations from second year field studies

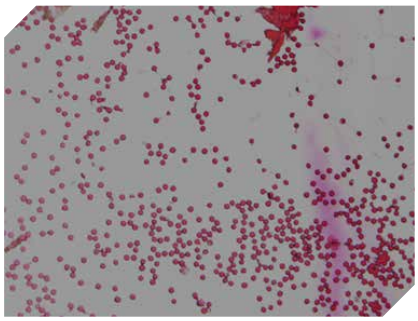
We have observed better vegetative growth and increased hermaphrodite flower numbers in this season due to various control measures that we have adopted. The pollen collected from hermaphrodite flowers of lines 537B-14 and 537B-15 have successfully set fruits when crossed with wild-type female plant. On the other hand, the hermaphrodite female flowers 537B-14, 537B-15, 537B-46 and 537B-50 successfully set fruits when crossed with pollen collected from wild-type male plants. However, the fruits collected from hermaphrodite plants are not of marketable size and mostly devoid of any seed. This could be due to parthenocarpy. To confirm this, we have carried out viability test on the pollen collected from wild-type male plant and hermaphrodite plants. The pollen staining data clearly indicated that there is either very low or no pollen in hermaphrodite flowers compared to wild-type male plant (Fig. 2). In addition, we have also observed fused stigma in hermaphrodite female flowers, which makes it difficult for pollination. So, further studies are required to delineate the features observed in hermaphrodite flowers and see if we can produce marketable size fruits from these plants.

Hermaphrodite flowers

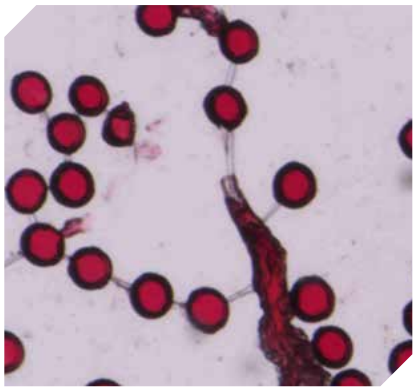
Female flower (Wt)

Male flower (Wt)

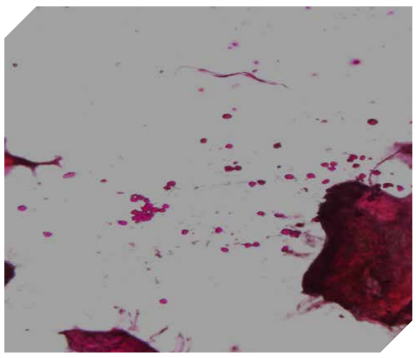
Fig. 1 Flowering pattern observed in hermaphrodite, wild-type (Wt) female and wild-type male plants



Pollen grains collected from wild-type male plant



Hermaphrodite flower with few pollen grains



Hermaphrodite flower without any pollen

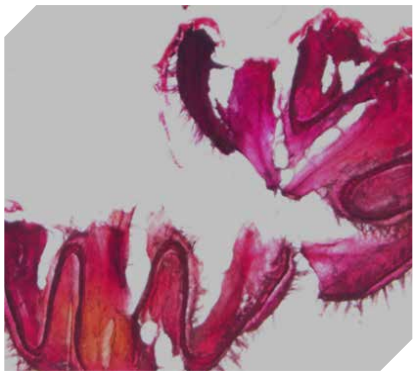


Fig. 2 Pollen viability test – pollen grains collected from different plants were stained with acetocarmine and observed under microscope.

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

Kamal K Malukani

[in collaboration with CSIR-CCMB and ICAR-IISS]

India is facing a dual challenge of malnutrition and obesity. A significant portion of the population suffers from deficiencies in essential micronutrients like iron, zinc, and vitamins, lacks adequate protein in their diet, and is either diabetic, pre-diabetic, or affected by multiple nutritional deficiencies. Rice is the staple food for most of the Indian population. Unpolished brown rice contains good amount of nutrients but white polished rice, the common form of rice consumed in India, does not provide adequate amounts of micronutrients. Phytic acid is an antinutrient that is enriched in brown rice, but it reduces the bioavailability of minerals. We aim to generate rice lines with beneficial traits like low glycemic index (GI), and high iron, zinc, and protein content. We also aim to make rice with low phytic acid that may lead to brown rice with better palatability, cooking quality as well as better nutritional values.

As part of this collaborative work, we have generated a new mutagenized rice population in the background of Improved Samba Mahsuri (ISM), the bacterial blight tolerant, low GI rice variety. These lines are being advanced at CSIR-CCMB, Hyderabad, and Indian Institute of Seed Science (ICAR-IISS), Bengaluru to stabilize the traits. The harvest from 4th generation of mutants (M4) will be screened for nutrition content. Additionally, we are testing rice mutant lines previously developed by CSIR-CCMB in collaboration with ICAR-IIRR for nutritional traits.

Nutrition assessment facility at TIGS (NuTIGS)

We are establishing a nutrition assessment facility to measure key nutrients that are relevant to address major nutrition deficiencies in India (Fig. 1). The target traits include high iron, zinc, total protein, and low sugar release rates in the white rice and low phytic acid in unpolished rice. Plans are underway to expand the facility's capabilities to include vitamin and amino acid quantification in polished rice grains. We also plan to extend the facility to new collaborators and partners to find neglected food sources with better nutritional values.

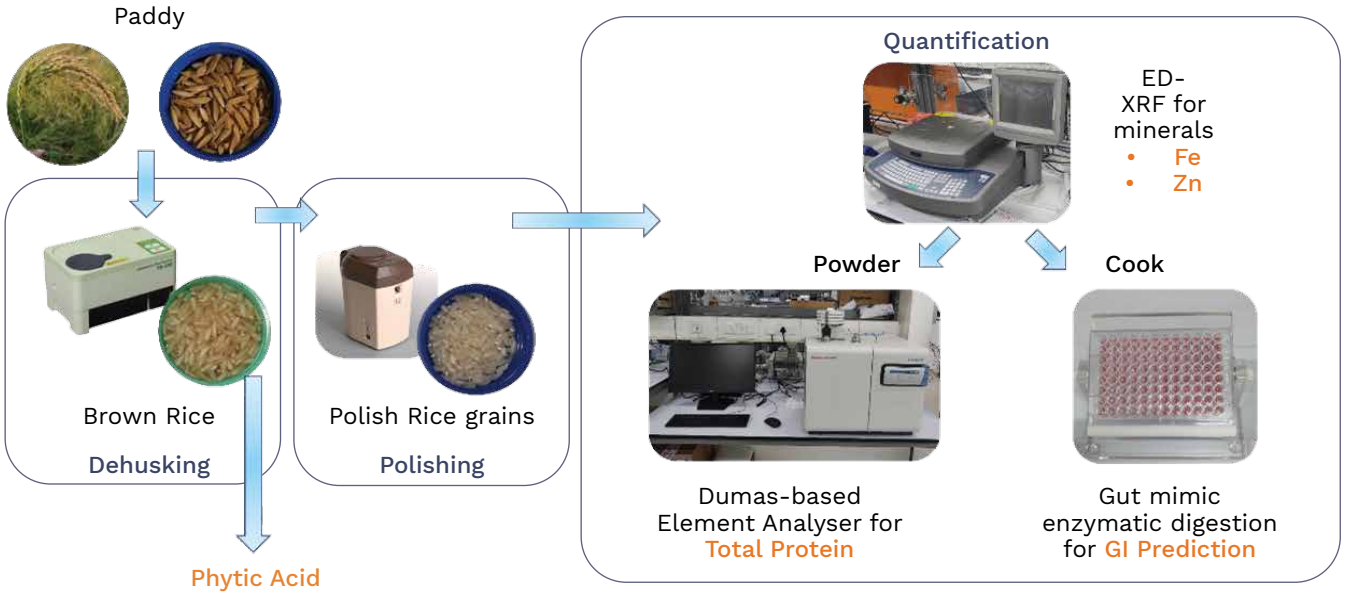


Fig. 1: Workflow for nutrient quantification at NuTIGS.

While we develop a new mutant population, we have screened 213 previously selected mutant lines, varieties, or landraces for iron, zinc and total protein 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 6 lines that show higher zinc than the parent (ISM) in five successive generations (Fig. 2). One 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 (Fig. 3). Recent screening of same 213 lines for total protein content led to identification of mutants with higher grain protein content (Fig. 4). However, this needs to be tested for subsequent generations.

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 and mutants tested for zinc, iron and total protein content.

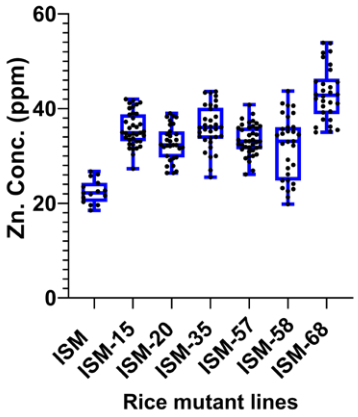
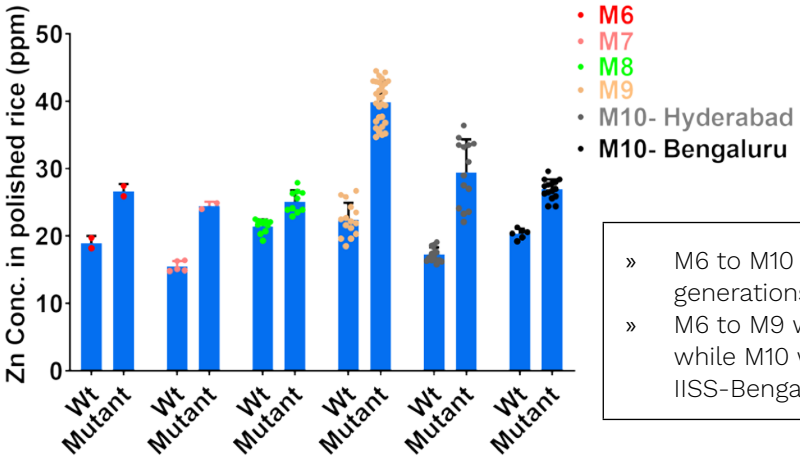


Fig. 2: Zinc content in M9 generation of polished rice of 6 mutant lines that show higher zinc than the parent (ISM). Each dot represents Zn concentration observed in individual plants from respective lines.



» M6 to M10 represents different generations of mutants.
» M6 to M9 was grown in CCMB-Hyderabad while M10 was grown in CCMB aswell as IISS-Bengaluru

Fig. 3: Zinc concentration across five generations in polished rice in 1 of the high zinc mutant rice and the respective parent (Wt, ISM). Each dot represents Zn concentration observed in individual plants from respective lines.

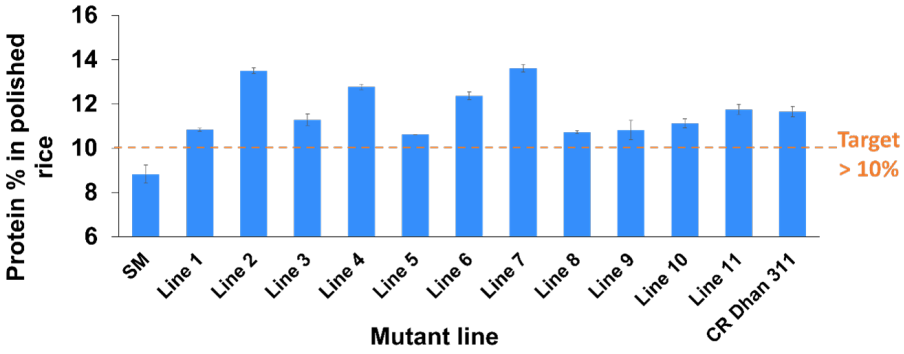


Fig. 4: Protein percentage in polished rice of some mutant rice lines.

Fig. 4: Protein percentage of 11 potential high protein rice lines and respective parent (SM). CR Dhan 311 is a released high protein rice variety.

While testing for the iron and zinc content in rice grains we observed polishing leads to a severe loss of iron and a significant loss of zinc (Fig. 5). Washing rice with distilled or tap water does not have significant effect on iron or zinc content. Brown rice is traditionally soaked for a few hours or sometimes cooked in excess water which is drained out after cooking. We observed both practices lead to significant loss of iron and zinc.

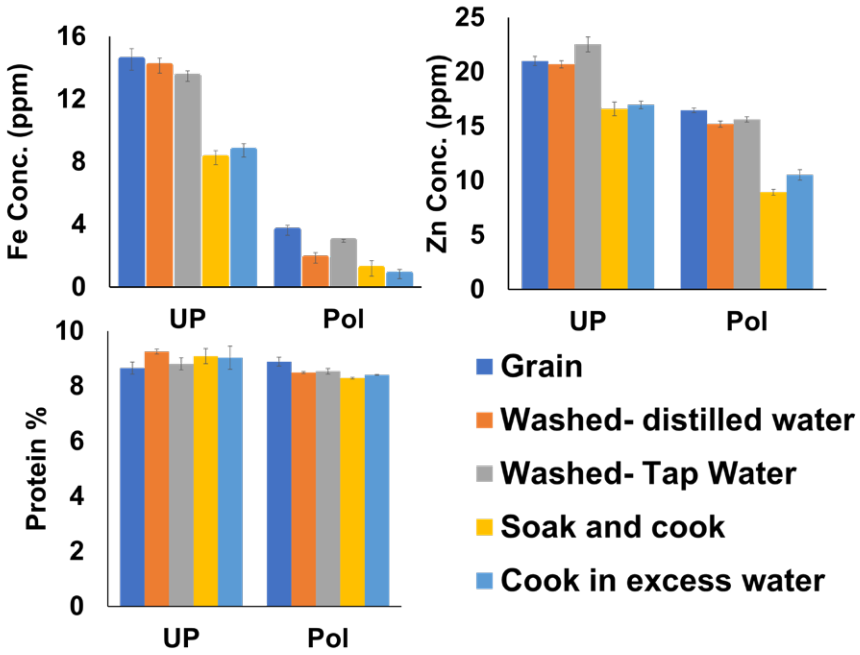


Fig. 5: Effect of polishing and other cooking practices on nutritional values of rice. UP: Unpolished rice, Pol: Polished rice

Disease and Pest Management

Effective disease and pest management is crucial for tackling agriculture's pressing challenges, especially in an agricultural powerhouse like India. At TIGS, advanced scientific research, stakeholder engagement, and innovative surveillance toolkits are employed to monitor and manage pests and diseases.

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.

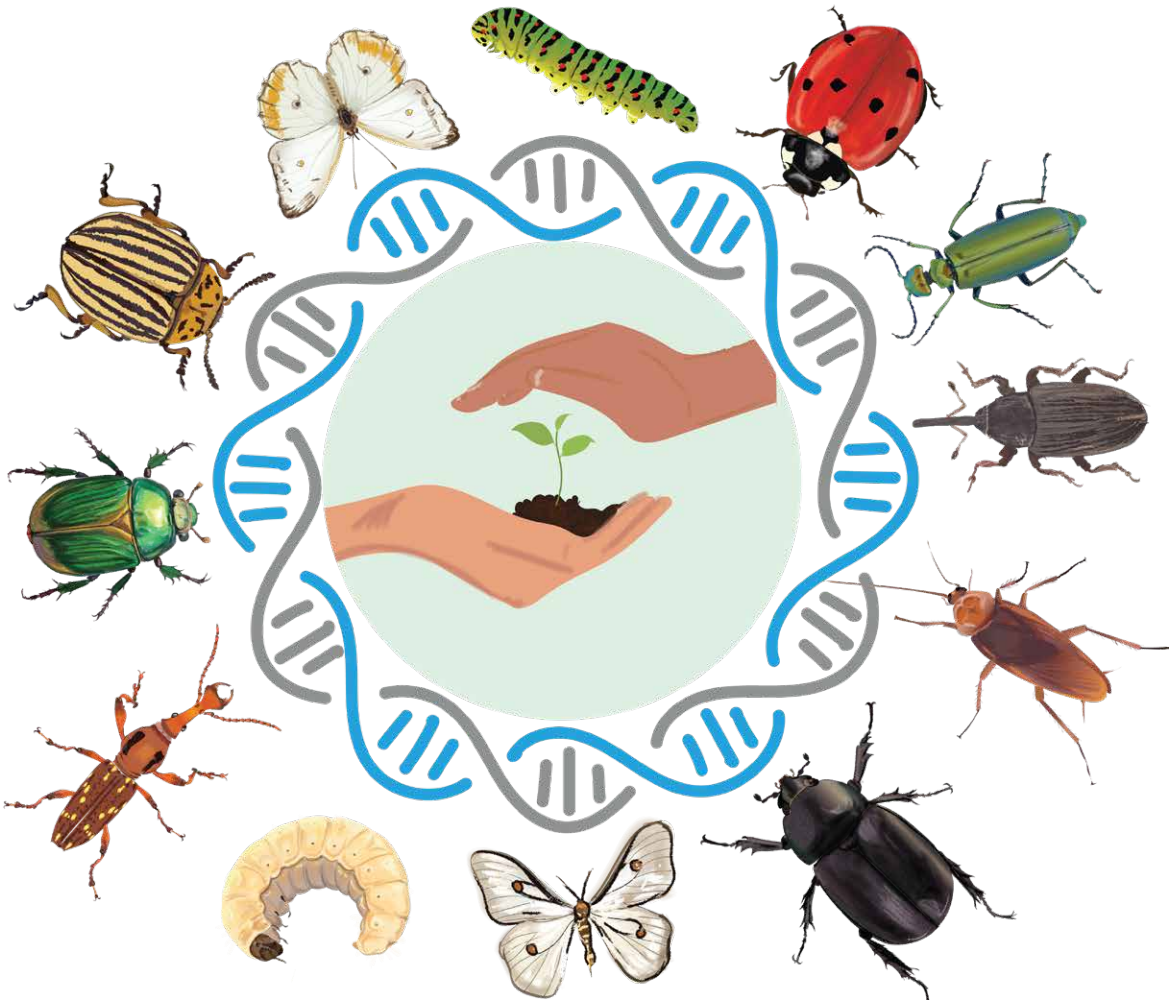


Image ideation by Sampath Kumar

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

Sampath Kumar

[Inputs from Central Coffee Research Institute (CCRI), Chikmagalur, and Indian Institute of Science (IISc), 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. 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)

b)

c)

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]

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:

1. Address the gap in knowledge regarding resistance status of FAW
2. Develop novel combinations of bio-pesticides
3. 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

Mass Rearing of Fall Armyworms

Leaf dip assay to study insecticide resistance

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Technology Platforms

Technology Platforms

Harvinder Kour Khera

Rajesh V Iyer

Satyaprakash Pandey

Vasanth Thamodaran

TIGS aims to harness the untapped potential of cost-effective diagnostics and therapeutics for disease elimination by creating platforms to support our infectious and rare disease programs and enable rapid implementation of emergent technologies. The lack 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 due to high costs and the 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 diseases that are refractory to small molecule therapy.

Since most of these technologies were created in the developed world, the cost of reagents and equipment is considerable for a country like India. Translational research towards the development of new and improved diagnostics and therapeutics is the need of the hour. Another of our focus areas, therefore, is the indigenization of technologies used in nucleic acid-based diagnostics development and stem cell-based therapies. Key initiatives include leveraging genomic technologies for disease detection and genome editing capabilities for deriving diverse disease models. The disease-in-a-dish models initiated at TIGS will be invaluable in identifying potential drug targets, followed by validation of these targets through the application of novel or existing drug molecules to rescue disease phenotypes. We also focus on the development and evaluation of biotherapeutic interventions, especially mRNA therapeutics in these systems.

Diagnostics Development Platform

Diagnostic development platform is dedicated to bridging critical gaps in early and accurate disease diagnosis, which is fundamental for effective treatment and improved patient outcomes. Molecular diagnostics, which offer advanced tools for early detection and precision medicine, are at the core of our efforts. Early and accurate diagnosis is essential for timely interventions, especially for infectious and rare diseases. However, challenges such as the lack of cost-effective diagnostic methods, delays in diagnosis, and inaccuracies continue to hinder healthcare progress.

To address these challenges, we are developing a comprehensive diagnostic platform that leverages cutting-edge technologies like CRISPR, digital PCR, isothermal amplification methods (such as LAMP and RPA), and next-generation sequencing (NGS) panels. This platform is specifically designed to provide affordable and reliable diagnostic solutions for a wide range of diseases, from common infections to rare conditions.

A key focus of this initiative is the creation of low-cost, point-of-care diagnostic tools that can be deployed in field settings across India. By ensuring that these solutions are rapid, robust, and accessible, we aim to enhance early detection capabilities, making them available even in the most remote and underserved areas of the country. Our goal is to revolutionize disease diagnostics with innovative technologies that improve healthcare access and outcomes nationwide.

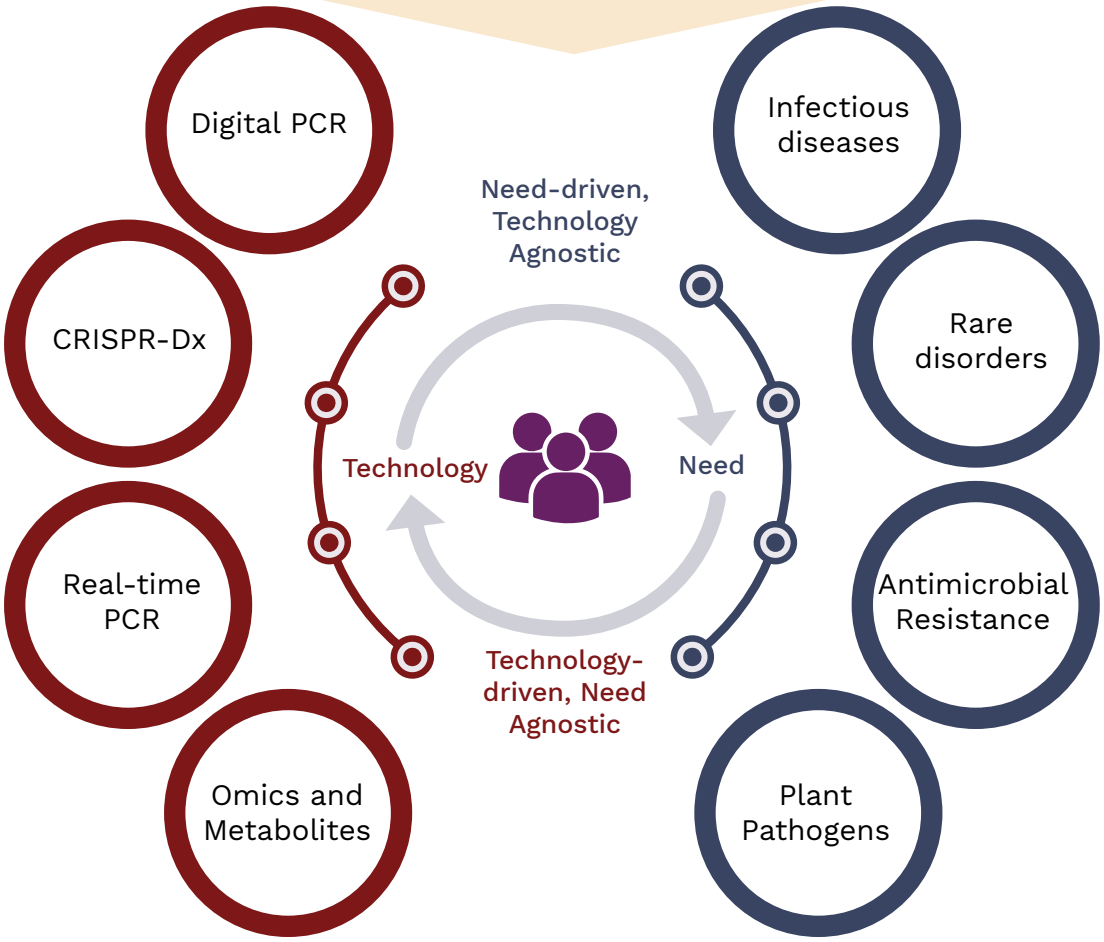


Image ideation by Harvinder Kour Khera and Satyaprakash Pandey

Developing indigenous diagnostics solutions for One Health

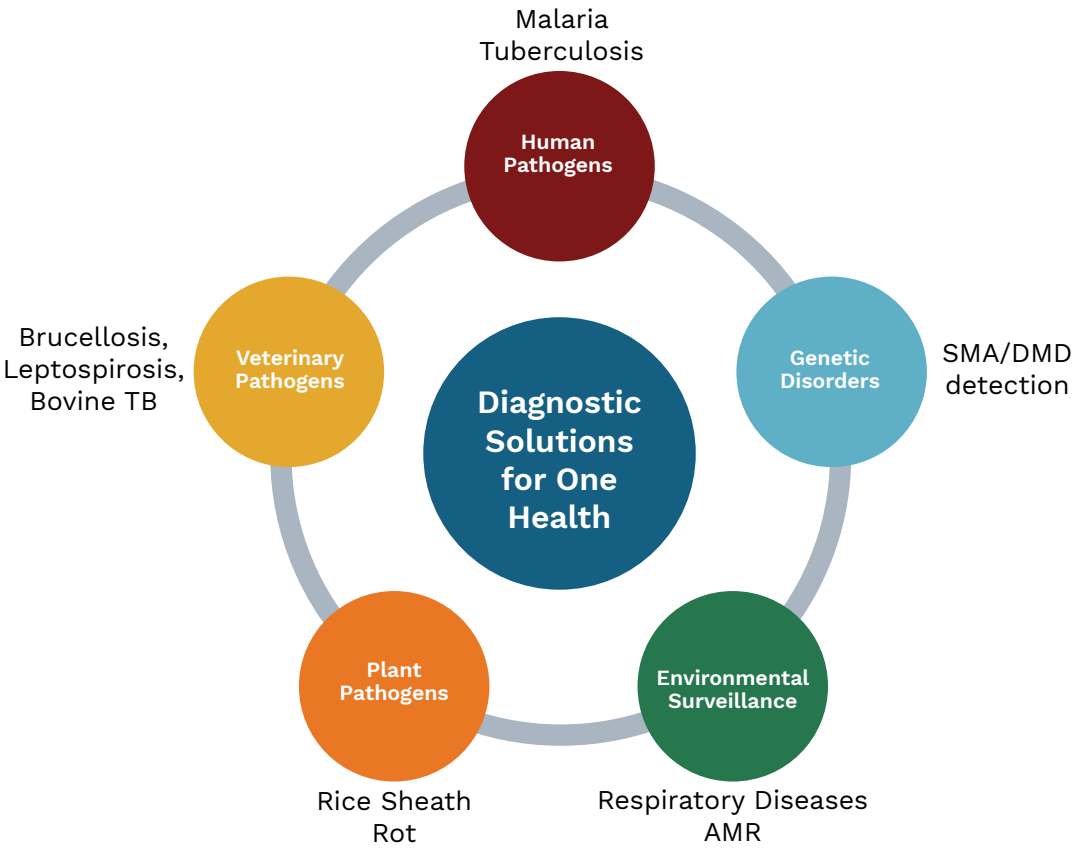
Harvinder Kour Khera

India, with its vast population and diverse ecosystems, faces complex health challenges that require integrated One Health approaches. One Health emphasizes the interconnectedness of human, animal, and environmental health. As India confronts rising zoonotic diseases, antibiotic resistance, air and water pollution, and inadequate healthcare infrastructure, there is an urgent need to develop diagnostic solutions that can bridge these domains.

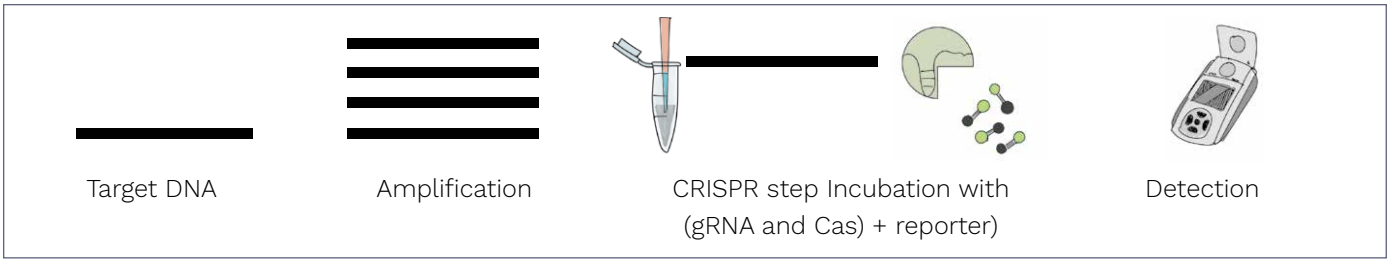
According to the World Health Organization (WHO), 60% of emerging infectious diseases are zoonotic, making early detection and rapid response crucial. Additionally, the growing threat of antimicrobial resistance (AMR) poses a critical risk to both human and animal health, further exacerbating the challenge.

Developing diagnostic solutions for One Health in India requires innovation in multiplex diagnostic platforms that can simultaneously detect pathogens across humans, animals, and the environment. Additionally, expanding surveillance systems, integrating AI-based tools for rapid diagnostics, and establishing cross-sector collaboration are key strategies. Challenges include resource constraints, lack of infrastructure in rural areas, and data-sharing issues. Addressing these will require public-private partnerships, capacity building, and investment in localized solutions tailored to India's diverse epidemiological landscape. At TIGS, we are focused on developing low-cost, diagnostic solutions suitable for field applications in India. The aim is to provide innovative solutions for early diagnostics/ surveillance kits that are rapid, robust, affordable, and accessible to the remotest part of the country.

Recent achievements in the diagnostic platform have led to the successful establishment of protocols for the expression and purification of various proteins, including Cas proteins and polymerases. This advancement contributes to indigenization and cost reduction. Efforts have concentrated on developing CRISPR-based diagnostics for malaria and tuberculosis, with current innovations undergoing validation for technology transfer.



We plan to expand into plant, veterinary, and environmental applications using CRISPR-Cas and digital PCR technologies. Notably, CRISPR-based methods are being developed for detecting significant plant pathogens such as Sarocladium and Magnaporthe, as well as veterinary diseases like Bovine Tuberculosis and Brucellosis, alongside various collaborations. Additionally, efforts are underway to detect Mycobacterium tuberculosis in wastewater using CRISPR and digital PCR. Efforts are being made for the development of CRISPR diagnostics for genetic disorders like Spinal Muscular Atrophy (SMA) and Duchenne Muscular Dystrophy (DMD). Future advancements are anticipated in point-of-care testing and the integration of digital health, which will enhance disease diagnostics and surveillance, ultimately transforming healthcare and improving global health outcomes.



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.*

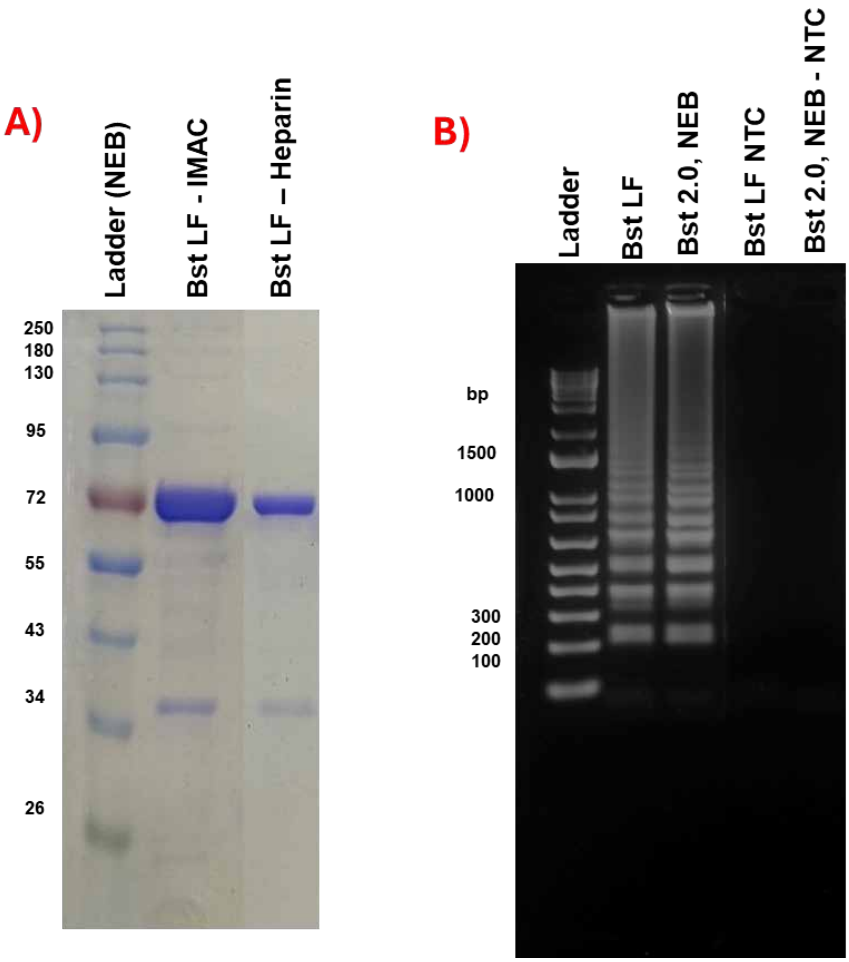


Fig. Indegenization of Bst Polymerase A) Ni-NTA purified Bst DNA Polymerase loaded onto a 10% SDS PAGE Gel. B) Activity assay – LAMP products loaded onto a 1% TBE Agarose gel. NTC stamds for no template control.

Strip Assay for Malaria detection

The LAMP-CRISPR based strip assay for malaria detection has been optimised. This assay enables rapid, field-deployable diagnosis with visual readout, eliminating the need for complex laboratory infrastructure. Its precision and ease of use make it a promising tool for malaria surveillance and point-of-care testing

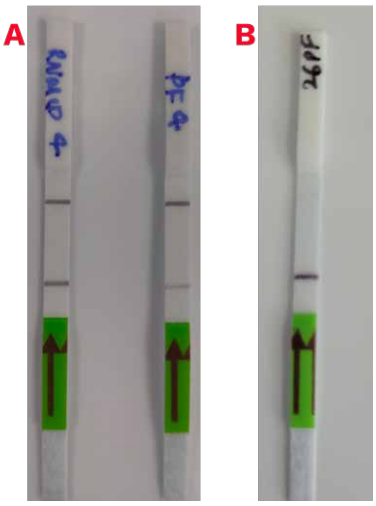


Fig. Strip assay standardized for detection of malaria. A: Positive sample B: negative sample.

Clinical validation of CRISPR-based MTB detection:

The CRISPR-based assay for *Mycobacterium tuberculosis* (MTB) detection developed at TIGS underwent clinical validation using DNA extracted from 38 sputum samples. The study assessed the assay's sensitivity, specificity, and reliability in comparison to conventional diagnostic methods. Results demonstrated its potential for accurate and rapid MTB detection in clinical settings. Further validation is in process.

CRISPR assay for Plant pathogens

Rice sheath rot has been reported to cause yield losses of up to 85%, posing a serious risk to farmers and rice-producing nations worldwide. In this context, the research aimed to accomplish the sensitive and rapid detection of S. oryzae from infected rice sheaths, seeds, and environmental samples.

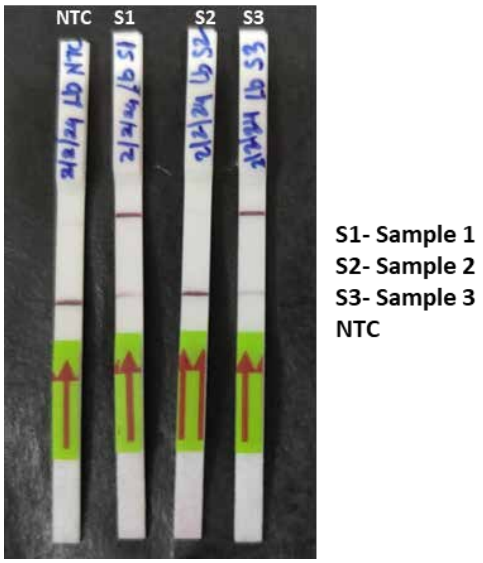


Fig. Strip based assay for detection of Sarcocladium oryzae. S1, S2 and S3 are the three field samples tested for Sarcocladium using the assay developed in lab. S1 and S2 are positive while S2 is negative. NTC is no template control.

Rice blast disease is caused by the fungus *Magnaporthe oryzae*, is another devastating disease. The disease affects all growth stages of rice and can infect leaves, necks, and seeds, leading to substantial yield losses that range from 10% to 50% under favorable conditions. Rapid and precise detection of *M. oryzae* is essential for effective disease management, enabling timely intervention and minimizing crop damage.

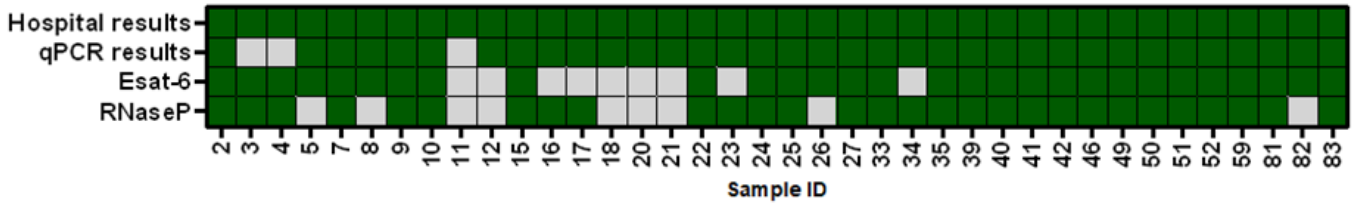


Fig. Clinical Validation of TB-CRISPR assay (Positive Samples). DNA isolated from a total of 38 sputum samples, determined as positive by the hospital was evaluated using the TB CRISPR assay. The assay targets included Esat-6 and RNaseP. The results are shown as a single gradient heatmap, with positive detections indicated for each target alongside qPCR and hospital results for comparison. (Chart interpretation: Green – Positive, Grey – Negative). Hospital Positive/qPCR Positive/TB-CRISPR Positive= 27, Hospital Positive/qPCR Negative/TB-CRISPR Positive = 2, Hospital Positive/qPCR Negative/TB-CRISPR Negative = 1, Hospital Positive/qPCR Positive/TB-CRISPR Negative = 8. Further validation is in process.

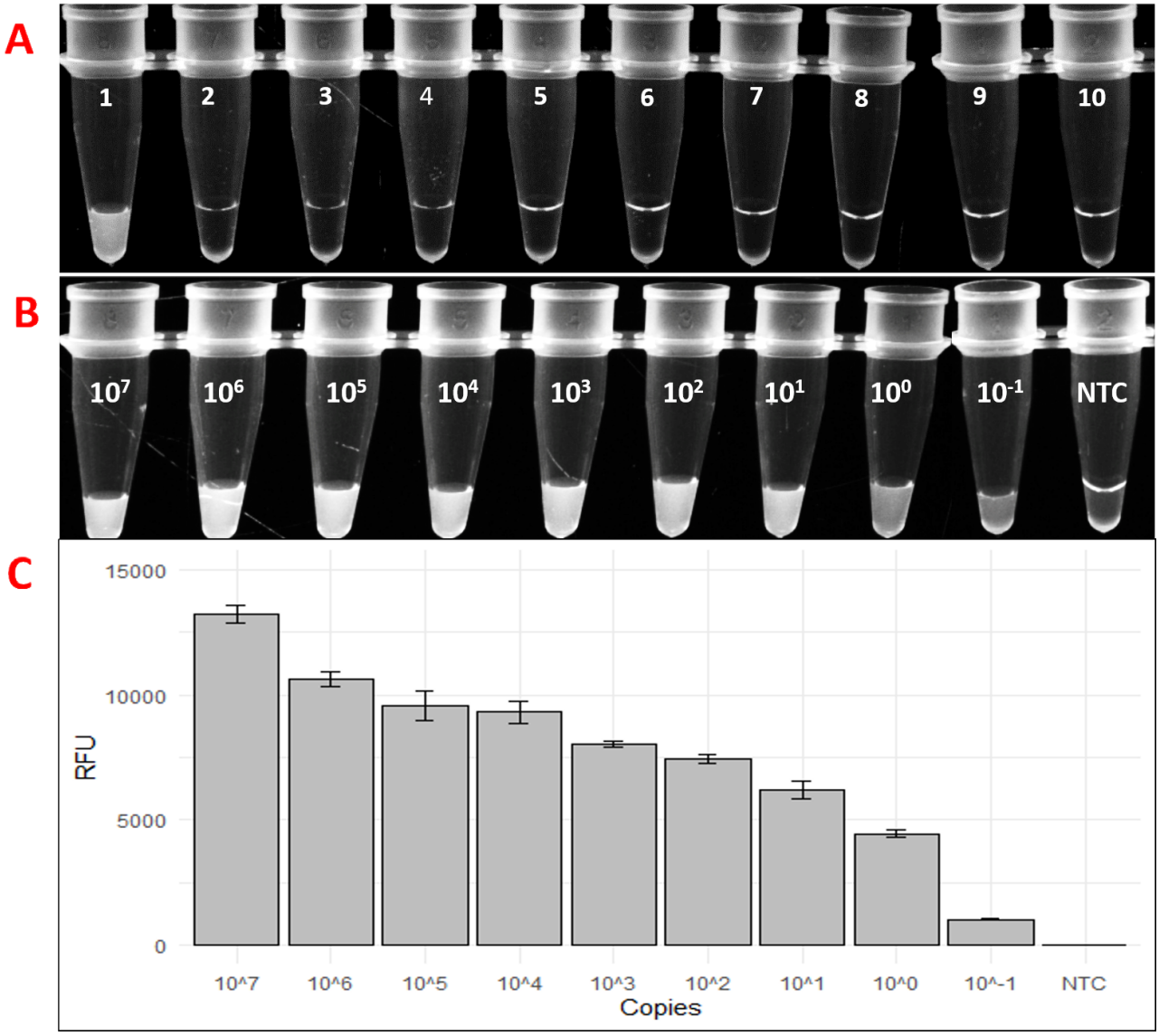


Fig : CRISPR Cas12a assay for detection of M. oryzae: 3A: Colorimetric assay demonstrating the specificity of RPA aided CRISPR cas12a assay 1 - Magnaporthe oryzae, 2 - Bipolaris oryzae, 3 - Curvularia lunata, 4 - Sarocladium oryzae, 5 - Exerohilum rostratum, 6 - Ephelis oryzae, 7 - Rhizoctonia solani, 8 - Fusarium equiseti, 9 - Ustilaginoidea virens, 10 – NTC. 3B: Sensitivity analysis of the RPA aided CRISPR cas12a assay using RPA product of serial dilutions of M. oryzae from 107 to 10-1copies of DNA: 3C: Fluorescence intensity (RFU) measured using Biorad CFX96 qPCR system for sensitivity assay.

Multiplexed molecular diagnostic platform for pathogen detection

Satyaprakash Pandey

COVID pandemic highlighted the importance of molecular diagnostic assays to trace, track and treat pathogens with cost-effective, reliable and robust solutions catering to the remotest areas and under-resourceful populations. At TIGS we are focusing on developing molecular diagnostics platforms to overcome such challenges in the future. Our criteria are based on

Patient-centric innovation: IVD tests are becoming closer to patient reducing dependence on large labs. New technologies like CRISPR diagnostics, lab-on-chip and micro-fluidics are emerging to reduce costs and increase the quality and efficiency of the assays with minimal infrastructure requirement. This has led to higher adoption of innovative techniques and approaches, increasing efficiency and facilitate speedy detection of infectious diseases and genetic disorders e.g., multiplexing / paneling.

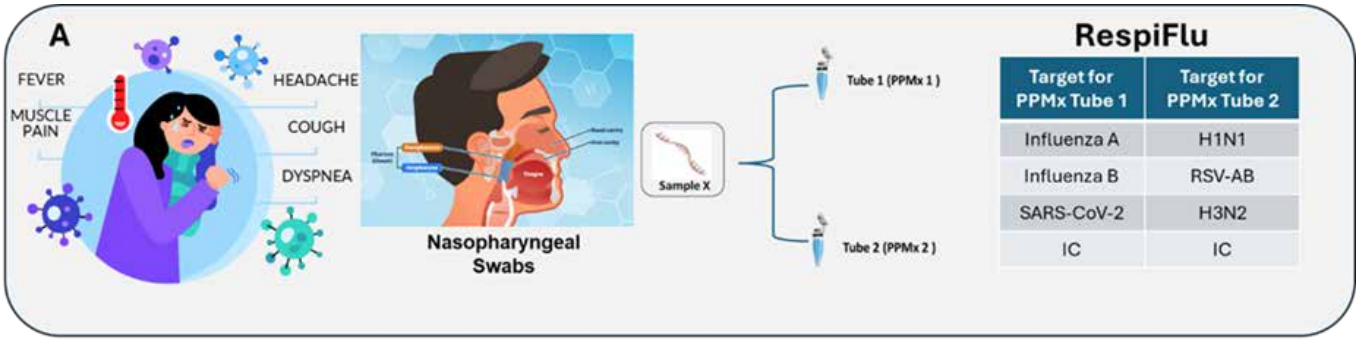
Neglected diseases and lack of frugal solutions for remote testing: Emergence of new pathogens, drug resistance of variants, mass-testing requirements with a focus to capture presence of multiple pathogens with minimal testing has led to development of newer assays with focus on multiplex assays that utilize the existing infrastructure or require minimal to no infrastructure.

A. Detection of respiratory pathogens from clinical human samples and wastewater samples

Influenza, Respiratory Syncytial Virus (RSV), and COVID-19 are three distinct respiratory viruses, each belonging to different viral families, yet collectively responsible for a significant portion of severe respiratory infections globally. These viruses often present with overlapping symptoms such as fever, cough, and difficulty breathing, complicating the clinical identification of the specific causative agent.

An innovative approach to bridge the diagnostic gap lies in environmental surveillance, particularly through the analysis of wastewater for pathogen signatures. This non-invasive method enables the monitoring of pathogen prevalence on a community-wide scale, providing a comprehensive insight into the spread and dynamics of diseases. By identifying the genetic markers of these viruses in wastewater, public health authorities can detect potential outbreaks at an early stage, allowing for prompt and targeted public health responses to curb transmission and alleviate the burden on healthcare systems.

Currently, while individual assays exist for the detection of these viruses, the development of a single multiplex assay capable of simultaneously identifying and differentiating among these pathogens stands to significantly enhance clinical diagnostics and public health management. Such an assay would enable more efficient outbreak monitoring and patient categorization, reducing the risk of cross-infection and the spread of these viruses.



RespiFlu

Target for PPMx Tube 1	Target for PPMx Tube 2
Influenza A	H1N1
Influenza B	RSV-AB
SARS-CoV-2	H3N2
IC	IC

Our goal is to develop a comprehensive assay capable of detecting and distinguishing among key respiratory pathogens, including Influenza A, Influenza B, RSV A and B, and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), as well as subtyping Influenza A strains H1N1 and H3N2 from both clinical and environmental wastewater samples.

We are currently in the phase of evaluating the performance of this assay with clinical and wastewater samples and are actively seeking partnerships with industry stakeholders for its commercialization. Our efforts are directed towards cost-effective respiratory virus detection and management, ultimately contributing to more effective outbreak control and patient care.

B. Detection and differentiation of HPV high risk genotypes for early screening and patient management

Cervical cancer, predominantly caused by the Human Papillomavirus (HPV), poses a significant health threat to women worldwide. In India, the statistics are particularly alarming, with one woman succumbing to cervical cancer every seven minutes. It is estimated that 5% of Indian women will encounter an HPV infection at some point in their lives. However, cervical cancer stands out as the only female cancer that is not just entirely preventable but also curable when detected and treated in its early stages. Although there are multiple HPV genotypes, notably, over 80% of cervical cancers are linked to HPV genotypes 16 and 18.

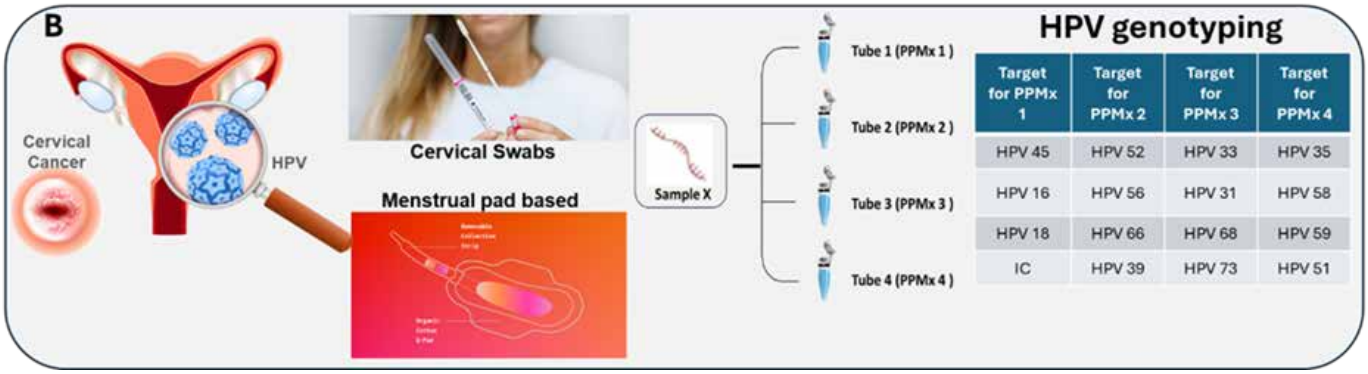
Recognizing the critical nature of this issue, the World Health Organization (WHO) has advocated for a comprehensive approach to combat cervical cancer, encapsulated in the 90-70-90 model:

- **90% Vaccination:** Ensuring full vaccination by the age of 15.
- **70% Screening:** Conducting high-performance tests by the ages of 35 and 45.
- **90% Treatment:** Providing timely treatment for those identified with cervical disease, whether for precancerous lesions or invasive cancer.

HPV screening plays a pivotal role in increasing the detection rate of cervical cancer, thereby significantly reducing mortality rates. While the Pap Smear assay has been commonly used, its limitations in sensitivity and scalability highlight the urgent need for DNA-based molecular diagnostics for a more accurate, robust, and scalable HPV screening program.

Our mission is to enhance early screening and patient management for cervical cancer by detecting and differentiating between HPV genotypes 16, 18, and thirteen other high-risk (HR) types (45,31,33,35,39, 51,52,56,58,59,66,68,73). To achieve this, we are developing a qualitative PCR test for the detection and differentiation of HPV genotypes 16, 18, and the thirteen other HR types. A very critical barrier is sample collection without privacy invasion in women. We are working with partners on a “do-it-yourself” self-sample collection methodology that is compatible with the assay.

We have successfully developed the assay and are currently seeking industry partners for its commercialization. In terms of self-sample collection, our goal is to incorporate CDSCO approved sample collection devices into our assay’s workflow to facilitate efficient HPV detection.

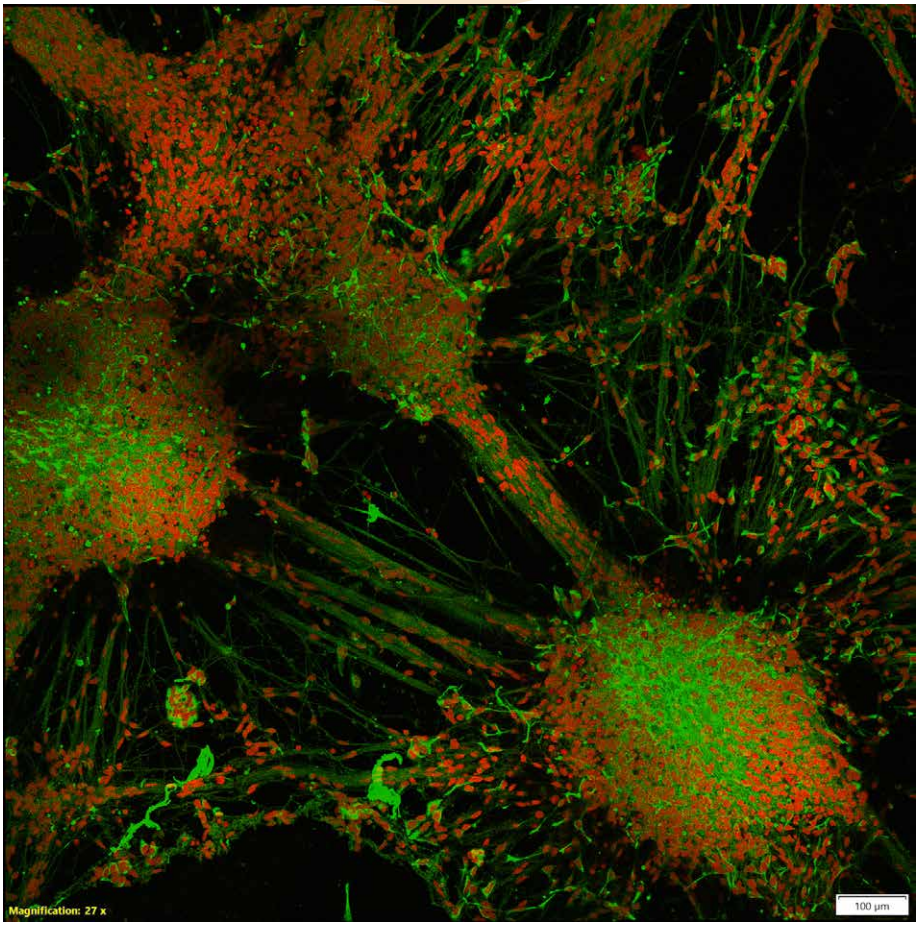


Cell-Based Therapeutics Platform

Induced pluripotent stem cells (iPSCs) developed from patients have enabled the investigation of disease mechanisms in the lab without dependence on animal models, which do not always mimic human disease conditions. Cells differentiated from patient iPSCs recapitulate the disease phenotype and are valuable in drug screening and testing. Human pluripotent stem cells generated from an individual with a specific genetic disorder can speed up personalized therapies, with the in vitro derivation of patient-specific cell types helping in studying the disease pathogenesis. However, obtaining patient samples can have ethical and access concerns and may not represent the most prevalent disease variants, necessitating gene editing approaches for such disorders.

Using CRISPR-Cas based gene editing, it is possible to disrupt a gene function by introducing the mutation of interest and to correct a disease-associated mutation. To study a specific genetic disorder, the mutation of interest is introduced in the target gene in a pluripotent stem cell derived from a normal donor, and the resultant cell line differentiated into the relevant lineages to study disease pathogenesis or drug screening.

These approaches have been successfully developed at TIGS, generating a disease-agnostic iPSC-based therapeutic platform that can enable the development and testing of novel drugs and therapies.



Motor neurons derived from IPSCs.
Image credit: Karthik K and Vasanth Thamodaran

Human pluripotent stem cell-based disease models for testing biotherapeutics

Vasanth Thamodaran

The Organisation for Rare Diseases India (ORDI) has listed about 250 rare genetic disorders (RGDs) that are prevalent in India. The lack of cell-based models for a majority of these RGDs has hindered the development of therapies tailored to these patients. At TIGS, we have developed a platform to enable the generation of stem cell-based disease models for a variety of disorders. 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.

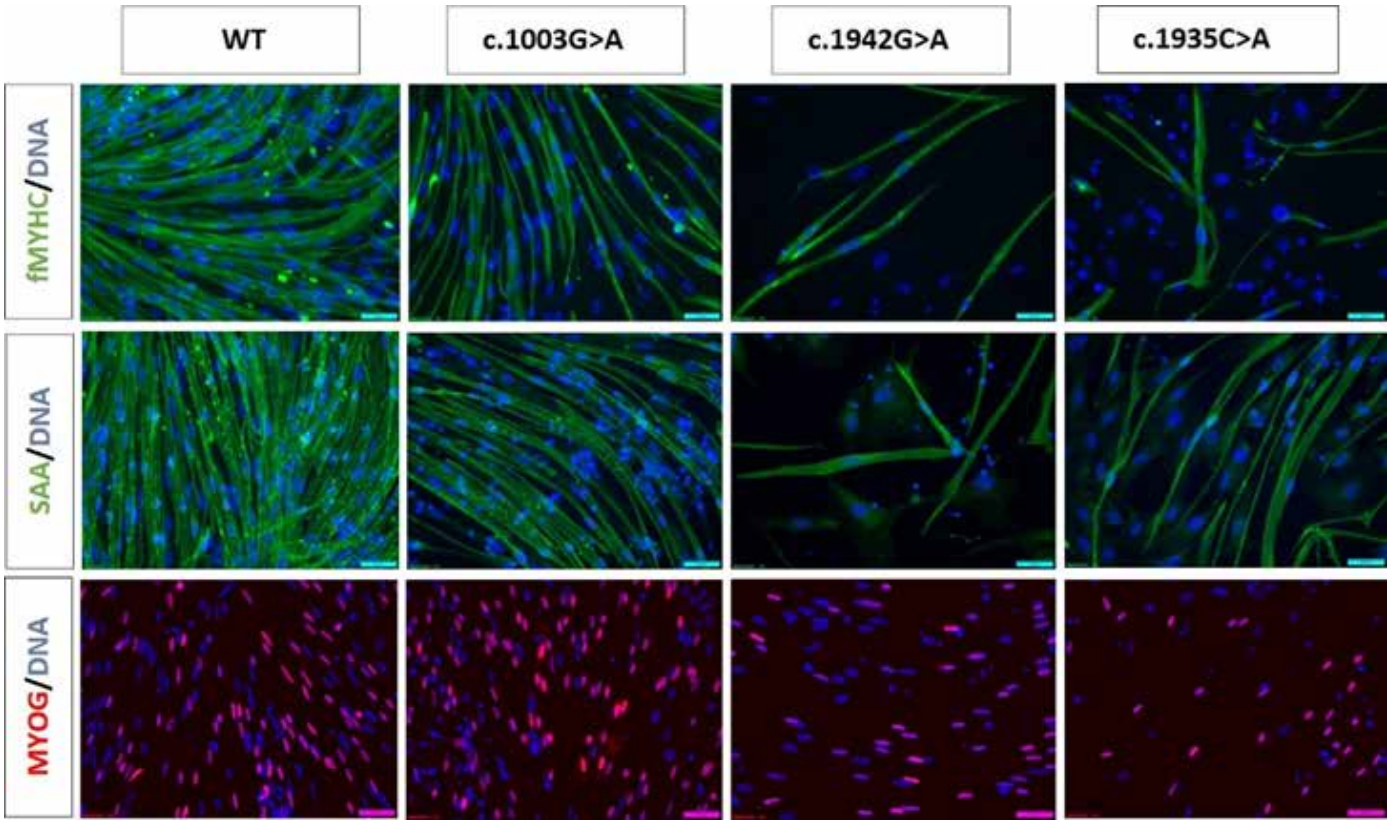
We have been working on generating mutant iPSCs carrying the mutation of interest using CRISPR-Cas9 (for RGDs such as lysosomal storage disorders (LSDs), Duchenne Muscular Dystrophy (DMD), and fatty acid metabolism), as well as by programming patient-derived cells (for Osteogenesis Imperfecta (OI) and Spinal Muscular Atrophy (SMA). The mutant lines are characterised for pluripotency marker expression, trilineage differentiation potential, and genome integrity. Further, the mutant cell lines are differentiated to lineages that are affected in each genetic disorder e.g., cardiac and skeletal muscle lineages in the case of LSDs such as Pompe disease, and motor neurons in the case of SMA. The defects associated with these disorders will then be validated in the differentiation process. The disease model so established will be used in evaluating and developing therapeutic interventions for these disorders.

Disease-in-a-dish platform for disease modelling and evaluating biotherapeutics for lysosomal storage disorders (LSDs)

Lysosomal storage disorders (LSDs) collectively have a worldwide prevalence of 1 in 7,700 births. LSDs are caused by defects in lysosomal enzymes resulting in the accumulation of unprocessed cellular components like proteins, lipids, carbohydrates and nucleic acids. Though there are about 50 different LSDs, in India defects associated with processing of the following cellular components are more prevalent - glycogen (Pompe's disease), fat molecules like sphingolipids (Gaucher disease), glycosphingolipids (Fabry disease) and gangliosides (Tay-Sachs disease). All these disorders are fatal and require lifelong management with enzyme replacement therapy (ERT), externally administering the missing lysosomal enzymes. However, the treatment cost is expensive and investigation of new treatment options can be beneficial for the patients. Further, all the studies have been on the prevalence of associated genetic mutations in non-Indian patients and many of the identified mutations are different from the Caucasian population. Thus, establishing pluripotent stem cell models for these genetic disorders will provide us insights on the disease pathogenesis in the Indian context and can also serve as a platform for drug screening and testing bio-therapeutics.

We use CRISPR-Cas based approaches to introduce mutations associated with LSDs that are widely prevalent in the Indian population. After the cell lines carrying the desired mutation are generated, the cell lines can be differentiated to lineages either as 2D or 3D (organoids) systems to understand the disease mechanisms. Finally, the cell lines will also be used as a therapeutic platform for developing therapeutic interventions for LSDs.

We have overcome the difficulties associated with obtaining patient samples by using gene editing to introduce specific mutations and a human pluripotent stem cell (hPSC) model for Pompe disease model have been established. The system was able to recapitulate skeletal muscle loss phenotype observed in patients. Currently, the approach is being applied to other LSDs such as Gaucher's disease.



Skeletal muscle cells showing Pompe disease phenotype. Human ESCs carrying Pompe mutations prevalent in India were differentiated to skeletal muscles. The Pompe myotubes showed severe cell death compared to control, a phenotype that mimics muscle loss in the patients.

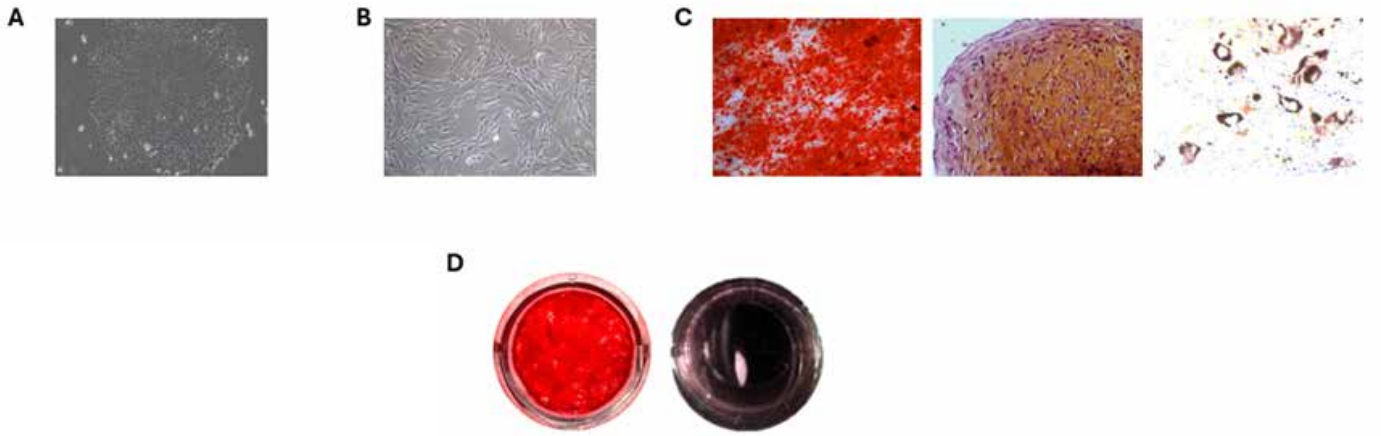
Generation of iPSCs from patients with Osteogenesis Imperfecta (OI)

Osteogenesis imperfecta (OI) or brittle bone disease is a genetic disorder characterized by low bone mass and multiple fractures. The severity of the disease ranges from subtle increase in the fracture frequency to perinatal death. Worldwide approximately, 6-7/100,000 people are affected with OI due to the mutations in one of the collagen genes. 85-90% of OI cases are associated with mutations in the procollagen type I genes (COL1A1 or COL1A2). Type I collagen is a heterotrimer, containing two □1(I) and one □2(I) chains. It is synthesised as a procollagen molecule, with N-terminal and C-terminal globular pro-peptides flanking the helical domain. The helical domains contain uninterrupted Gly-Xaa-Yaa triplets because the small glycine side chain fits in the internal helical space. The most common structural defects in type I collagen causing OI are glycine substitutions in the helical domain. In addition, defects in 17 other genes have identified to be responsible for OI phenotypes. In the past years, several genes encoding proteins involved in type I collagen synthesis, processing, secretion, and post-translational modification, as well as in proteins that regulate the differentiation and activity of bone-forming cells have been shown to cause osteogenesis imperfecta (BMP1, CRTAP, FKBP10, LEPRE1, PLOD2, PPIB, SERPINH1, TMEM38B, CREB3L1, SERPINF1, SP7, WNT, PLS3 and MBTPS2).

Currently there is no cure and no effective treatment for OI patients, though several studies have reported that the cyclical intravenous therapy with bisphosphonates is beneficial in children and adolescents with moderate to severe forms of OI. This treatment decreases pain and increases the density and size of lumbar vertebral bodies, decreases fracture rate, and improves mobility. However, recently, several preclinical studies using stem cell therapy have shown promising effect in the treatment of OI.

We are generating iPSC-based disease models for OI from the fibroblasts of patients with different variants and looking for the molecular and biochemical profile in

respect to bone formation and bone resorption. One of the main objectives is to use these iPSC-based disease models for testing different therapeutic approaches for treating impaired bone formation. We have around 180 patients from our centre, with NGS data available for 150 subjects, and 56 novel mutations identified so far. 18 different genetic mutations are found in these 150 subjects (both autosomal dominant and recessive). With an ultimate goal to develop therapeutic interventions, iPSC-based disease models for both dominant and recessive OIs will be developed. To study the OI associated disease phenotype, iPSCs have already been derived from OI patient derived mesenchymal cells for mutations associated with COL1A1, COL1A2 and SERPINF1. Osteogenic cells derived from the patient iPSCs showed defect in maintaining the structural integrity leading to detachment of bone cells.



A cell based model to study OI using patient derived iPSCs. A) COL1A1 OI patient derived iPSC showing typical morphology of a pluripotent stem cell colony. C) iPSC derived MSCs were successfully differentiated to all three lineages including osteogenic cells. D) The COL1A1 mutant osteogenic cells detached from the surface and lacked staining for alkaline phosphatase, indicating defective osteogenic differentiation.

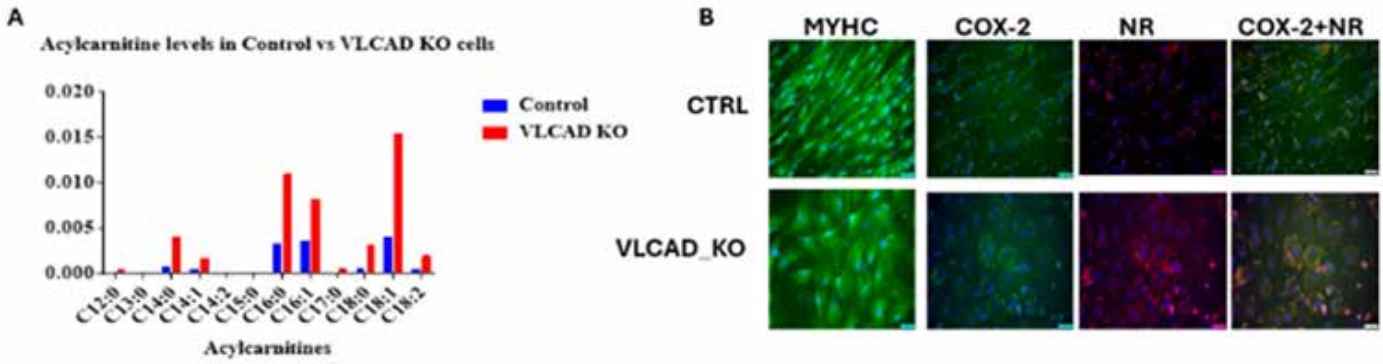
Disease-in-a-dish platform for fatty acid oxidation (FAO) metabolic disorders

Fatty acid oxidation disorders (FAOD) are a group of inborn errors of metabolism caused by gene mutations affecting the oxidation of fatty acids in the mitochondria or disruption in the transport of fatty acids into the mitochondria. Fatty acids are oxidised to produce energy during prolonged fasting or an increased energy demand during illness. A defect in the oxidation usually results in the accumulation of intermediate fatty acid metabolites, which is responsible for the disease pathology. In neonatal condition, the symptoms appear within few hours of fasting resulting in cardiomyopathy, liver dysfunction and fatal within few days or weeks. The infantile-onset disease is associated with severe illness, liver dysfunction, hypoglycaemia and death. The adult form displays muscle weakness and renal dysfunction. Depending on the gene associated with the fatty acid metabolism, about 11 disease variants have been identified. We are working on the disorder associated with very long chain fatty acid oxidation (VLCADD). VLCADD is caused by a defect in the gene ACADVL, which codes for the enzyme acyl-CoA dehydrogenase very long chain. The enzyme is present in the inner mitochondrial membrane and catalysis the first step of oxidation of long fatty acids with 14-20 carbon length. It plays a crucial role in fatty acid oxidation in liver, heart, skeletal muscles and skin fibroblasts. Individuals with VLCADD deficiency may have fat deposits (fatty infiltration) and abnormal enlargement of the liver (hepatomegaly); poor muscle tone (hypotonia); and/or evidence of cardiomyopathy. It is an autosomal recessive disorder and has a prevalence of 1:50000 to 1:100,000.

VLCADD is not yet well studied in the Indian context. Mouse models have been developed to study VLCADD associated disease pathogenesis. Vlcad knockout mice, had an overall accumulation of palmitoyl-CoA and oleoyl-CoA 58% and 64% respectively. Vlcad-deficient hearts had microvesicular lipid accumulation and marked mitochondrial proliferation, and demonstrated

facilitated induction of polymorphic ventricular tachycardia. In contrast to the human disease phenotype, supplementing Vlacd knockout mice resulted in severe clinical manifestations similar to humans and there was a gender dependent variation observed as well. Such species-associated differences highlight the necessity of new disease models to study VLCADD41.

Presently, there are only two studies that have demonstrated generation of iPSCs from VLCADD patients and their utility for cellular assays. VLCADD-iPSCs expressed pluripotency markers and differentiated to all three germ layers, indicating that ACADVL gene is not crucial for iPSC generation. VLCADD cardiomyocytes displayed shorter action potentials (APs), more delayed after depolarizations (DADs) and higher systolic and diastolic intracellular Ca2+ concentration ([Ca2+]i) than control CMs. In addition, the studies also established the potential for using the iPSC models for drug testing. We aim to generate iPSCs based disease models for very long-chain acyl-CoA dehydrogenase deficiency (VLCADD) and to identify drug molecules that can rescue the VLCADD associated disease phenotype. Using CRISPR-Cas9 based gene editing approach, a novel VLCADD iPSC disease model is being developed – early results indicate that the skeletal muscle cells showed increased cell size and accumulation of lipids in mitochondria, successfully recapitulating the disease phenotype.



An iPSC-based model to study VLCADD. A) Mass spectrometry analysis showed accumulation of long chain fatty acid intermediates. B) VLCADD iPSC derived skeletal muscles showed increase in cell size and accumulation of lipids (Nile Red – NR) in mitochondria (COX2 staining).

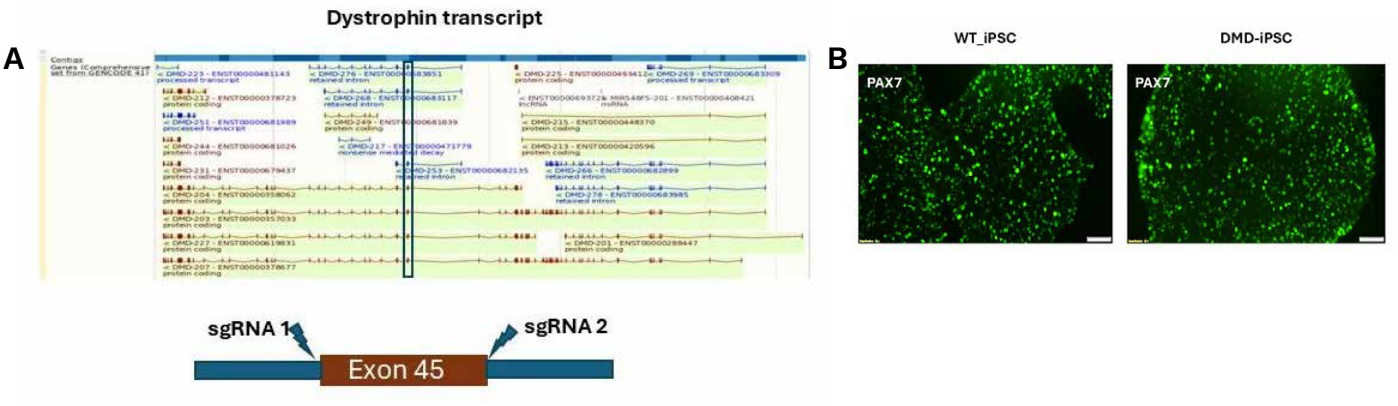
Generation of DMD iPSC and developing novel therapeutics

Duchenne muscular dystrophy (DMD) is one of the spectrum of genetic disorders affecting dystrophin function, which are collectively called as dystrophinopathy. DMD is the severe form, where the function of dystrophin is completely lost. DMD is associated with the loss of various voluntary muscle functions in the body and under severe conditions it affects heart and gut. Symptoms appear between 3 to 6 years of age and start affecting the upper legs, arms and shoulder area. As the disease progresses, muscular degeneration spreads to other regions of the body including lower legs, forearm and trunk. By 10 to 12 years of age the children require assistance in performing routine duties. In addition to the above disabilities, a few affected individuals develop cognitive impairment. DMD follows X-linked pattern of inheritance and thus the disorder predominantly affects the male population. It has a high prevalence rate of 1 in 5000 live male births.

Mouse models are the widely used animal model to study DMD, followed by the canine DMD models. However, there are about 60 different animal models for DMD, which also includes invertebrates like C. elegans and Drosophila, although all the models display many variations in disease manifestation, phenotypes and progression. Human iPSC-based DMD models are able to fill some of these gaps on understanding disease mechanisms and have provided evidence for high-throughput and cost-effective methods of drug testing that may be sufficient to replace animal models in some circumstances. With the improvement of iPSCs reprogramming and subsequent myogenic differentiation methods, the possibilities for pre-clinical and clinical research will considerably expand.

We aim to generate an iPSC-based disease model for DMD in India, and to develop a gene editing based therapeutic intervention to rescue the disease phenotype associated with DMD. Using gene editing, the most prevalent DMD associated mutation in India, exon

45 deletion, was introduced in a healthy male derived iPSC line. The DMD iPSC line expresses all the stem cell markers and maintains its differentiation potential. To rescue the disease phenotype using gene editing approach, guide RNAs that can at least partially restore dystrophin associated defects will now be studied.



An iPSC based model to study DMD. A) Dual sgRNs targeting exon 45 of dystrophin gene. B) DMD-iPSC showing deletion in exon 45 created using CRISPR-Cas9

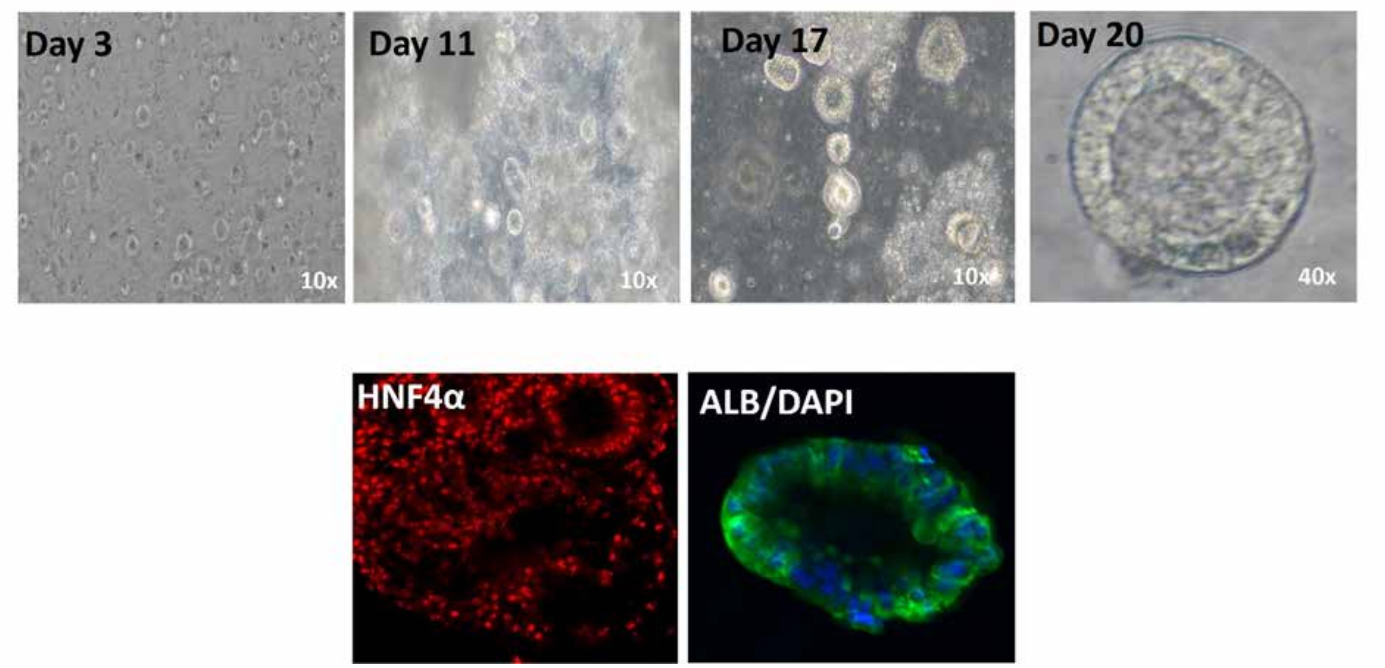
Development of a human pluripotent stem cell derived liver organoid model for malaria and drug toxicity studies

In a 2020 survey, malaria was found to affect about 240 million people, causing 6,27,000 deaths. Globally, malaria is predominantly caused by two Plasmodium species, *Plasmodium falciparum*, and *Plasmodium vivax*. Among the two, *P. falciparum* is the dominant pathogen associated with high mortalities, whereas *P. vivax* is a widely distributed species and has the ability to cause relapse of malaria.

***In-vitro* liver models to study malaria:** In the human host, Plasmodium matures in the liver and the mature form enters the erythrocytes for further maturation and proliferation, which results in malaria. The drugs that are routinely used for treating malaria, target the intra-erythrocytic stage of Plasmodium and very few drugs target the liver stage of the parasite. In addition, unlike the well-studied erythrocytic stage of Plasmodium, the liver stage maturation phase of Plasmodium is poorly understood. Existing primary human hepatocytes (PHH) based in vitro liver models come with batch-to-batch variability and due to its short in-vitro life span, it lacks sustainability. Thus, developing alternative in vitro human liver models will not only provide insights into the elusive liver stage maturation of Plasmodium, but will also enable the development of new drugs that can block the parasite before the disease causing intraerythrocytic stage.

***In-vitro* liver models for drug evaluation:** Pre-clinical drug studies are routinely performed in animal models such as mice. However, the drug metabolic pathways in the liver are dramatically different between mice and humans. For instance, the key drug processing protein complex cytochrome P450 is made of 72 different proteins, whilst only 27 protein components make up the cytochrome P450 complex in humans. Such differences bring in variations in drug processing, which often leads to the failure of drug candidates, which were previously tested in preclinical mouse models. Thus, the generation of pre-clinical liver models that can closely resemble the human hepatic system can enable successful drug discovery.

We are developing a multicellular human liver organoid model that can support the maturation of Plasmodium sp. in hepatocytes. The developed human liver organoid will enable drug toxicity or drug evaluation studies both in vitro and in vivo approaches.



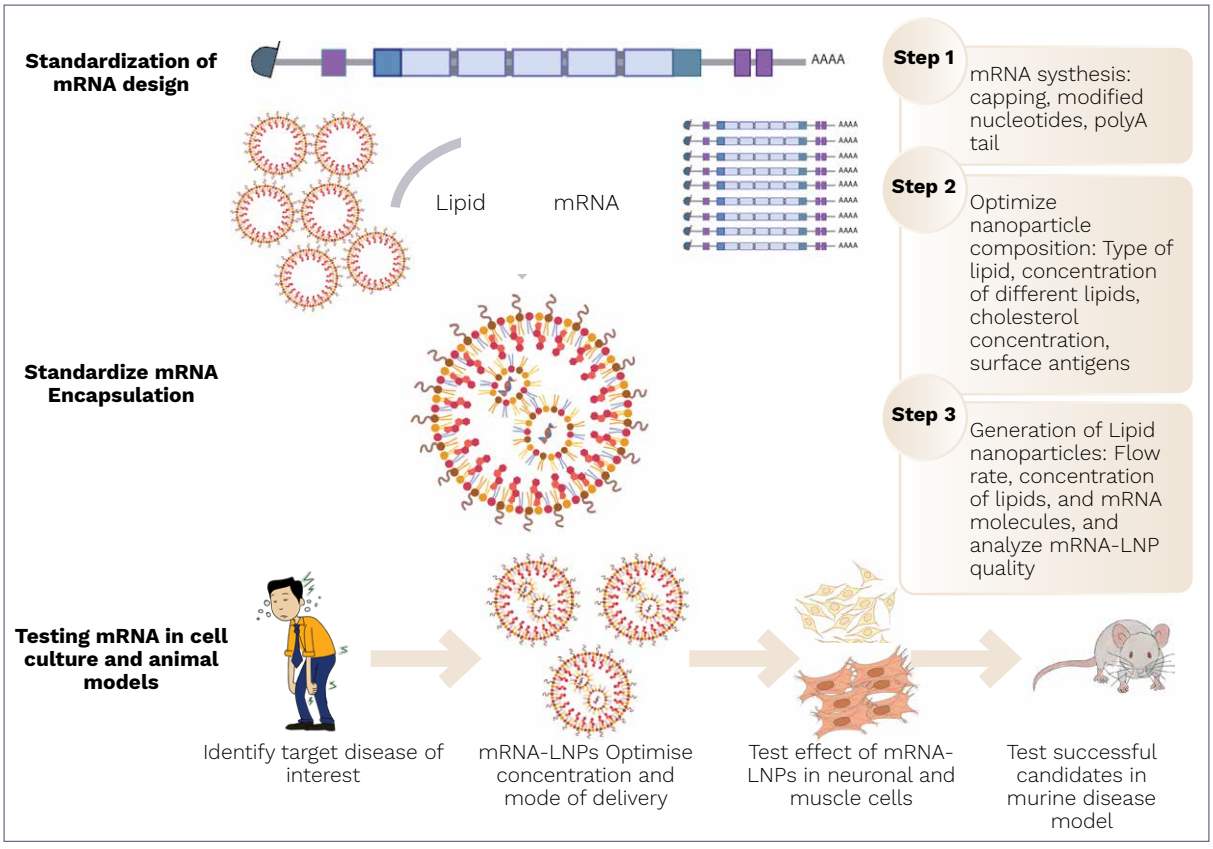
H9 ESC derived human liver organoids. Micrographs showing development of organoids at different days. Immunostaining showed expression of liver specific markers HNF4α and albumin.

mRNA Therapeutics 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 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.

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, is 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.

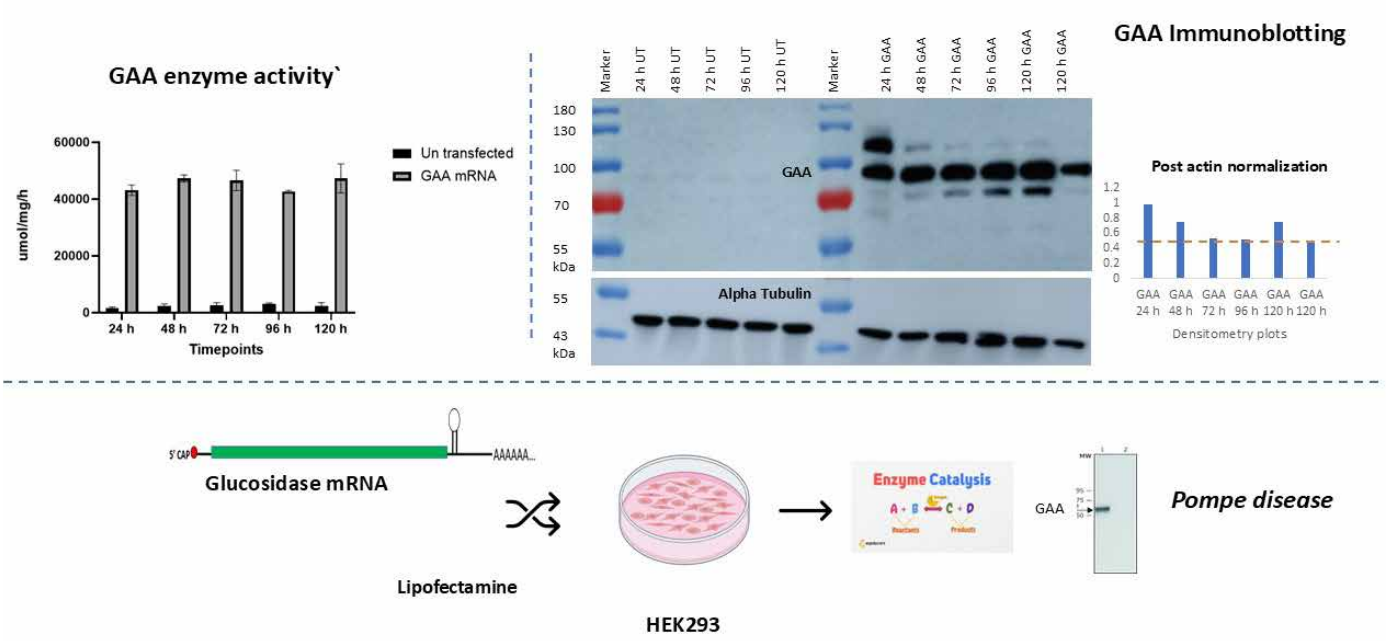


mRNA-based therapies

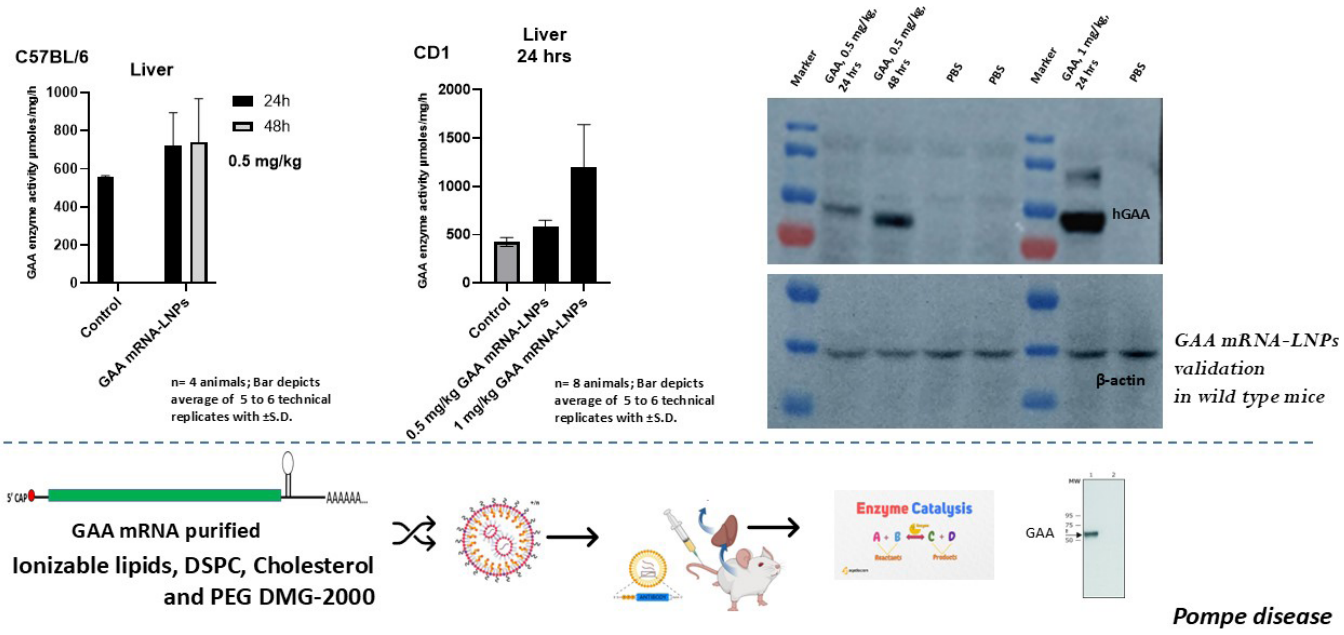
Rajesh V Iyer

Lysosomal storage disorders

Lysosomal storage disorders (LSDs) are a group of monogenic rare genetic disorders that occur due 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 ~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 ERT. The cost of these therapies is high 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 small 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, respectively, 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*. These formulations were also preclinically validated in mice and were found to facilitate the *in vivo* production of therapeutic proteins in the mice liver for 24 hours. We are further developing these potential preclinical leads for Pompe and Fabry disease, so that dosing formulation for the human phase-I clinical trials can be determined.

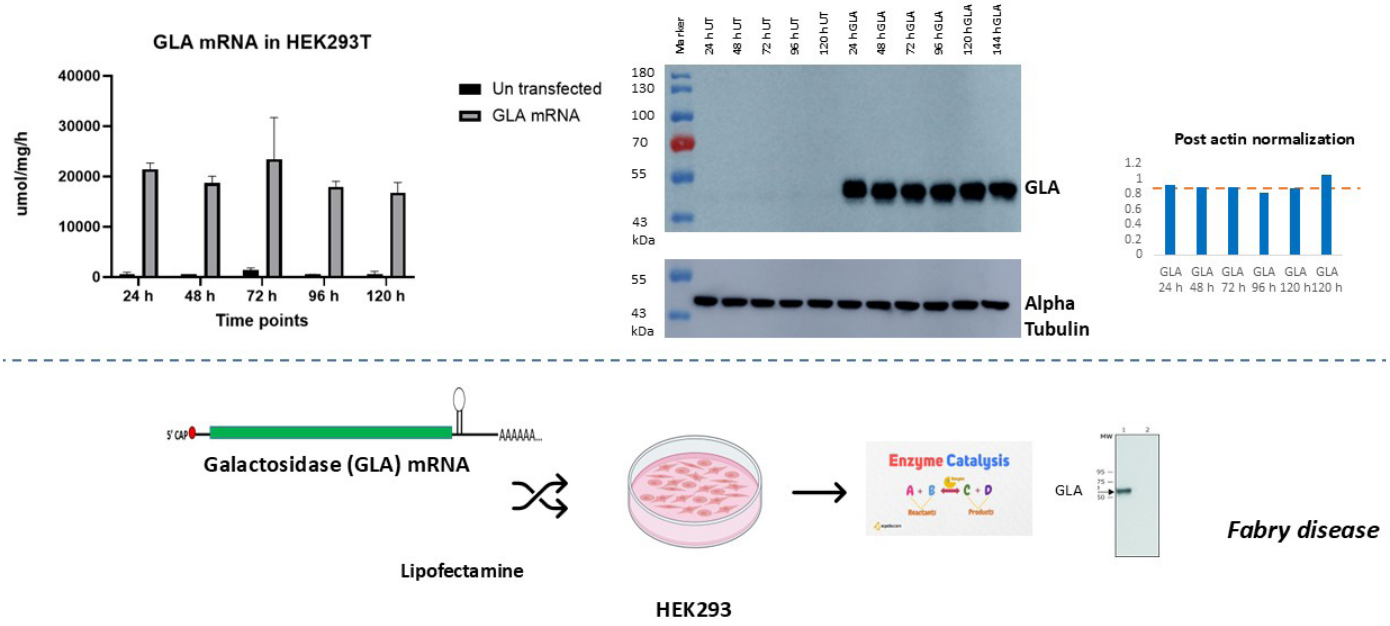


In vitro validation of mRNA therapeutic candidate for Pompe disease

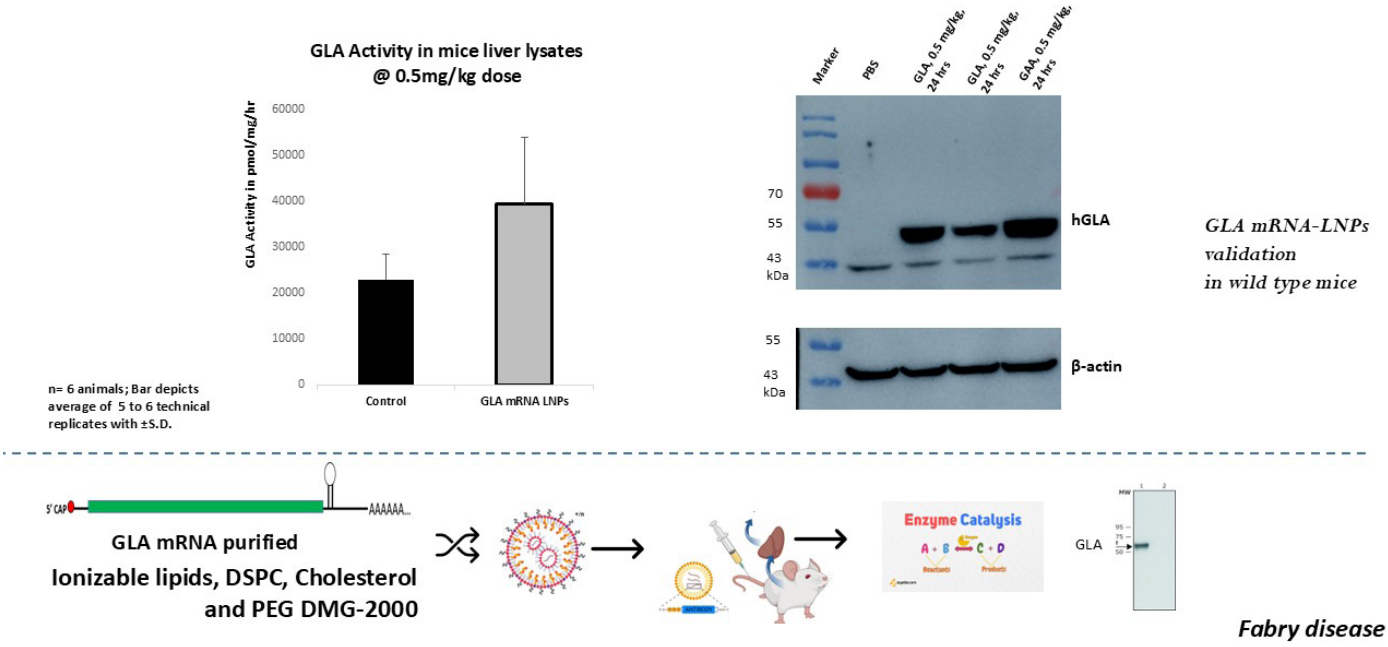


GAA mRNA-LNPs validation in wild type mice

In vivo validation of mRNA therapeutic candidate for Pompe disease



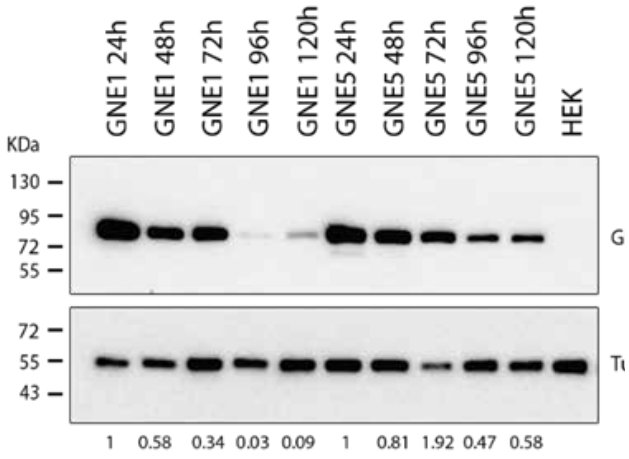
In vitro validation of mRNA therapeutic candidate for Fabry disease



In vivo validation of mRNA therapeutic candidate for Fabry disease

GNE myopathy

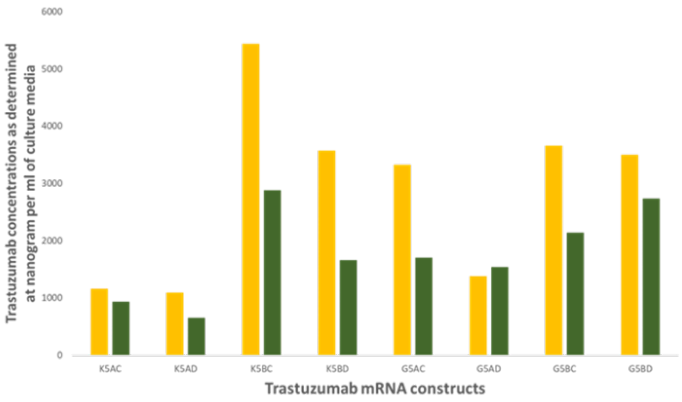
GNE myopathy is an adult-onset progressive neuromuscular disorder that generally leads to extreme disability in a few years. The disease is caused by mutations in the bifunctional enzyme Glucosamine (UDP-N-Acetyl)-2-Epimerase/N-Acetyl-Mannosamine Kinase involved in sialic acid biosynthesis. There is no approved treatment for this disease. TIGS is collaborating with World Without GNE Myopathy (WWGM), a patient advocacy group, to develop mRNA therapy for GNE Myopathy. 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.



In vitro validation of mRNA biotherapeutic candidate for GNE myopathy

Monoclonal antibodes for cancer

Monoclonal antibody therapy dominates the therapeutics protein market with worldwide sales of nearly $125 billion. In 2021, FDA approved the 100th monoclonal antibody “Dostralimab” (the antibody which worked wonders for colon cancer patients) developed by GlaxoSmithKline. However, the antibody treatment can cost up to 4 Lakhs per month and usually, patients have to be on the therapy for six months to a year. Such costs make it beyond the reach of a majority of the population in India. We are working towards this social issue by developing mRNA-based antibodies for cancer. These mRNA-based antibodies can potentially reduce monoclonal antibody treatment of cancer by 100 folds. To achieve this, we are developing antibody encoding mRNA based immunotherapeutic candidates which can be injected parenterally into the patient’s body. The mRNA is complexed with a suitable non-viral gene delivery system to enhance its stability as well as uptake into the cells. The internalized mRNA inside the patient’s cells then expresses the antibody and secretes it into the bloodstream of the patient to facilitate immunotherapy. Owing to the synthetic nature of mRNA therapy, it bypasses the expression and purification methods required for the therapeutic protein replacement therapy, thereby reducing the cost substantially.



3 microgram per ml of antibody production via transfection of dual mRNA-LNPs

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

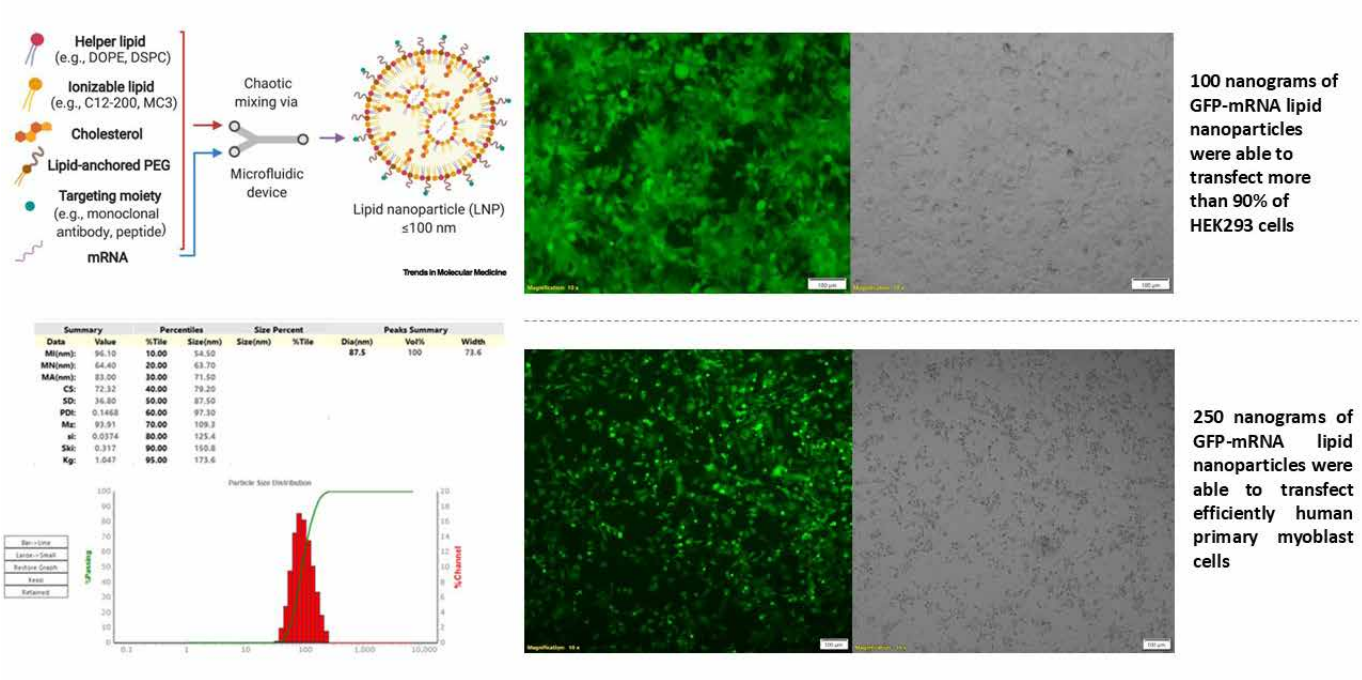
Apart from the mRNA solutions, we are also developing suitable *in vivo* delivery abd expression systems. We have successfully generated mRNA-lipid nanoparticles (mRNA-LNPs) using a customizable microfluidic device and validated them in cell & mice models. The size of mRNA-LNPs was found to be below 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. To further validate our lipid nanoparticle formulation, we developed luciferase mRNA-lipid nanoparticles and injected them into mice. Upon bioluminescence imaging, we observed strong signal from mice administered with luciferase encoding mRNA-LNPS whereas no signal was detected in the mock injected control group. This result asserts the *in vivo* transfectability of the custom developed mRNA-LNPs at TIGS.

Future outcomes

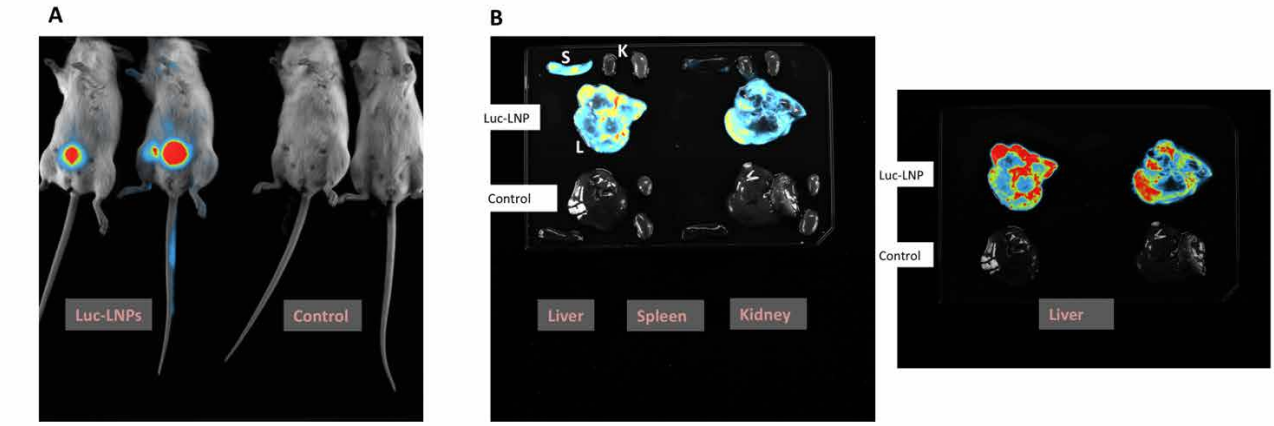
We have prospective mRNA candidates for numerous rare diseases, which are ready for packing into nanoparticles and testing in rodent models. Following proof of efficacy in animal models, we envisage a toxicological study to demonstrate that our therapy is safe for humans. Post toxicity studies, we want 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.

In the coming five years, we are aiming to develop preclinically validated mRNA based therapeutic candidates for the three lysosomal storage disorders (LSDs): Pompe disease, Fabry disease, and Gaucher disease. We would collaborate with industry partners for the setup of cGMP compliant synthesis of mRNA-based drugs and conduct preclinical toxicity studies for mRNA based biotherapeutic candidates for the three lysosomal storage disorders. TIGS also serves as the nodal centre for the ICMR (Indian Council of Medical Research, Govt. of India) funded multi-institutional project titled “Centre for

advanced research for neuromuscular genetic disorders (CAR-NMGD): Clinical data-based disease modelling, molecular diagnostics, and mRNA based biotherapeutic technology platform". As part of this program, we would collaborate with ICMR to conduct phase-I/II human trials and clinically validate mRNA-based drugs developed for the three LSDs by TIGS.



In vitro validation of GFP- mRNA lipid nanoparticles. They are generated using custom microfluidic pipeline. The average size of mRNA-LNPs were 73.6 nanometres with a net negative surface charge. The transfection ability of the developed mRNA-LNPs was close to 95% in HEK 293 cells.



0.5 mg/kg dose of secretory luciferase mRNA-lipid nanoparticles or PBS were administered intravenously to female CD1 mice. ***(A)*** *At 24 hours, mice were injected intraperitoneally with luciferase substrate and subjected to in vivo luminescence imaging.* ***(B)*** *At 48 hours, mice were injected intravenously with luciferase substrate. Mice were sacrificed, organs were harvested and imaged. n=2 per group.*

In vivo transfection of Luciferase mRNA- lipid nanoparticles

Technology Platforms team

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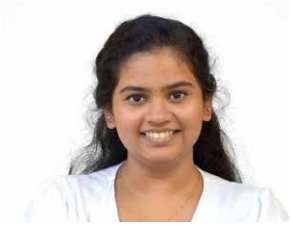

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Research Facilities

Research Facilities

Sunita Swain
Insectary

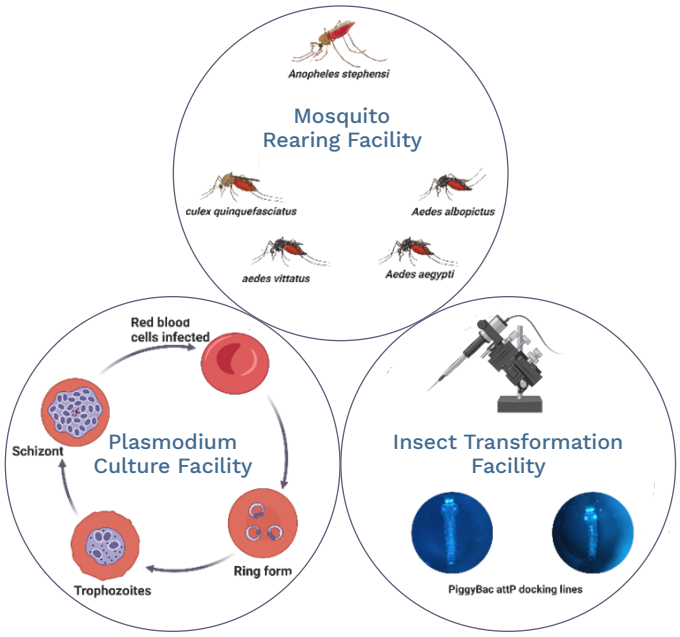
V S Sresty Tavva
Greenhouse

Insectary Facility

Sunita Swain

Mosquitoes, extensively studied for their vital role in disease transmission, represent a diverse group of over 3,500 species globally. Among this diversity, only a few species act as vectors for human diseases, which has made them the primary focus of most scientific studies.

The TIGS mosquito-rearing facility aims to establish itself as a National-level hub for mosquito vector research in India, with a specific emphasis on species from the Indian subcontinent. The facility is organized into three key components:



» **Mosquito Rearing Facility:**

This facility houses mosquito lines, including *Anopheles, Aedes,* and *Culex,* to support vector-related research. Areas of focus include vector competence, behavior, genetics, and host-pathogen interactions. The facility also develops isofemale and mutant mosquito lines tailored for specific experimental needs.

» **Parasite Culture Facility:**

Dedicated to *Plasmodium falciparum* research, this facility supports studies on parasite biology, drug testing, and vaccine development.

» **Insect Transformation Facility:**

This component facilitates advanced bio-manipulations in insect pests and vectors, opening new avenues for diverse entomological studies.

Collaborations and Research Initiatives:

» Partnering with Integri-Biotech, we are developing the Tele-Epidemiology Based Vector Identification and Disease Prevention System (Tevi-Dps), an AI-driven tool for real-time mosquito surveillance.

» Collaboration with inStem focuses on exploring the impact of odors on mosquito immunity and vector competence.

In-house projects include:

» Creating mutant Aedes aegypti lines for repellent screening.

» Developing a human pluripotent stem cell-derived liver organoid model for studying malarial pathogenesis, a platform with applications in anti-malarial drug evaluation.

» Establishing *Anopheles stephensi* lines refractory to Plasmodium infection through *Wolbachia* trans-infections.

Training Programs:

» The facility hosted a national-level workshop, “Beyond the Bites: Exploring Essentials of mosquito biology and rearing,” from November 5th to 7th, 2024. This successful event featured engaging sessions by experts, hands-on training for participants, and networking opportunities within the entomological community.

» As part of the BLiSc cluster, the insectary facility has actively organized orientation programs, training modules, and research services. Additionally, the facility has been involved in impactful outreach initiatives, including:

Community Engagement and Outreach:

» Participating in Facility Day, where the insectary showcased its operations and research capabilities.

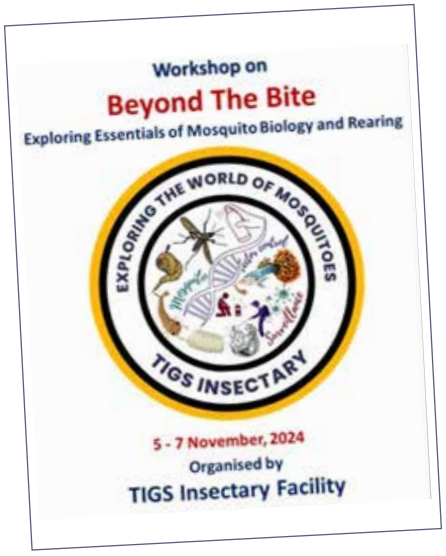
» Contributing to the One Health Awareness Program, where individuals from diverse backgrounds learned about mosquitoes and vector-borne diseases.

» Engaging in the Dengue Warrior Educational Series, where the team educated school children on vector-borne diseases and mosquito biology.

Hosting 54 ambassadors as part of the Sustainability Ambassadors of Global Exchange Program, focusing on raising awareness about the importance of combating vector-borne diseases.

Actively participating in NCBS Open Day, interacting with the public, and educating them about mosquito behavior and the diseases they transmit.

These initiatives highlight the facility’s dedication to community education and fostering awareness about the global challenges posed by vector-borne diseases.



Insectary Workshop hands-on session: A workshop on mosquito rearing techniques provided hands-on training to 19 participants, including students and faculty

One health awareness program at The Visvesvaraya Museum

APSI Degue warriors education series, Creative Circus

APSI Dengue warriors education series, NCBS colonnade

SAGE program

RIKEN-BDR (Japan) delegates visit

Public Outreach and Awareness Program of the Insectary Facility

Greenhouse Facility

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.

» State-of-the-art greenhouse facility for growing transgenic and non-transgenic plants under controlled conditions.

» 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*.

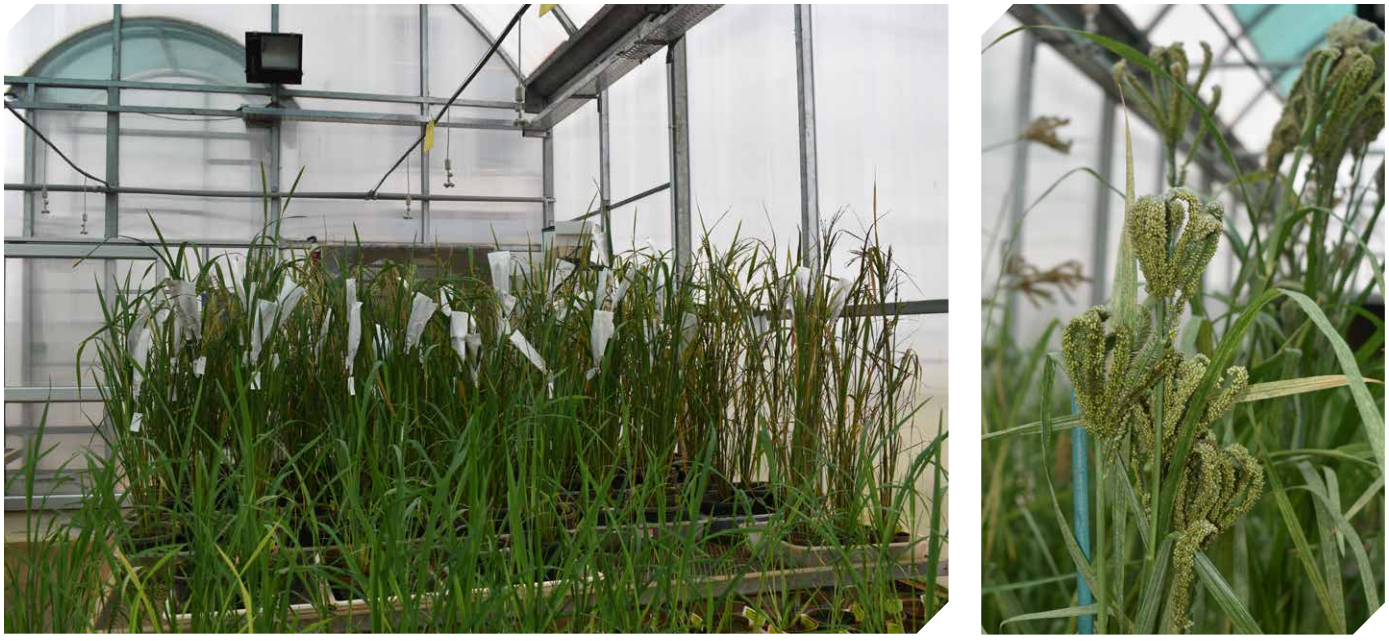
» Greenhouse is also equipped with pollination chamber to perform crosses between selected GE plants and wild-type parent controls.

» The pollination chamber is designed to generate heat and humidity required to perform crossing experiments.

» We maintain different varieties of rice, finger millet and pigeonpea all year long in TIGS greenhouse to make available embryos for tissue culture and transformation experiments and pollen for backcross breeding.

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

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 maintain plant product integrity during research activities in containment facilities.



Rice (L) and Finger millet (R) crops growing at the Greenhouse

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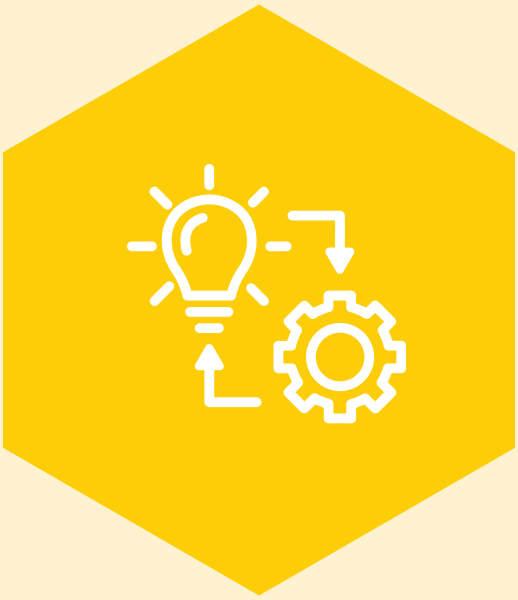
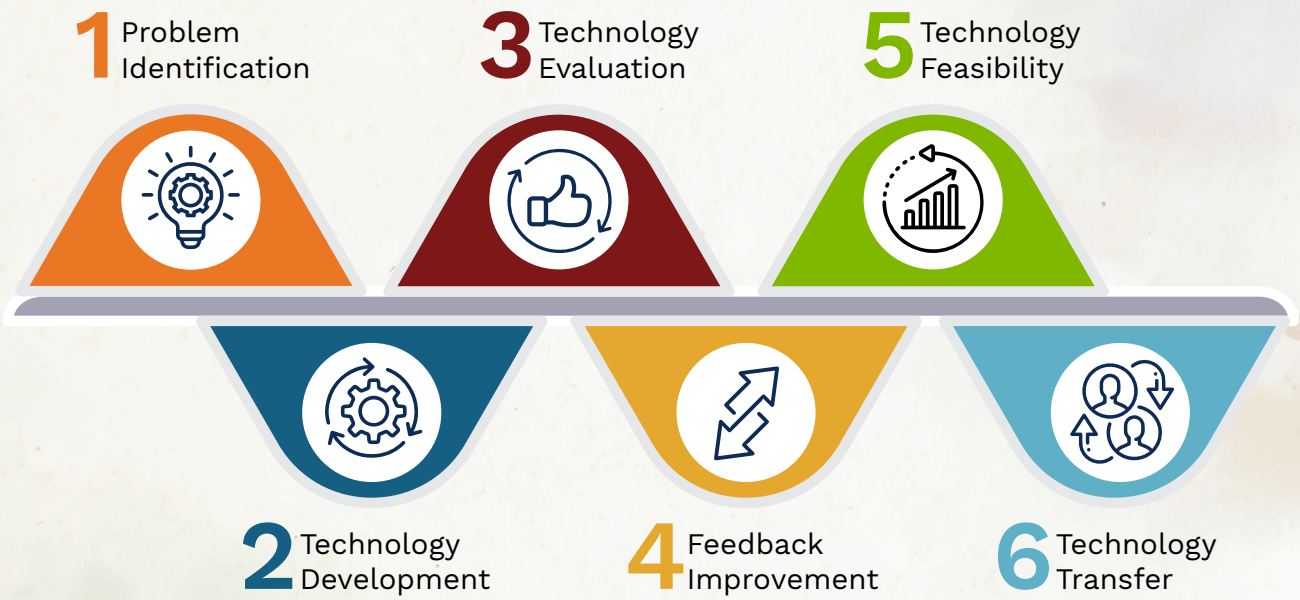
Technology Implementation




1 Problem Identification
3 Technology Evaluation
5 Technology Feasibility
2 Technology Development
4 Feedback Improvement
6 Technology Transfer

Technology Implementation

Satyaprakash Pandey

Enabling technologies to reach society

At TIGS, our efforts do not stop at developing the technology in the lab, but we measure our impact by ensuring that the technologies developed at TIGS reach society and the target group identified at the start of every project.

The journey of transforming lab technologies into societal solutions is pivotal for societal advancement and economic growth. This requires working together with project scientists, government, regulatory and industry partners to translate the technology from TRL1-3 to TRL 4 and above. TIGS has a dedicated Technology Implementation team for taking the technological solutions developed at TIGS to the society via market.

The Technology Implementation Group actively engages important stakeholders, such as scientists, clinicians, industry partners and Government labs, from the first step of the development of the technology for gap identification, differentiation of the offered solution and measures the predictable impact of the technology to the society. This team uses a structured approach to evaluate, assess feasibility, and transfer technology for commercialization, ensuring that groundbreaking innovations reach those who need them most.

At TIGS, the Technology Implementation team works closely with the Project Scientist and onboards relevant dependable partners to effectively scale and implement the solution. The process workflow from lab to society (via the market) requires multiple steps which are technology specific but process through multiple stages.

1. Technology evaluation

Once the technological solution is developed in the lab, the technology prototype is transferred to the Technology Implementation Group who work with the Project Scientist and other partners to perform a technology Evaluation. The first crucial step in transitioning lab-developed technologies to the market is a comprehensive technology evaluation. This phase involves:

a. **Problem Identification:** Understanding the User need to ensure the technology addresses a significant problem or need.

b. **Competitive Landscape Assessment:** Evaluating existing solutions to identify a unique value proposition for the developed technology.

c. **Performance Assessment:** Assessing the developed technology for its performance as per the established guidelines. Parameters such as stability, precision, repeatability, reproducibility are tested using International Standards in accordance with the established guidelines.

The main purpose of Technology Evaluation stage is to determine the performance of the technology in controlled field settings. We collaborate with multiple stakeholders (Industry partners, hospitals and government agencies) and onboard them at this stage for their feedback on the performance of the technology. This stage is pivotal for determining the technology's potential impact and viability in the market.

2. Technology feasibility

Most technologies suffer from failure due to lack of compatibility with the end-user's needs. At TIGS, we focus on high-quality and user requirement in parallel with cost-effectiveness. Technology feasibility analysis is a continuous iterative process. The feasibility analysis starts from the step of problem identification and is refined to develop a product as per the target product profile (TPP) and user requirement. Following a positive evaluation, the technology undergoes a feasibility analysis to ascertain its readiness and potential for commercial success. Key components include:

a. **Technical Readiness Assessment:** Examining the technology's development stage and what is required to bring it to a commercially viable product.

b. **Viability Analysis:** Assessing the aspects from the implementation lens, including cost of raw materials and production, manufacturing capability of partners, infrastructure availability for deployment in the field.

c. **Regulatory Pathway:** Identifying any regulatory requirements or certifications needed for the technology to go to market.

At this step, we develop strategies that will maximise the adoption and the reach of the technology. We perform gap analysis, identify the suppliers and logistics for quality but cost-effective raw materials, and compare our performance with the available solutions, if any. This continuous feedback allows us to generate data across multiple parameters and aids in optimizing the solutions as per the User needs to be more effective, scalable and implementable in the field. This stage ensures that the technology is not only viable but also ready for the challenges of commercialization.

3. Technology transfer

The final step is the transfer of technology from the lab to a commercial entity, through licensing to an existing company to deliver the technology to the User. To achieve this, dependable partners are needed. Technology Implementation Group pitches the technologies to multiple stakeholders (both from public and private domain) to seek their interest in the developed technology. A guideline document for technology transfer and revenue sharing supports the commercialization of the developed technologies for implementation and scalability. This stage involves:

a. **Partnership Development:** Identifying and engaging with potential industry partners or entrepreneurs with the expertise and resources to bring the technology to market.

b. **Commercialization Strategy:** Developing a detailed plan that covers product development, mapping the requirement of the product by multiple Users such as government, private sector and hospitals, not for profit organizations and patient groups.

c. **Support and Scaling:** Providing ongoing support to the commercial entity, and planning for scaling the technology to meet the User needs and demand.

The technology transfer costs including the development, licensing and commercialization is calculated on a project-to-project basis keeping the end goal of delivering the technology to the User in sight. Successful technology transfer requires careful planning, strong partnerships, and a commitment to navigating the complexities of commercialization.

Taking lab-developed technologies to society through the market is a journey fraught with challenges but rich with potential for positive impact. Through a structured approach to technology evaluation, feasibility analysis, and transfer for commercialization, we can ensure that innovations reach their full potential in improving lives and driving economic growth.

Overview of Technology Implementation at TIGS

Enabling technologies from lab to market

Technology	Description	Potential impact	Industry partner onboarded	Licensing status
Hepatitis A	RT-PCR diagnostics for Hepatitis A	Indigenous solutions for affordable, accessible and scalable molecular diagnostics	Yes	Licensed
Hepatitis E	RT-PCR diagnostics for Hepatitis E		Yes	Licensed
RespiFlu	RT-PCR diagnostics for respiratory pathogens (Influenza, COVID, RSV)		Yes	Licensed
HPV Genotyping	RT-PCR diagnostics for high-risk Human Papilloma Virus (HPV)		Yes	Licensed
African Swine Fever	RT-PCR diagnostics for African Swine Fever		Yes	Ongoing clinical validation
H5N1	RT-PCR diagnostics for H5N1 virus		Yes	Ongoing clinical validation
Growth Factors	Purified and characterized growth factors for stem cell culture	Affordable cell and gene therapy solutions	Yes	Pre-validation stage
Natural Mosquito Repellent	Formulation for mosquito repellent	Traditional knowledge of plant oils for mosquito control	Yes	Formulation testing stage
Combating Coffee Stem Borer	Electromagnetic pulse approach to combat coffee stem borer	Minimizing economic losses and use of harmful chemicals	Yes	Proof-of-concept established
Environmental Surveillance for AMR	Complete solution for Environmental surveillance from sampling to detection for a One Health approach	Early detection of pathogens and antimicrobial-resistant signatures for community screening	Yes	Validation stage complete

Technology Implementation team

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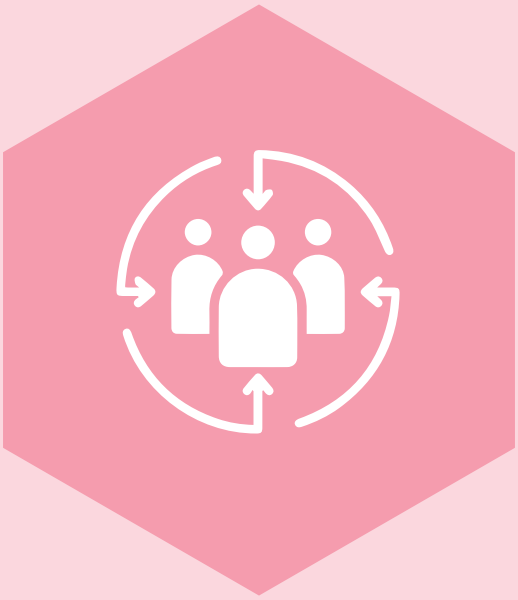
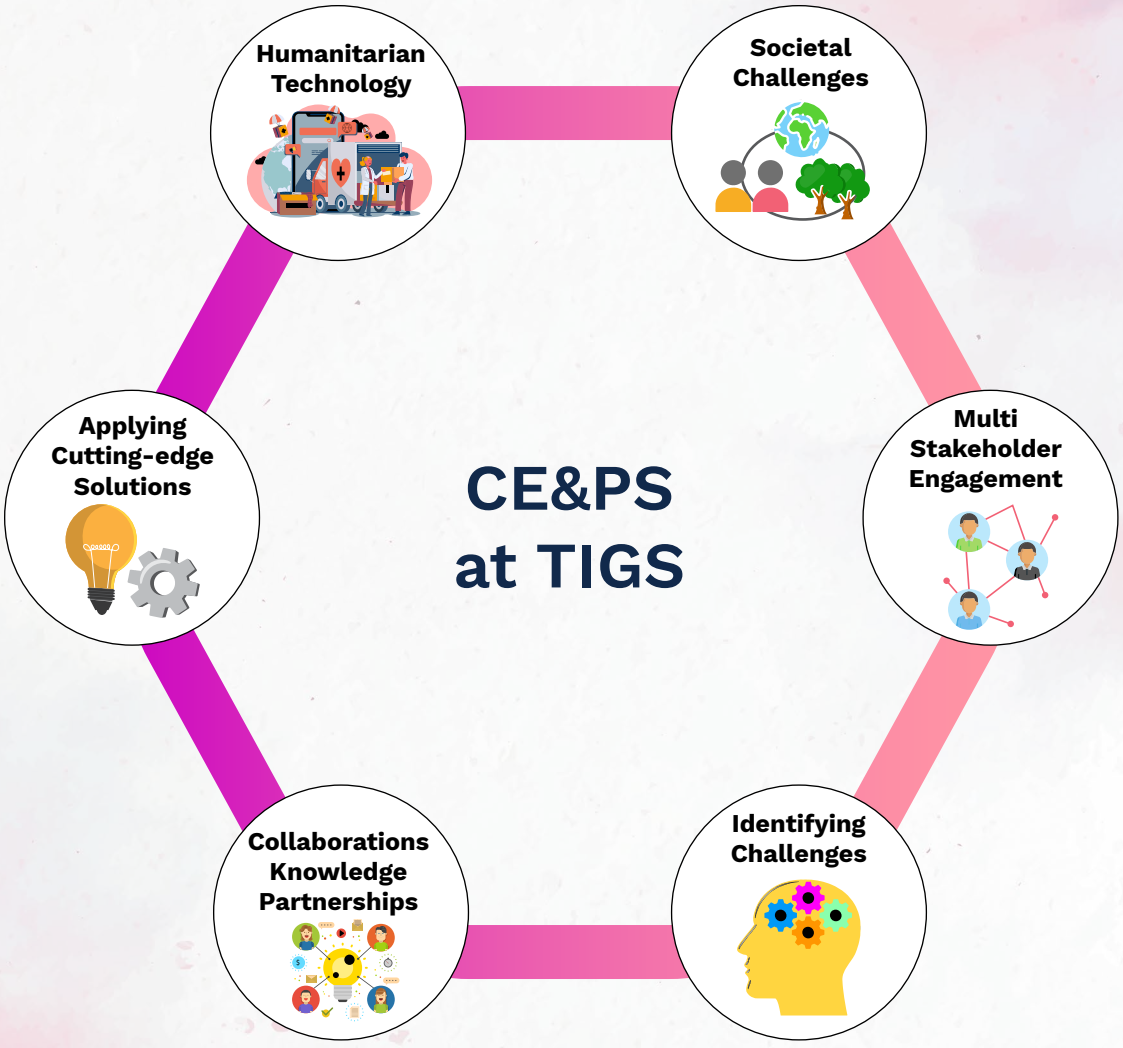
Community
Engagement and Policy
Stewardship
WHAT'S IN YOUR DNA?

Community Engagement and Policy Stewardship




Humanitarian Technology
Societal Challenges
Applying Cutting-edge Solutions
CE&PS at TIGS
Multi Stakeholder Engagement
Collaborations Knowledge Partnerships
Identifying Challenges

Community Engagement and Policy Stewardship

Saveetha Meganathan

The Community Engagement and Policy Stewardship program at TIGS aims to integrate scientific advancements with a comprehensive approach to community engagement and policy advocacy, in alignment with India's Science, Technology, and Innovation Policy 2013. This includes promoting open science, transparency, public consultation, scientific temper, and translating science into societal benefits. The program aims to achieve health equity and nutrition security by addressing community concerns through clear and consistent science communication and fostering societal connections.

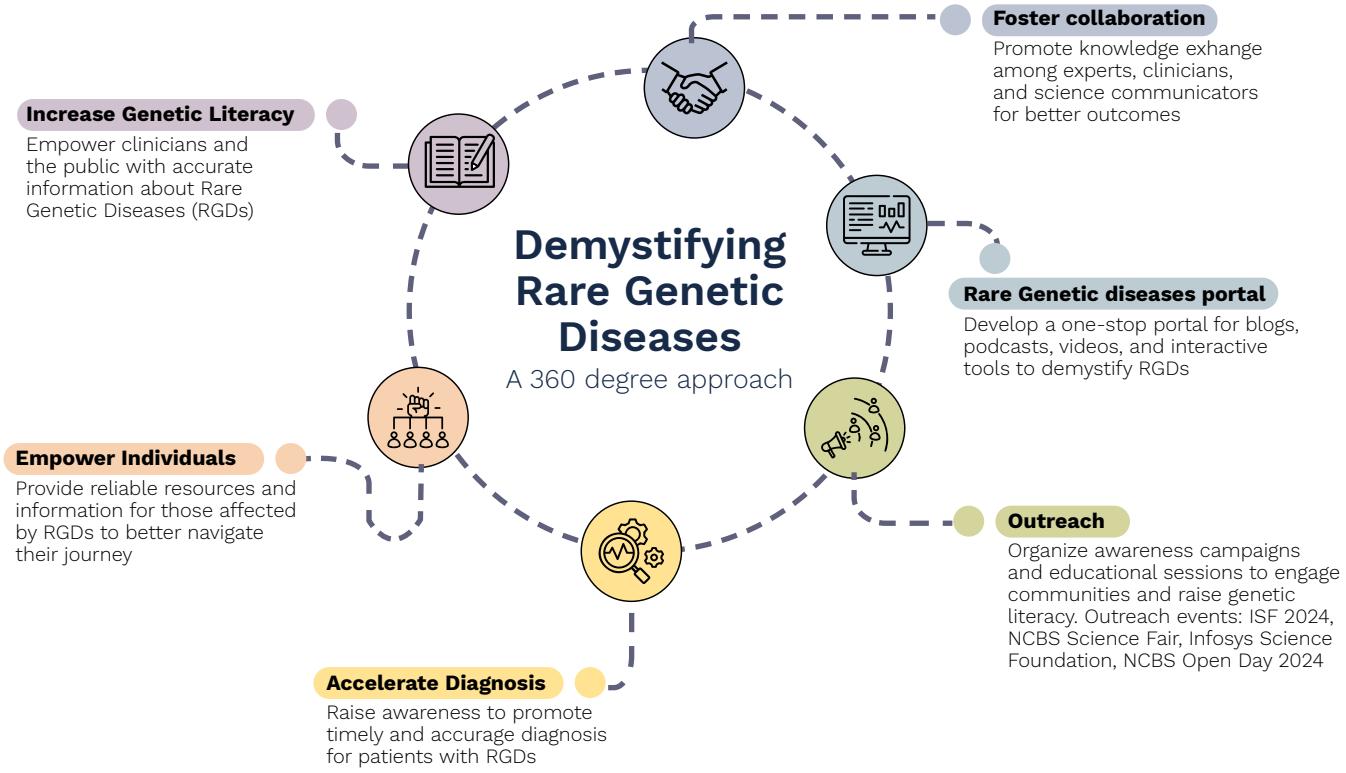
TIGS' proactive community engagement amplifies concerns and builds trust through effective science communication. Exploratory and action research projects lead to policy advocacy, funding opportunities, and system strengthening, focusing on improving lives through practical solutions. The program also emphasises the dissemination of scientific knowledge to communities with varying literacy levels, using innovative tools to ensure social inclusion in scientific progress.

TIGS is committed to creating socially conscious, ethically grounded research programs that develop low-cost, scalable humanitarian technologies. These technologies are designed to meet the contextual needs of Indian society, with a particular focus on the most vulnerable and disadvantaged populations. The institute also prioritizes networking with humanitarian groups, building global coalitions, and facilitating technology transfer to ensure that advancements in agriculture and health are accessible to stakeholders.

Through its efforts, TIGS plays a critical role in areas such as epidemiological surveillance and the development of affordable healthcare technologies for infectious diseases, precision diagnostics and treatments for rare genetic disorders, and the creation of nutrient-rich, climate-resilient crops. Partnerships with institutions and researchers across India enhance these efforts, enabling TIGS to tackle pressing challenges in human health and agriculture while ensuring that the benefits of science reach those who need them most.

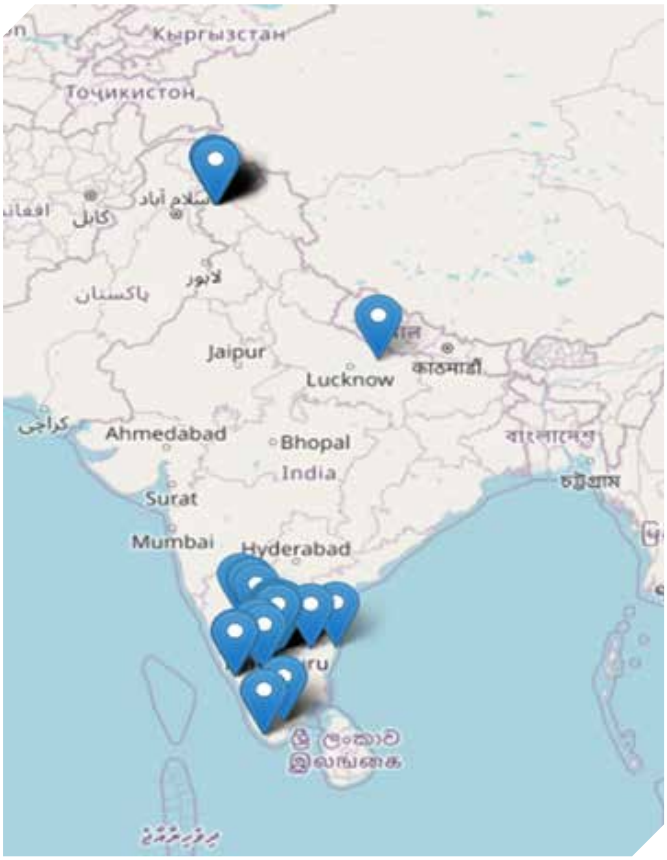
Community Engagement

Demystifying Rare Genetic Diseases



The Tata Institute for Genetics and Society (TIGS) is advancing diagnostics, therapeutics, and public awareness of rare genetic diseases (RGDs) through its “Demystifying Rare Genetic Diseases” project. This initiative enhances understanding among clinicians and the public, enabling timely diagnoses and empowering individuals with reliable information while fostering collaboration among experts and science communicators to improve genetic literacy. TIGS is developing a comprehensive “Rare Genetic Diseases” portal featuring expert blogs, the “Demystifying Rare Genetic Diseases Podcasts,” and visual materials aligned with the National Policy for Rare Diseases (NPRD). The institute promotes multi-stakeholder engagement through events like the Rare Genetic Diseases Research Summit (REDRESS) and innovative formats such as hackathons. Additionally, the platform will provide interactive learning resources, including educational videos and games for high school students, along with outreach activities at colleges. Through these efforts, TIGS aims to demystify RGDs and improve the overall well-being of affected individuals and communities.

This year, our GNE Myopathy awareness campaign achieved great success across India, led by the Community Engagement and Policy Stewardship team. Starting in Bangalore, the campaign distributed 117 educational posters to health centers nationwide, with the support of 31 dedicated volunteers and guidance from Dr. Rakesh Mishra.

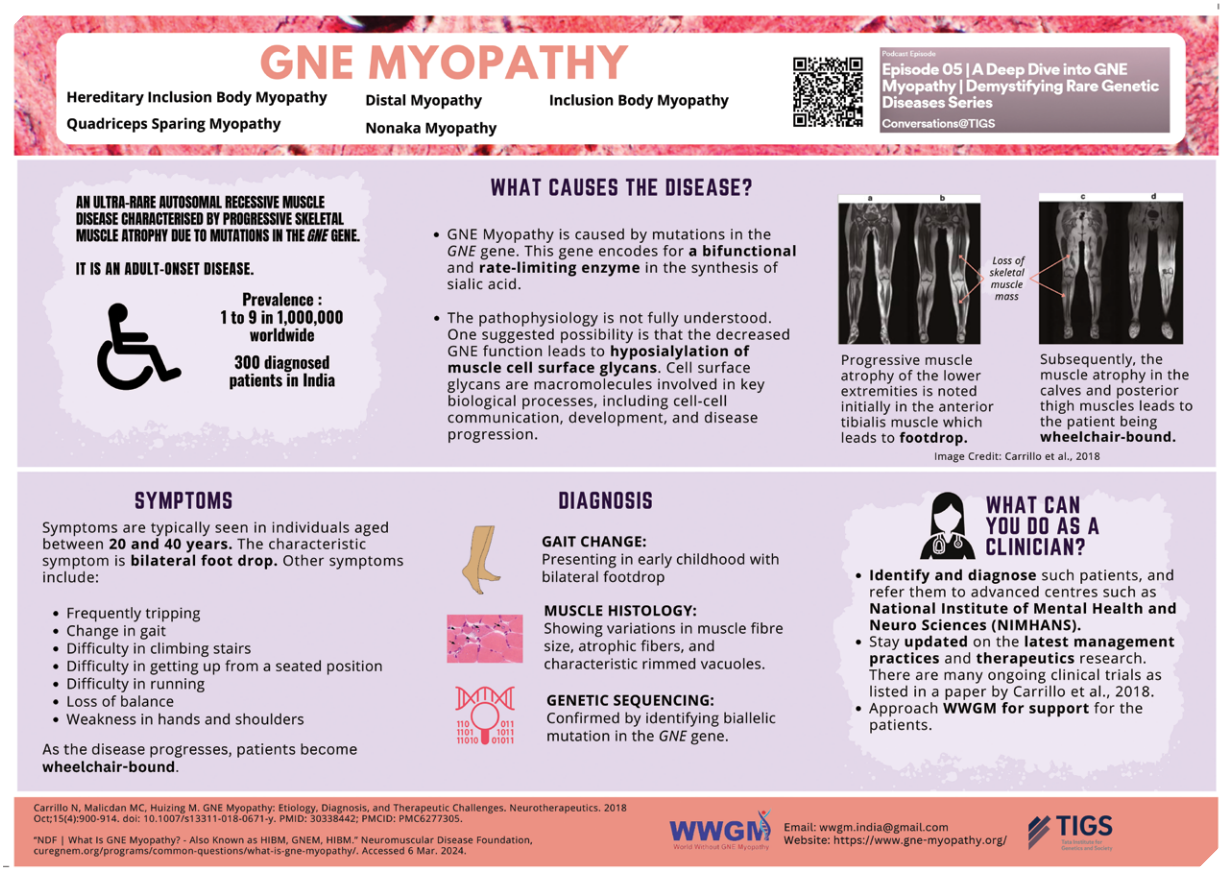


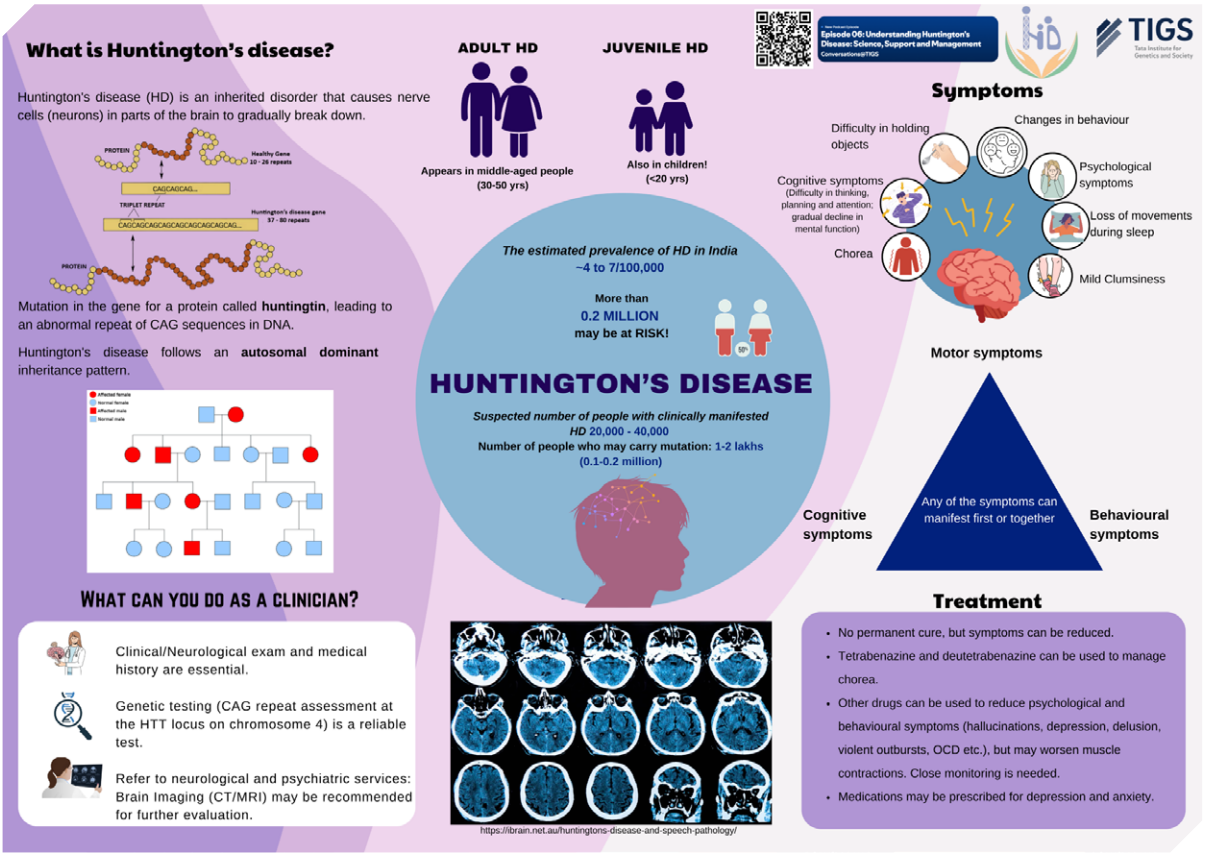
A snapshot of the poster dissemination of GNE Myopathy

Building on the success of the GNE Myopathy campaign, a new Huntington's Disease (HD) awareness campaign was launched with posters curated under the guidance of Dr. Sanjeev Jain and Dr. Meera Purushottam from NIMHANS, India. The campaign aims to raise awareness among clinicians, healthcare practitioners, and the public.

Two posters were created: one for clinicians, offering insights for early diagnosis and management strategies, and another for the public, presented as a storyboard that shares lived experiences of those affected by HD. The visuals simplify the complex science, , encouraging conversations and breaking the silence around the disease.

On February 27, 2024, we launched the podcast *"A Deep Dive into GNE Myopathy,"* featuring Prof. Bhattacharya, Head of Biology at Ashoka University. Combining professional expertise with personal stories, he discussed the disease, challenges in diagnosis, therapeutics, clinical trials, and rare disease policies. The episode also explored cutting-edge technologies like gene editing and iPSCs in advancing diagnostics and therapeutics, offering valuable insights for patients, researchers, policymakers, and curious listeners.





We also released a podcast episode titled *'Understanding Huntington's Disease Science, Support, and Management'* as part of the *'Demystifying Rare Genetic Diseases'* series. The episode featured Dr. Meera Purushottam (NIMHANS) and Dr. Rakesh Mishra (TIGS), who discussed the genetic origins, diagnostic challenges, and management of Huntington's disease. Aimed at raising awareness and fostering expert conversations, the podcast seeks to educate researchers, clinicians, and patient communities about rare genetic conditions and their broader impacts.

The recent campaign launched was the Epidermolysis Bullosa (EB) initiative, featuring a conversation between Dr. Rakesh Mishra and Dr. K. Thangaraj on our latest podcast episode. In this episode, they explored the groundbreaking research on epidermolysis bullosa (EB), a rare genetic skin disorder with significant implications for the Indian population.

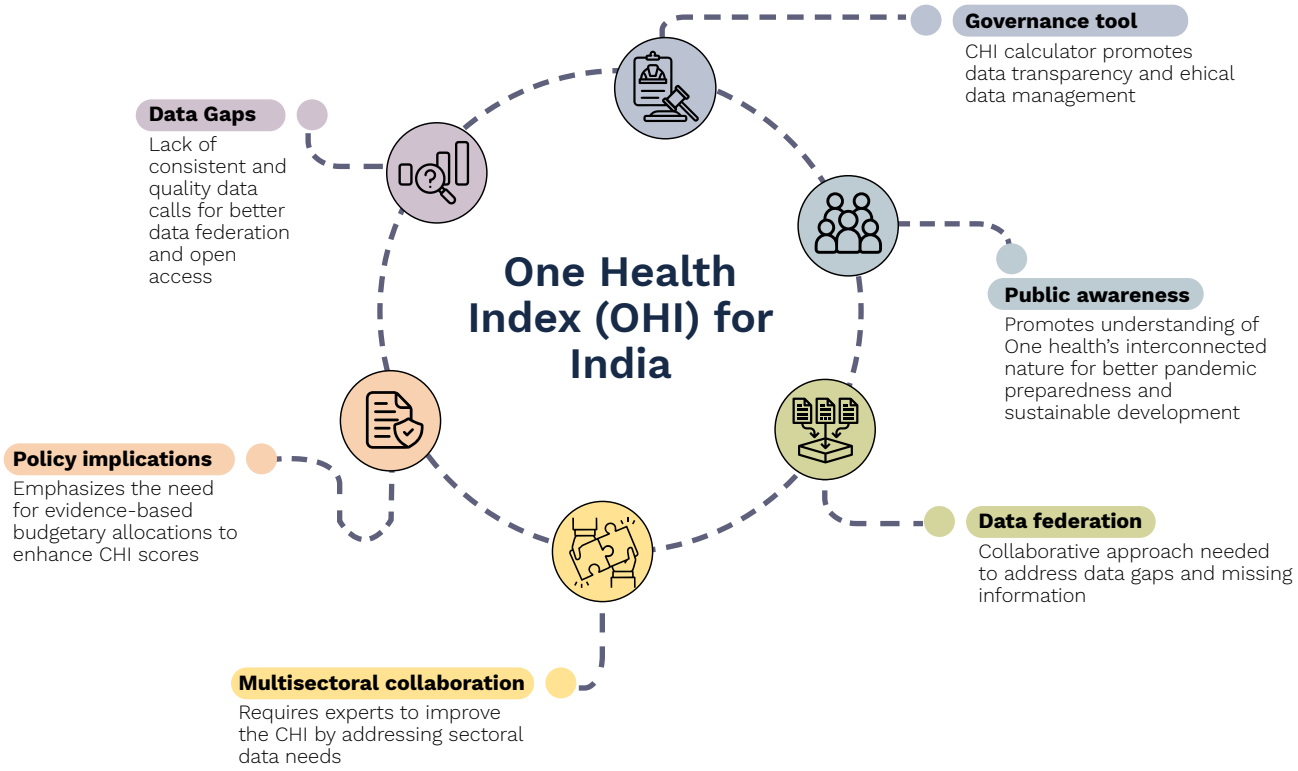
Genetic literacy Initiative

The Tata Institute for Genetics and Society is enhancing genetic literacy through a multimedia initiative that includes posters, podcasts, and engaging games for the public at events like the Infosys Science Foundation, REDRESS 2024 and NCBS Science Fair. Additionally, TIGS is collaborating with the Centre for Brain Research at IISc on a review paper to further advance genetic literacy. These efforts aim to create a more informed society and improve communication with healthcare professionals.

DRGD: Digital Portal

The "Demystifying Rare Genetic Diseases" (DRGD) portal serves as a comprehensive resource for patients, clinicians, and researchers. It provides access to curated information on rare genetic diseases, fostering a deeper understanding and supporting timely diagnosis and treatment through podcasts, clinical posters, storyboards, blogs, etc.

Policy Stewardship



One Health Index Framework for India

The One Health approach integrates human, animal, and environmental health to enhance global health security, with the One Health Index (OHI) serving as a key tool. The OHI simplifies complex health data, providing a standardized metric for policymakers, healthcare providers, and the public to evaluate health indicators at regional, state, and national levels. By offering a unified score on a scale from 0 to 100, the OHI enables stakeholders to understand and monitor health metrics effectively. In the Indian context, the OHI calculator will be crucial for policy recommendations, guiding targeted initiatives to improve health outcomes. Additionally, establishing a data federation model and open science communication platform will facilitate data access and sharing among stakeholders, fostering collaboration among government agencies, researchers, and policymakers to enhance health security.

One Health Calculator: Digital Portal

The future strategy for the One Health Index (OHI) focuses on developing a digital platform that will serve as a comprehensive resource for various stakeholders, including clinicians, policymakers, researchers, and the public. This platform will allow users to input data on specific indicators, enabling real-time calculation of the OHI score and highlighting data gaps. By digitizing the OHI, it will improve the ability to assess and track One Health indicators with greater accessibility and real-time updates. This tool will provide a strong foundation for evidence-based policy formulation and health system improvements aligned with One Health principles.

One health index calculation

(in collaboration with Indian Institute of Public Health, Gandhinagar)

This project aims to create a One Health Index (OHI) for India to assess the interconnected health of humans, animals, and the environment, addressing challenges like zoonotic diseases and antimicrobial resistance and

was taken up as a dissertation study by a student from the Indian Institute of Public Health, Surekha. S. By adapting the Global One Health Index (GOHI) framework, the project provides a context-specific evaluation tool that enables monitoring and benchmarking of One Health status, guiding policy decisions for enhanced collaboration among health sectors. Utilizing the primary data collected from experts and the Fuzzy Analytic Hierarchy Process (FAHP), the OHI will identify strengths and gaps in data collection, inform policymakers on priority intervention areas and support comprehensive data efforts for effective One Health strategies in India.

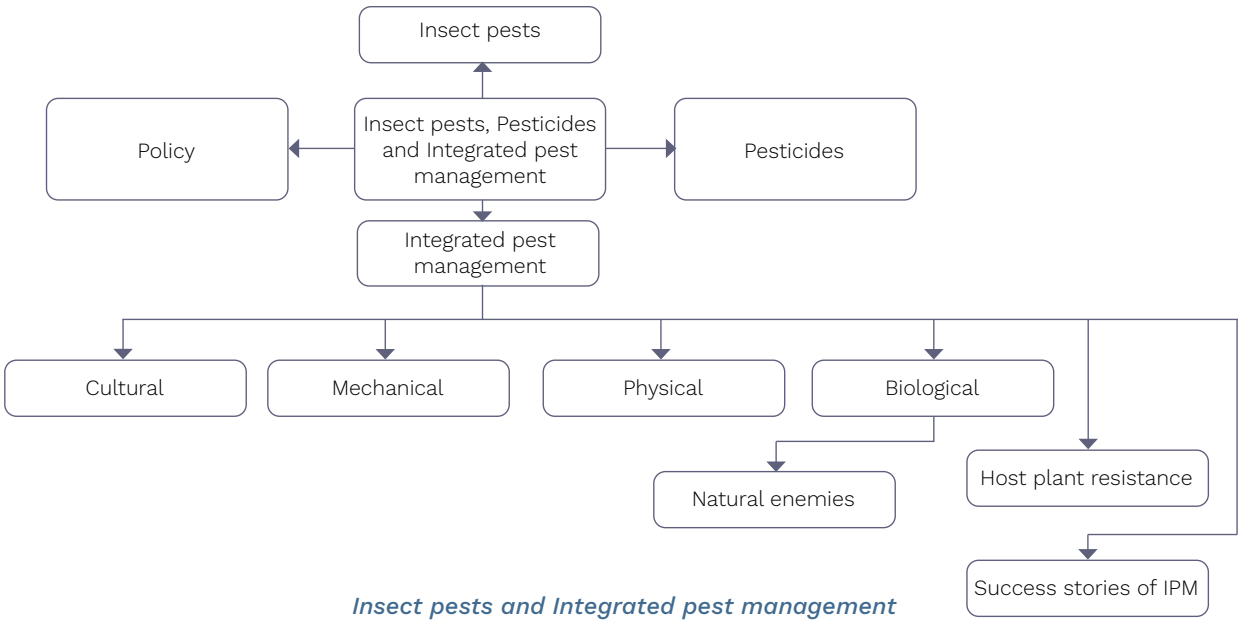
Evaluating KAP of Medical Officers in Bengaluru: AMR and ASP

(in collaboration with Indian Institute of Public Health, Gandhinagar)

Antimicrobial resistance (AMR) poses a significant global public health threat, exacerbated by excessive antibiotic use in human, animal, and agricultural sectors. This study evaluates the knowledge, attitudes, and practices (KAP) of 73 primary health center medical officers in Bengaluru, India, regarding AMR and Antimicrobial Stewardship Programs (ASP) and was done as a part of dissertation study by a student from the Indian Institute of Public Health, Akshay Das K. The research identifies critical knowledge gaps that lead to inappropriate antibiotic prescribing, emphasizing the need for targeted interventions like Continuing Medical Education (CME) and specialized training. Additionally, the study highlights the importance of policy stewardship in implementing evidence-based strategies for responsible antibiotic use, ultimately informing national AMR initiatives and promoting a collaborative, cross-sector approach to effectively combat AMR.

Insect pests and Integrated pest management

Insect pests pose a significant challenge to agriculture, causing substantial losses. This project explores the impact of insect pests on Indian agriculture, with a focus on the role of climate change in altering pest behaviour. To address these issues, policies must prioritize in-depth studies to identify vulnerable regions and crops, enabling the development of adaptive solutions to minimize the overuse of chemical pesticides. A comprehensive assessment framework is needed to evaluate pesticide misuse, considering factors such as frequency, dosage, and safety compliance. Promoting Integrated Pest Management (IPM) as a policy priority is crucial. IPM encourages biological control, resistant crop varieties, and reduced reliance on chemicals, aligning with sustainable agricultural practices and protecting both productivity and environmental health.



Insect pests and Integrated pest management

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CCMB
IBAB
Institute of Bioinformatics and Applied Biotechnology
JSS
JSS ACADEMY OF HIGHER EDUCATION & RESEARCH
(DEEMED TO BE UNIVERSITY)
MYSURU
BLiSC
Bangalore Life Science Cluster
UC San Diego
Dystrophy Annihilation Research Trust
JASLOK HOSPITAL
A lifetime of care
Integri Biotech
ORDI
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ASHOKA UNIVERSITY
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Empowering through awareness
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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 translational 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 the context of pandemic preparedness. Comprehensive surveillance calls for monitoring the prevalence of pathogens, and is the first step in disease control and elimination. Enabling inclusive networks that encompass One Health approaches will be the way ahead to monitor for infectious pathogens and prevent future pandemics. Global problems such as tackling antimicrobial resistance (AMR) or addressing the gaps in rare genetic disease research similarly require comprehensive and collaborative approaches.

TIGS is a leading partner in multiple such initiatives, both at the state and national level. We have been working towards bringing together stakeholders trying to address these difficult problems onto a common platform via annual summits that involve researchers from across the country as well as clinicians, patients, industry partners, regulatory and government bodies. We also engage in policy advocacy by interacting with relevant regulatory arms of the Government of India, and contribute to evidence-based policy recommendations within the existing frameworks.

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

The One Health Bengaluru City Consortium (OHBC), supported by Bengaluru Science and Technology Cluster https://www.bestkc.in/funded-projects/), aims to enhance public welfare through cross-sector collaboration. Funded by the Principal Scientific Adviser (PSA) to the Government of India, the consortium addresses interconnected issues like biodiversity loss, climate change, food insecurity, non-communicable diseases, and other health challenges, based on input from over 50 organizations. Formally launched on 3rd March 2023, the consortium's approach spans multiple disciplines, leading to the development of an integrated health system with comprehensive, real-time databases and analytical tools for predicting risks to human and animal health. It also emphasizes transparent stakeholder engagement to encourage citizen participation, innovation, and entrepreneurship for local solutions and sustainability.

The Bruhat Bengaluru Mahanagara Palike (BBMP) consented on 23.12.2021 to collaborate with BeST and stakeholders from various city-based institutions to work on One Health, disease ecology, environmental surveillance, disease risk, public health, infectious disease, antimicrobial resistance tracking, innovation, public engagement, education, and outreach. This consortium of experts will generate scientific evidence and knowledge, as well as co-create intervention strategies and adaptive risk management for zoonotic outbreaks in Bengaluru City. As the responsible governance organization and primary implementation stakeholder, BBMP will be the end user of the knowledge and data generated by the OHBC.

Approach

Our data-driven approaches, including pathogen surveillance through wastewater and vector-borne diseases, can inform policy. Coupled with One Health frameworks, engaging multi-disciplinary scientists, NGOs, municipal bodies, and citizens in surveillance will create a community prepared for disease outbreaks, identifying gaps and equipped with sustainable solutions. Our One Health model consists of four components:

1. Infectious Disease Surveillance with citizen/ government participation in science
2. Disease Ecology with citizen awareness
3. Citizen Science for disease surveillance in urban and peri urban areas.
4. Policy planning, management, and implementation of safe wastewater reuse

Goals

The OHBC goals align with the National One Health Mission to pilot a one-health approach using evidence-based decisions to facilitate health in the city, streamline data and information linkages and access across sectors, and ensure community participation.

Short-term	Medium-term	Long-term
» Draft concept note » Ownership and Leadership to One Health by BBMP » Meeting with stakeholders » Prioritisation of key diseases » Identification of key partners in science (disease specific) and policy » Develop vision	» One Health cell with a coordinator from BBMP » Surveillance teams at zonal/ PHC levels » Integration of real-time surveillance » Involvement of local institutions	» Plan in place to predict and mitigate outbreaks of prevalent diseases » Citizen-science involvement » Social groups and political groups involvement for implementation

BBMP One Health Cell

The first Kick-off meeting on 23.11.2022 was organized and chaired by the Special Health Commissioner, BBMP, with attendees from the BeST cluster and the Animal Husbandry and Veterinary Department, CHO. The Special Health Commissioner, BBMP, approved the establishment of the BBMP One Health Cell.

On 29th March 2024, BBMP is implemented the One Health approach across Bengaluru on the lines of National One Health Mission setup to integrate all health activities of different ministries under One Umbrella. BBMP has constituted One Health Cell consisting of 5 committee i.e. Clinical Health, Public Health, Animal Health, Environmental Health, and Digital Health.

Launch of BBMP One Health Cell on 20th March 2024

TIGS has integrated efforts under the OHBC. TIGS is working on infectious diseases, vector ecology, and environmental surveillance. By collaborating with other institutions and pooling expertise and resources, we contribute to the development of new methods and innovations beneficial to our region and nation.

We are developing a consistent sampling strategy and robust laboratory testing protocols to enhance sensitivity. These will be part of the national wastewater surveillance programme and the Swachh Bharat Abhiyan (Clean India Mission), aiming to influence water and sanitation policy creation and refinement.

Currently, the mosquito control strategy mainly focuses on removing larval habitats and spraying anti-larval agents. However, entomological surveillance is often passive and biased toward areas with disease outbreaks. Cities, as heat islands, have diverse landscapes with varying temperature regimes, vegetation, and infrastructure. These differences can create microclimates that affect mosquito abundance and disease transmission. One limitation for dengue control has been the lack of structured surveillance, diagnostics, awareness, and collective effort, leading to a high number of cases. Bengaluru (Karnataka, India) is a densely populated metropolis with a gradient of urbanization, poor sanitation, improper waste management, and inadequate water supply, particularly in unauthorized settlements. This leads to water storage practices that support Aedes mosquito breeding. Studying the health effects of these changes in Bengaluru is important and can provide lessons for cities nationally and worldwide.

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]

APSI - 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.

Screenshot of the APSI website

APSI all cluster meet held at BLiSC campus. 23-24 May 2024

RF-APSI Outreach at BLiSC, 2024-2025

As the APSI's public health surveillance work covering environmental surveillance, clinical surveillance, AMR and development of low-cost PCR based pathogen and AMR detection kits are near completion, BLISC (TIGS-NCBS) have organized several capacity building/training and educational workshops as part of outreach.

» The first set of events started off on June 30, in collaboration with Bangalore Baptist hospital for practicing clinicians for AMR surveillance and clinical approaches, with talks by TIGS team Dr. Rakesh Mishra, Director, Dr. Farah Ishtiaq, Principal Scientist, Dr. Shivranjani Moharir, Senior Scientist and Dr. Mansi Malik, Scientist, medical doctors, WHO-India and GoK authorities. The workshop was co-organized and led by Dr. Carol George, Head of Community Health, Palliative care and Research Division, Bangalore Baptist Hospital and Dr. Sufia Sadaf, Program Manager, Outreach, RF-APSI, NCBS

» This was followed by 4 events (July 24, July 29, August 12 and Sept 17) for Dengue warriors: education and awareness series, covering dengue bionomics, vector surveillance and use of AI for data integration, including live-hands on exhibits by TIGS insectary team and other ground partners (ARTPARK, Initiative for Climate action, BeST cluster, BBMP, ECHO network, MSCH, VITM, Ministry of Culture and Ministry of Education), with a final felicitation for social media campaign participants by BBMP on Sept 17. The target audience was school students and teachers.

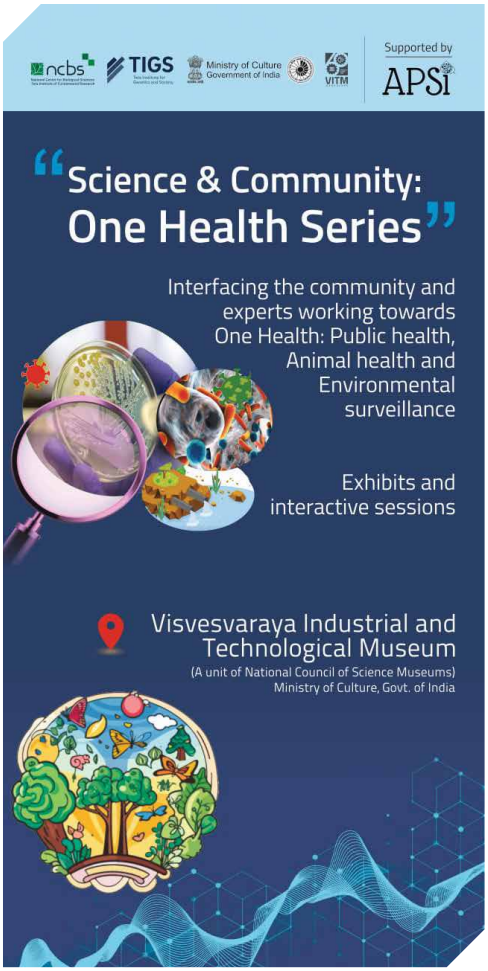
» Further outreach activities were conducted during NCBS's open day Sept 13, with APSI and TIGS insectary team covering wastewater surveillance, clinical surveillance for pathogens and AMR, vector-borne diseases and novel molecular surveillance methods for 300 students and 200 community members.

» Sept 16-18, 2024: The first hands-on training for capacity building was organized for 15 selected candidates (microbiologists, health technicians and researchers) for capacity building on environmental surveillance and molecular diagnostic approaches for clinical surveillance of pathogens, vector borne pathogens and AMR traits. It was a rigorous 3-days training workshop, with plenty of hands-on experiments and expert talks by the mentors, reinforcing the learning through engaging games, led and organized by Dr. Sufia Sadaf, Dr. Shivranjani Moharir and Dr. Mansi Malik.

» Sept 30, Oct 14: 2 sets of AMR education and awareness, stewardship advocacy workshops were conducted for Bangalore medical college students and Research Institute, Sept 30 and Saptagiri Institute of Medical Science and Research Institute, Oct 14 respectively, led by APSI's outreach partner, Superheroes against superbugs (SaS), with NCBS-TIGS and in collaboration with the Department of Medical Education, Govt of Karnataka. Prof. LS Shashidhara, Director, NCBS, joined the Sept 30 workshop, and Dr, Mansi Malik joined the Oct 14 workshop

» Nov 6 and Nov 11, 2024: AMR workshop led by SaS team for medical colleges, with NCBS-TIGS and in collaboration with the Department of Medical Education, Govt of Karnataka at Sri Siddhartha Medical College and Hospital, Tumkur, Nov 6 and Sri Atal Bihari Vajpayee Medical College and Research Institute, Nov 11 and Mysore Medical College and Research Institute on Nov 27th. mentored by Dr. Shivranjani Moharir, Dr. Mansi Malik, Dr. Arati Ramesh and Dr. Rakesh Mishra, respectively.

» Nov 12, 2024-Feb 2025: The program 'Science and Community, One Health Series' was pre-launched, to showcase RF-APSI' outreach and public health strategies and relevance, with Visvesvaraya Industrial and Technological Museum, NCBS and TIGS. It consisted of expert talk by Dr. Shivranjani Moharir, community interaction and curated hands-on exhibits, films, engaging games developed by the teams. The main launch is scheduled for Dec 20 at VITM for a full-scale exhibit and public outreach. This will be followed by bi-weekly expert talks and curated hands-on activities, catering to school students, teachers, college students and various organizations and public, until Feb 2025. This program series is conceptualized and co-led by Dr. Sufia Sadaf and Ms. Jyoti Mehra, Curator, VITM, with expert talks and exhibits by several organizations including TIGS.



» Dec 10, 2024: Roundtable stakeholder meeting, "Developing Blueprint for Strengthening Surveillance-Alert-Response System" for govt public health authorities, leading scientists and directors, co-organized by ACESS health, NCBS, TIGS and RF-APSI.

Rare Genetic Diseases Research Summit (REDRESS)

28–29 November 2024

We are thrilled to announce the successful completion of the 3rd edition of the Rare Genetic Diseases Research Summit (REDRESS 2024), organized by TIGS and Organization for Rare Diseases India along with the Indian Council of Medical Research (ICMR) as the knowledge partner.

This one-of-a-kind 2-day transformative event brought together leading scientists, clinicians, government agencies, patient advocacy groups, and industry experts to brainstorm and drive advancements in rare genetic disease research in the country.

REDRESS 2024 had a participation of over 180+ individuals from various walks of life with an intent to learn about the advancements and encourage cross talk between stakeholders of Rare Genetic Diseases (RGDs) field in India. Over the past few days, REDRESS 2024 became a hub of discussions, collaborative opportunities, and impactful presentations to ensure a holistic approach to address the RGD burden of India.

The sessions included short talks on diagnostics, therapeutics and disease management for prevalent RGDs, Population & Newborn screening in Indian contexts, and on the status of clinical research on RGDs – its challenges and opportunities.

REDRESS 2024 also witnessed two important panel discussions, one on the Status of orphan drug development, treatment protocols and clinical trials for Rare Diseases in India and the other on Industry perspective on RGD diagnostics and therapeutics in India.

The sessions were led by 42 expert speakers and panelists who shared their insights. Several participants also showcased their contribution to the RGD field via vibrant poster sessions. A total of 53 posters were presented during the 2-day summit.

A heartfelt thank you to our speakers, panelists, poster presenters, patient advocacy groups, attendees and all others for their invaluable contributions and dedication to the RGD field in India. Together, we are making strides in coming up with meaningful solutions for the rare disease community.

Group photo of participants from the 3rd REDRESS 2024

Few snippets from the poster sessions at REDRESS 2024

Glimpses from the sessions of REDRESS 2024

AMR Research Conference

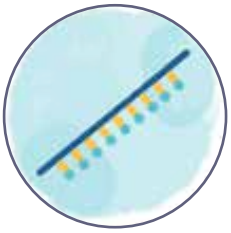
22–23 August 2024

The Antimicrobial Resistance (AMR) Research Conference 2024, organized by the Tata Institute for Genetics and Society (TIGS) in collaboration with the National Centre for Biological Sciences (NCBS) and the Alliance for Pathogen Surveillance in India, brought together experts from around the world to discuss one of the biggest threats to public health: antibiotic resistance.

Why AMR Matters

Antimicrobial resistance happens when bacteria and other microbes develop the ability to withstand the drugs designed to tackle them. This makes infections harder to treat, leading to prolonged illnesses and increased mortality. The conference focused on new treatments, diagnostic tools, and policies needed to combat AMR.

Key Highlights from the Conference



The conference opened with insights from Dr. Rakesh Mishra (TIGS) and Dr. LS Shashidhara (NCBS), emphasizing the need for new antibiotics, better diagnostic methods, and stronger governmental policies. Dr. Kamini Walia from the Indian Council for Medical Research (ICMR) provided critical data on AMR's alarming spread and ongoing efforts to contain it.

Researchers shared breakthroughs in developing new antibiotics and therapies. Dr. Colin Jamora (Shiv Nadar University) explained how natural peptides in our bodies fight bacterial infections. Balasubramanian (BugWorks) presented a newly discovered antibiotic that could save countless lives by tackling multi-drug-resistant bacteria. Dr. Garima Khare (University of Delhi) focused on treating drug-resistant tuberculosis using peptide-based therapies. Dr. Chandradhish Ghosh (Helmholtz Institute) explored how modified genetic materials could help kill bacteria more effectively. Dr. Arati Ramesh (TIGS) demonstrated how targeted gene therapies could restore the effectiveness of antibiotics that bacteria had previously resisted.

A panel discussion led by Dr. Farah Ishtiaq (TIGS) and Dr. Deepa Agashe (NCBS) covered AMR surveillance. Medical experts from hospitals and research institutions discussed how data helps doctors prescribe the right antibiotics and prevent further resistance. The panel members included Dr. Carolin E. George (Bangalore Baptist Hospital), Dr. Mary Dias (St. John's Medical College Hospital), Dr. Sachin Jadhav (HCG), Dr. Tavpritesh Sethi (Indraprastha Institute of Information Technology) and Dr. Punyasloke Bhadury (IISER Kolkata). They discussed many aspects of AMR and how the clinicians deal with it. It also touched up on how hospitals develop their own antibiogram from patient samples to be able to prescribe the right antibiotics since lab testing takes 24-48 hours.

In another session, academic experts from explored how bacteria develop resistance to drugs. Dr. Raju Mukherjee (IISER Tirupati) examined how antibiotics impact bacterial energy production, sometimes leading to resistance. Dr. Sarika Mehra explained how bacteria pump out antibiotics to survive, but combining different drug types can outsmart them. Dr. Amit Singh (IISc Bangalore) showcased a new biosensor that helps scientists understand bacterial survival strategies at a microscopic level.

Bacteriophages (viruses that infect bacteria) are emerging as an alternative to antibiotics. Researchers discussed the advances in bacteriophages in this session. Dr. Urmi Bajpai (University of Delhi) shared research on using phages to kill antibiotic-resistant bacteria. Mr. Pranav Johri (Vitalis Phage Therapy) spoke about his personal experience overcoming drug-resistant infections using phages, inspiring his company's mission to make this treatment available in India. Dr. Jason Gill (Texas A&M University) presented real-world cases where phages successfully treated drug-resistant infections. Dr. Geetha Kumar (Amrita University) discussed using natural plant extracts and phage combinations to fight AMR. Dr. Victor

Nizet (UC San Diego) introduced a futuristic approach using nanosponges—tiny particles that can trap and neutralize bacterial toxins.

Early detection of AMR can save lives. Researchers in this session presented new tools to speed up diagnosis. Dr. Tushar Shaw (MS Ramaiah University) discussed new tests that quickly identify resistant bacteria. Dr. Satish Kalme (Rapiddx Technologies) introduced a microfluidic device that can rapidly test bacteria's response to antibiotics. Dr. Chetana Baliga highlighted how special antimicrobial peptides produced by honeybees could be used to treat infections.

A panel of experts discussed India's AMR policies and challenges. Key take aways from the session included:

- The importance of a "One Health" approach, integrating human, animal, and environmental health strategies to curb resistance.
- The role of hospitals, government bodies, and industries in implementing better antibiotic usage policies.
- Dr. Krishna Reddy (ACCESS Health International) emphasized how public awareness and responsible antibiotic use can help slow down resistance.

A Platform for Future Solutions

The conference also featured poster presentations by scientists and students from across India, showcasing innovative ideas to tackle AMR. The discussions and collaborations sparked at the event are expected to lead to new research initiatives and solutions to one of the most pressing global health threats. The AMR Conference 2024 successfully brought together experts, researchers, and policymakers to discuss solutions for antibiotic resistance. The event reinforced the importance of collaboration between scientists, doctors, and government agencies to develop new treatments and strategies. With ongoing research and innovation, the fight against AMR continues, offering hope for a future where antibiotic resistance is no longer a major threat to public health.

Group photo of participants from the AMR research conference 2024

Sustainable Ambassadors Global Exchange (SAGE) Program 2024

18 July 2024

Co organized with Echo Network and Nordic Centre in India (NCI)

The second cohort of the senior and junior ambassadors of SAGE program got an opportunity to interact with the scientists and visit the facilities at TIGS to know more about our work.

Dr. Rakesh Mishra walked the students through the vision, mission and the research programs we undertake at TIGS. Dr. Mansi Malik and Dr. Shivranjani Moharir gave a brief on infectious disease surveillance and diagnostics, antimicrobial resistance and the impact it has on the public health systems.

The students got to visit the green house facility where Dr. Sresty Tavva and team where thy learned about the crop improvement program at TIGS. They also got a walk-through tour of the operations of the unique insectary facility at TIGS led by Dr. Sunita Swain and team.

Dr. Saveetha provided a comprehensive overview of the Community Engagement and Policy Stewardship (CE&PS) program at TIGS, emphasizing the critical role of science communication through diverse multimedia platforms to ensure holistic stakeholder engagement. The students experienced firsthand how the CE&PS team ideates communicating science to the public through engaging and interactive methods. From jingle-making and meme creation to storyboarding and comic creation.

The visit showcased the fun and effective ways to promote science communication. They also participated in a genetic literacy crossword-solving contest, making the experience both educational and enjoyable.

Beyond the Bite: Exploring Essentials of Mosquito Biology and Rearing

5 -7 November 2024

The 2nd edition of the insectary workshop was conducted this year. It was planned to be an engaging workshop combining expert talks with hands-on practical sessions, offering participants an in-depth understanding of mosquito biology, vector research, and the latest developments in the field. The workshop was attended by a diverse group of 20 participants from six different states across the country, engaging in interactive discussions and activities that covered key topics such as mosquito rearing, collection techniques, and dissections. These sessions were designed to enhance participants' expertise in exploring the complex world of mosquitoes.

Workshop Highlights:

- **Expert-led Sessions:** Insights into mosquito biology, vector research, and biocontrol strategies, delivered by leading experts in the field.
- **Hands-on Practical Sessions:** Participants gained practical experience in mosquito collection, surveillance, handling and rearing in the insectary, as well as dissecting key epidemiologically significant tissues.
- **Network Opportunities:** Attendees had the chance to connect with professionals and fellow researchers in entomology, fostering collaboration and knowledge exchange. We extend our sincere gratitude to all the participants, speakers, and resource persons, including Dr. R S Sharma and Dr. S L Hoti, for their significant contributions to the success of the workshop.

A few snippets from the workshop

Centre for advanced research for neuromuscular genetic disorders (CAR-NMGD)

Clinical data-based disease modelling, molecular diagnostics, and mRNA based biotherapeutic technology platform

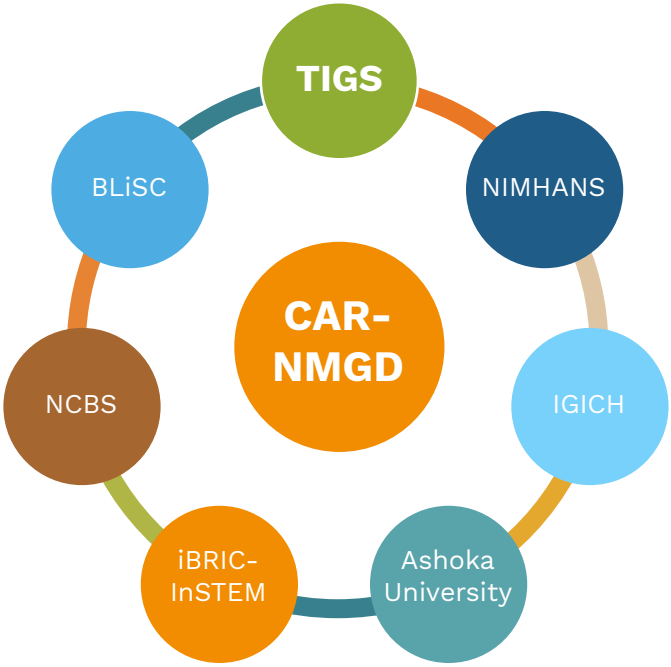
Neuromuscular genetic disorders (NMGDs) are a set of diseases affecting people of different age-groups, causing extreme disability and loss of life. For most NMGDs there is no treatment and where available, it is unaffordable. India lacks research resources, therapeutic and diagnostic platforms, cell/animal models, well-characterized patient cohorts for NMGDs. Consequently, this makes drug-discovery implausible. Centre for advanced research for neuromuscular genetic disorders (CAR-NMGD) would be an integrated center where scientists, clinicians and patient-support-group collaborate to develop research resources, preclinical/clinical models, diagnostics, and aid in NMGDs drug discovery.

For this project we intend to:

- Develop natural history-based quantitative clinical models for disease progression.
- Develop cellular and animal models for facilitating pan-India NMGD research.
- Develop diagnostic assays for NMGDs.
- Develop mRNA-based therapeutic and gene editing platform with muscle targeting non-viral delivery systems.

CAR-NMGD would be built up on strong interinstitutional collaborations of TIGS with National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Indira Gandhi Institute Of Child Health (IGICH), Bengaluru, National Centre for Biological Sciences (NCBS), Institute for Stem Cell Science and Regenerative Medicine (iBRIC-inStem), Bangalore Life Science Cluster (BLiSC), and Ashoka university, Sonipat.

The uniqueness of our collaboration lies in conglomeration of eminent clinicians; expert scientists working on disease modelling, molecular diagnostics, and mRNA therapeutic technology; world class infrastructure of NCBS and BLiSC; and patient advocacy groups, World Without GNE Myopathy (WWGM) and Organization for Rare Diseases India (ORDI) into a single centre. The centre already had preliminary data to support its objectives and with the support of ICMR, we believe we would be able to reach our goals even faster.



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 a few partnerships developed in 2024

May 2024

MoU signing with AIIMS Bhopal to work on joint collaborative projects focusing on infectious diseases, antimicrobial resistance, surveillance and control of vector-borne and zoonotic infections

July 2024

TIGS and CSIR – NEIST signed an MoU to conduct joint research on plant disease diagnostics, AMR surveillance, insect pesticides and vector borne diseases

August 2024

MoU with JNCASR, Bengaluru to work on joint research projects to develop diagnostics and therapeutics for Rare Genetic Disorders.

October 2024

MoU with IOTA diagnostics to conduct advance research in the field of newborn screening and STD diagnostics

October 2024

TIGS and ICAR – Indian Institute of Rice Research sign MoU to develop climate-resilient rice varieties, while also improving the nutritional value of rice through mutation breeding and genome editing.

December 2024

MoU with Shiv Nadar Institution of Eminence to work towards advancements in healthcare, agriculture, and education.

List of collaborators

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

All India Institute of Medical Sciences (AIIMS), Bhopal
To work on projects of environmental surveillance, clinical surveillance, AMR and blood disorders

Ashoka University, Sonipat
Co-operation in the field of rare genetic disorders

Aster Hospital Bengaluru
To work on joint projects on rare genetic disorders and infectious diseases

Aura Biotechnologies Private Limited, Chennai
To develop and commercialize technologies for health care and agriculture

Bangalore Baptist Hospital, Bengaluru
Research and academic activities in the area of infectious diseases and rare genetic disorders

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 Human Genetics, Bengaluru
Research and academic activites in the area of infectious diseases and rare genetic disorders

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

CSIR - Centre for Cellular and Molecular Biology (CCMB), Hyderabad
To run collaborative projects in crop limprovement and rare genetic disorders

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

CSIR-North-East Institute of Science and Technology (NEIST), Jorhat
To conduct joint research on plant disease diagnostics, AMR surveillance, insect pesticides and vector borne diseases

Cure SMA Foundation, Gurugram
To work on collaborative projects on SMA diagnostics

Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad
Co-operation in the field of rare genetic disorders

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

DY Patil Medical College, Pune
To work on joint projects on rare genetic disorders and infectious diseases

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

FRIGE - Institiue of Human Genetics, Ahmedabad
To conduct collaborative research activities on rare genetic disorders

Gujarat Biotechnology Research Centre, Gandhinagar
To conduct joint research in the areas of healthcare and agriculture

Huwel Lifesciences Private Limited, Hyderabad
To develop and commercialize surveillance and diagnostic kits

iBRIC - Institute for Stem Cell Science and Regenerative Medicine
Institutional Collaboration

ICAR- National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI), 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-Indian Institute of Rice Research (IIRR), Hyderabad
To develop climate-resilient rice varieties, and to improve the nutritional value of rice

ICAR-National Bureau of Agricultural Insect Resources (NBAIR)
To work on projects relating to crop improvement and pest management

ICMR - National Institute of Malaria Research (NIMR), Delhi
To develop antibody assays

ICMR-National Institute of Virology (NIV), Pune
To work on KFD drug repurposing

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

Indian Angelman Foundation
To work on joint projects of Angelman syndrome diagnostics

Indian Prader-Willi Syndrome Association, Kolkata
To conduct joint research and outreach for Prader-Willi syndrome

Institute of Bioinformatics. Bengaluru
Cooperation in the field of disease biology and genomics

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

Iota Diagnostic Private Limited, Ahmedabad
Co-develop health care technology solutions

Jaslok Hospital, Mumbai
To conduct joint research on imprinting disorders

Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru
To work on joint projects on rare genetic disorders and infectious 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

Karnataka Institute of Endocrinology Research (KIER), Bangalore
To conduct collaborative research activities on rare genetic disorders

Kasturba Medical College (KMC), Manipal
To work on joint projects on rare genetic disorders and infectious diseases

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

National Institute of Animal Biotechnology (NIAB), Hyderabad
Joint collaborative work on Infectious diseases in animals, Brucellosis, Leptospirosis, JEV, Toxoplasmosis

National Institute of Mental Health and Neurosciences, Bengaluru
To conduct joint research on neuromuscular disorders

Neuberg Anand Reference Laboratory, Bengaluru
To work on infectious diseases especially for the surveillance of dengue, chikungunya and AMR

Nordic Centre in India, New Delhi
Institutional collaboration to conduct SAGE program

Organization for Rare Diseases India, Bengaluru
Organizing joint programs, scientific events and creating awareness on rare genetic disorders

Peptris Technologies, Bengaluru
AI based drug screening for SMA

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

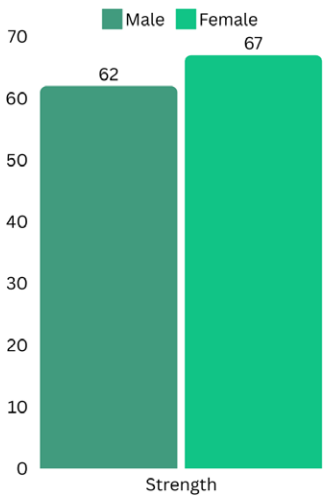
Shiv Nadar University, Delhi NCR
For academic and research collaborations

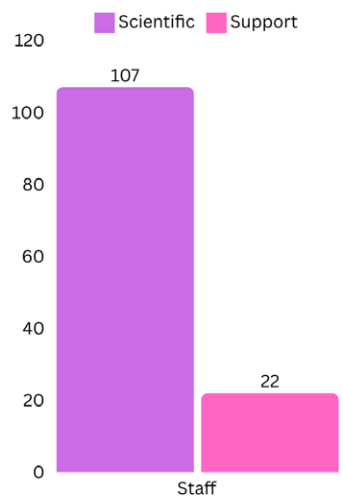
Social Alpha, Bengaluru
To work collaboratively for commercialization of TIGS R&D programs

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

University of California, San Diego
Joint collaboration for research in healthcare and crop improvement

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





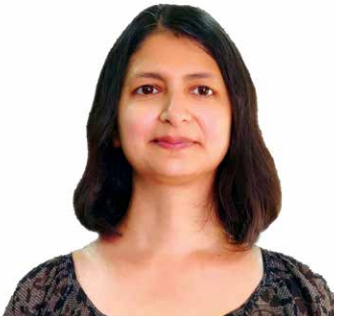
Total staff

129

Management and Administration

Director's Team

Rakesh K Mishra
Director



Surabhi Srivastava
Chief Scientific Officer

M K Sham Bharadwaj
Communications Coordinator

Hemanth Rao
Admin Manager and
Executive Secretary

Gottivedu Jyothirmai Office
Coordinator

Govardhan
Office Assistant

Program and Lab Management Team

Pankaj Gupta
Senior Program Manager

Kokilavani Varadharajan
Lab Manager

Namratha A
Senior Executive, Accounts

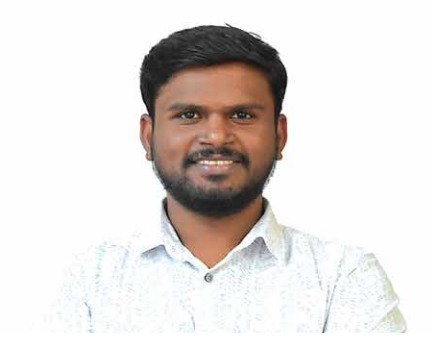
Sangeetha Ramdass
Executive, Procurement

Vinutha KS
Assistant Manager, Procurement

Vidyasagar YS
Lab Assistant

Human Resources Team

Naveen P
Senior Manager, HR



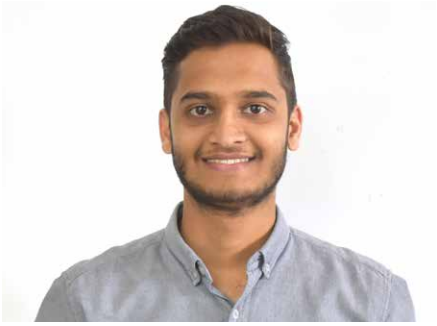
Likith Kumar V
Assistant Manager, HR

Medappa PK
Assistant Manager, IT

Finance and Accounts Team

Karthik Krishnan
Chief Financial Officer

Jyothi A
Assistant Manager, Accounts



Hardik Solanki
Assistant Manager, Accounts

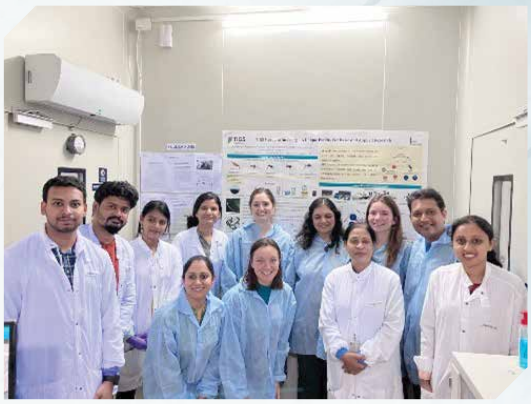
Pushpalatha V
Senior Executive, Finance

Goutham Raj B
Executive, Accounts


TIGS
Annual Report
2023
TIGS
HANDBOOK
TIGS
Annual Repo
2022
TIGS
THE 2nd RARE GENETIC DISEASE
RESEARCH SUMMIT (REDRES
TATA TRUSTS
HORIZONS
Ratan N Tata, 1937-2024
REMEMBRANCES
TATA INSTITUTE FOR
GENETICS AND SOCIETY
VISION

Knowledge Dissemination

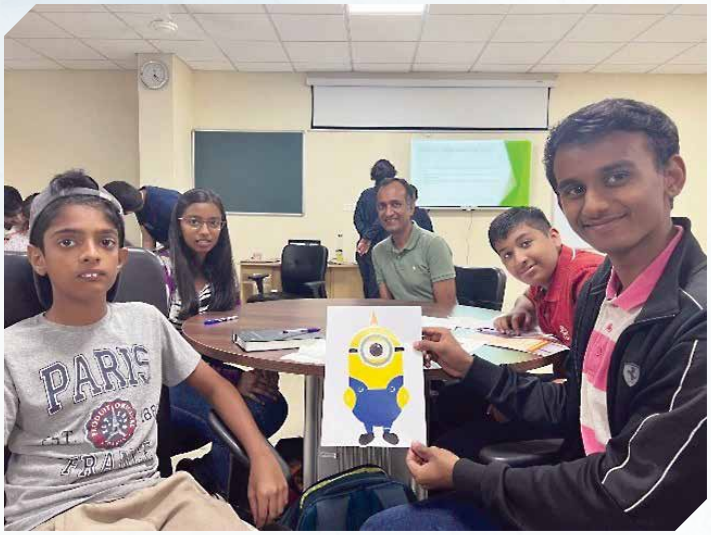
Talks, Events and Visits

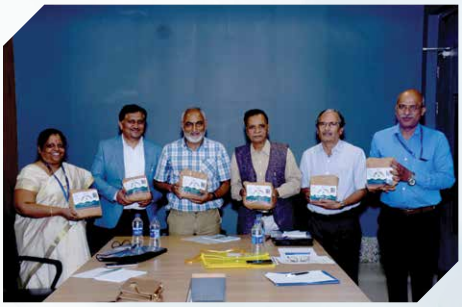

Visit by students and staff of the MIT Global Experiences Internship program. 18 January 2024

Dr. Rakesh Mishra talk on 'From cutting edge science to policy: Navigating the landscape of rare genetic diseases in India at KMC Manipal. January 20 2024.


BeST cluster organized a meeting to envision the future of #Brand Bengaluru in Digital Health. Dr. Farah Ishtiaq from TIGS took part in the meeting. 20 January 2024.



TIGS along with the Centre for Brain Research (CBR), IISc engaged with the public to talk about "What's in your DNA" through a booth and a workshop at IISER Pune for the Indian Science Festival 2024, 20 – 21 January 2024.



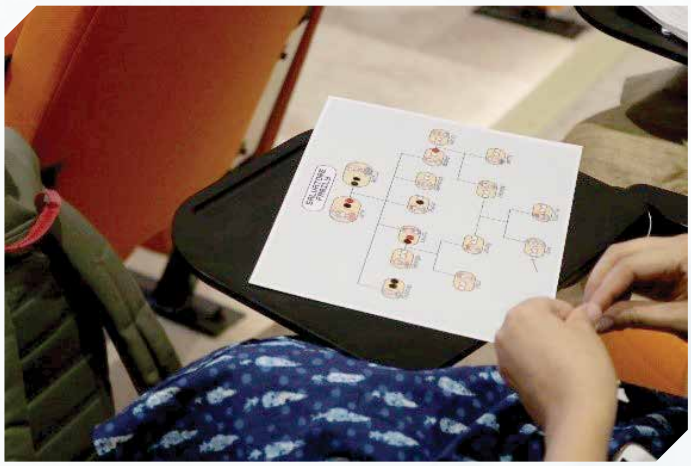
Dr. Rakesh Mishra inaugurated a session on 'Collaborative Research and Extension Activities' held at PES University, Bengaluru with the Karnataka Association for Advancement of Science (KAAS), along with others from various institutions. 2 February 2024

Celebrating 25 years of BLiSC campus

The campus felicitated Prof. CNR Rao and Dr. Indumathi Rao recognizing their contributions in establishing the BLiSC campus. As part of it, young students from various schools visited and interacted with scientists to know more on the research being done on campus. 14 February 2024.

Farah Ishtiaq's TEDx talk on Does Sewage hold the secret of the city's health? At MAHE Bengaluru. 16 February, 2024

Farah Ishtiaq presentation at the ICMR One Health webinar series titled Avian Influenza – A looming threat. 22 February 2024



TIGS along with NCBS, Bengaluru organized a session at Infosys Science Foundation, Bengaluru on the International Rare Disease Day 2024. 29 th February 2024

The Journal of Biosciences, Indian Academy of Sciences held a launch symposium for the release of a special issue on the 'Rare Genetic Diseases Landscape in India' edited by Prof. Alok Bhattacharya, Prof. Sudha Bhattacharya and Dr. Rakesh Mishra. 28 February 2024

TIGS staff participated in the Racefor7, a 7 km walk/run to spread awareness on Rare Diseases. This annual event is organised by our partner ORDI. 28 February 2024

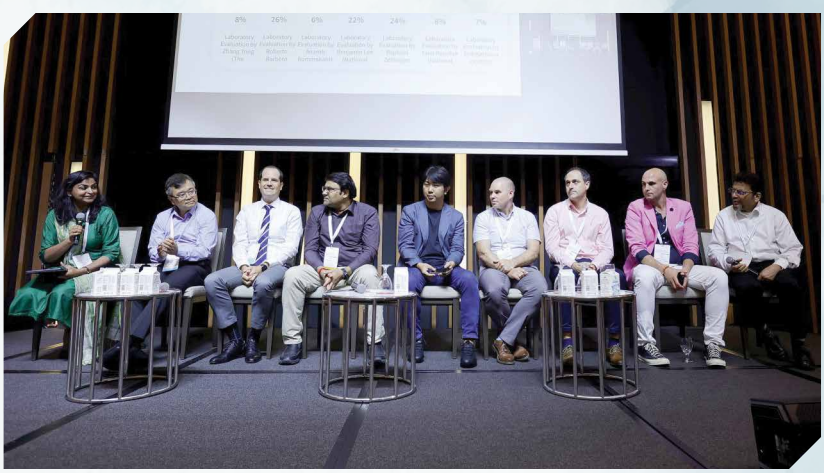
BeST Cluster facilitated an event on 'Stakeholder mapping for Bruhat Bengaluru Mahanagara Palike (BBMP)'s One Health Cell sub-committees - Environmental Health, Animal Health, Clinical Health, Public Health, and Digital Health' at the Indian Institute of Science (IISc). 20 March 2024.

Podcast by India Bioscience "SciTalks: Artful Explorations and Festival Chronicles" based on the experience conducting Genetic Literacy Initiative 'What's in your DNA' at the Indian Science Festival 2024. 19 March 2024

Launch of the first clinical poster for the ultra-rare genetic disease, GNE Myopathy in Sahakarnagara UPHC, Bengaluru. This is part of the 'Demystifying Rare Genetic Diseases' project initiated at TIGS. April 5, 2024

Dr. Rakesh Mishra part of the panel discussion on Environmental Surveillance during the APSI India workshop on Environmental Surveillance of AMR at Ashoka University, Sonipat. 10 April 2024

Establishment of the clinical biorepository at NCBS Bengaluru with generous funding support from HUDCO limited. 24 April 2024



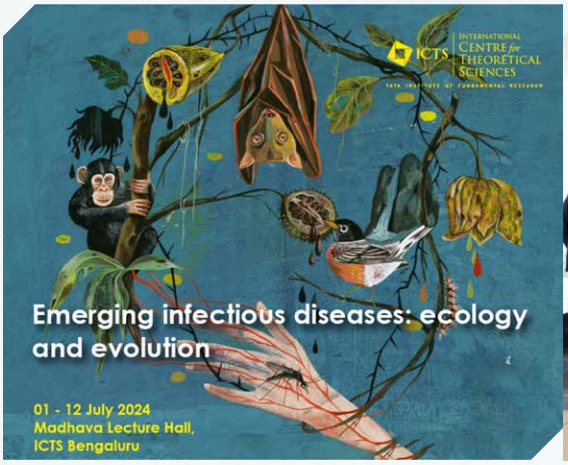
Dr. Farah Ishtiaq was a panelist at the event 'Defining research agenda on wastewater surveillance in Asia' in Asia PGI Conference, 24-28 June 2024, Singapore.

Visit by master's students of Public Health from M S Ramaiah University of Applied Sciences. 18 June 2024

TIGS scientists leading the Decoding AMR session during the AMR Surveillance strategies and clinical approaches event at Bangalore Baptist Hospital. 30 June 2024

Stall put up by TIGS Insectary team at Visvesvaraya Industrial & Technological Museum, Bengaluru as part of 'I am One Health' event, an interactive awareness program with experts on what we can do to mitigate dengue and other health related problems in the city. 5 July 2024

Talk on neural stem lineages by Dr. Sonia Sen at the NCBS RIKEN Joint meeting, NCBS Bengaluru. 11 July 2024



TIGS along with NCBS organized a 2 week workshop 'Emerging infectious diseases: ecology and evolution' at TIFR ICTS, Bengaluru. 1-12 July 2024

Dr. Mansi Malik attended a workshop 'Arboviral Surveillance in a Climate Evolving World' focused on the genomic surveillance of pathogens; dengue and zika viruses hosted by the Asia Pathogen Genomics Initiative, at Duke-NUS, Singapore. 3-9 July 2024

Dr. Shivranjani Moharir gave a talk on developing a rapid and a low-cost diagnostic assay for Spinal Muscular Atrophy at the SMArtCon 2024 conference organised by CureSMA India in Gurugram. 24 - 25 August 2024

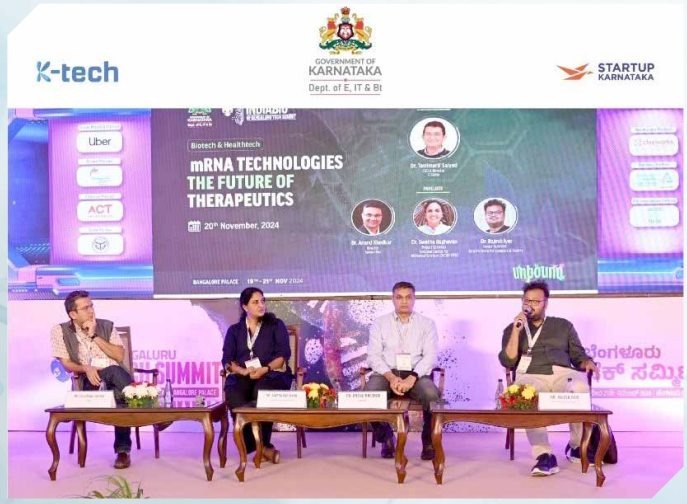
The Community Engagement and Policy Stewardship team from TIGS set up a stall with the theme 'Genetic Literacy' at the National Centre for Biological Sciences (NCBS) Open Day 2024. 13 September 2024.

TIGS insectary team showcased their inner workings at the National Centre for Biological Sciences (NCBS) open day 2024. 13 September 2024

Dr. Rakesh Mishra gave a talk at the Health Talk Series, conducted in collaboration with India Health Fund on Innovating for Public Health at the Pune Knowledge Cluster, 3 October 2024

Dr. Rakesh Mishra participated in a panel discussion at the Smart Protein Forum 2024 held at Transdisciplinary University, Bengaluru. 19 October 2024

Dr. Gayatri Iyer and team along with Aster CMI hospital conducted a multidisciplinary clinic for patients with Prader Willi Syndrome in association with India Prader Willi Syndrome Association. 18 November 2024



Dr. Rajesh Iyer participated in the session 'mRNA Technologies – The Future of Therapeutics' at the Bengaluru Tech Summit 2024. 19- 21 November 2024

TIGS scientists Dr. Farah Ishtaiq and Dr. Satyaprakash Pandey participated in the 1-day workshop Advancing Research Collaborations to tackle AMR at the Livestock, environment and human interface held at ICAR – NIVEDI, Bengaluru. 27 November 2024

TIGS scientists Dr. Rakesh Mishra, Dr. Farah Ishtiaq and Dr. Shivranjani Moharir along with APSI partners participated in the panel discussion on 'From Sewage to Strategy-Role of Wastewater Surveillance in Pathogen and AMR Surveillance' at MICROCON 2024 held at Pune. 21 – 24 November 2024

Dr. Satyaprakash Pandey and Dr. Surabhi Srivastava for a visit to the Tata Digital Nerve Centre (DiNC), Kolar and the primary health care center, Karnataka. December 2024

Dr. Farah Ishtiaq was an invited speaker on 'Evidence-based disease surveillance for vector-borne and neglected tropical diseases' in One Health and Climate Hub" in Tamil Nadu state. To kickstart this initiative, the Department of Health and Family Welfare is organized a one-day workshop on December 18, 2024

Other talks

1. Talk by Dr. Sresty Tavva on 'Crop improvement program at TIGS: Strategies to develop improved crop varieties' at the NCBS annual talks, NCBS Bengaluru on 10 January 2024.
2. Invited talk by Dr. Vasanth Thamodaran at the 48th annual meeting and international conference of the Indian Society of Human Genetics (ISHG) held in Ahmedabad. January 2024.
3. Dr. Mansi Malik gave a talk on the 'Overview of molecular surveillance of clinical samples at TIGS' at the InDx roundtable meeting held at C-CAMP Bengaluru. 16 March 2024.
4. Dr. Rakesh Mishra participated in a panel discussion on Environmental Surveillance workshop organized by Superheroes against Superbugs and APSI. New Delhi 10 April 2024.
5. Dr. Shivranjani Moharir was invited to give a talk at Ashoka University on 'Environmental Surveillance for Pathogens & Antimicrobial Resistance Landscape Using Open Drain Wastewater Samples'. New Delhi 10 April 2024.
6. Talk by Dr. Farah Ishtiaq on 'Environmental surveillance using wastewater and data interpretation' at ICAR - NIVEDI, Bengaluru. April 2024.
7. Dr. Gayatri Iyer presented a talk on 'Role of Genetic Counselling in Pediatric Rare Neurological Disorders with Case Studies' as part of the Continuing Medical Education talk for Bangabandhu Sheikh Mujib Medical University, Bangladesh, conducted by Strand Life Sciences. May 2024 (virtual).
8. Dr. Gayatri Iyer was participated as a panelist at Intersex Advocacy Roundtable webinar organized by the Intersex Children's Foundation of India. May 2024.
9. TIGS researchers Dr. Rakesh Mishra, Dr. Farah Ishtiaq, Dr. Shivranjani Moharir and Dr. Mansi Malik participated in the Decoding AMR session of the workshop 'Antimicrobial Resistance – Surveillance strategies and clinical approaches. Organised by APSI, TIGS, NCBS at Bangalore Baptist Hospital, Bengaluru. 30 June 2024.
10. Dr. Rakesh Mishra (panelist) and Dr. Gayatri Iyer (coordinator) participated in the panel 'Role of Genomics in Current day Healthcare' in the 9th Annual Board of Genetic Counseling India conference held at SAIACS CEO Centre, Bengaluru. 5-7 July 2024.
11. Dr. Mansi Malik attended a workshop 'Arboviral Surveillance in a Climate Evolving World' focused on the genomic surveillance of pathogens; dengue and zika viruses hosted by the Asia Pathogen Genomics Initiative (AsiaPGI), at The Duke-NUS centre. Singapore 2 – 10 July 2024
12. Dr. Rakesh Mishra and Dr. Shivranjani and her team participated in the SMArtCon 2024, A multistakeholder conference held by CureSMA India to share insights on indigenous research in Spinal Muscular Atrophy, latest advancements such as new disease-modifying therapies and multidisciplinary supportive care for SMA at New Delhi. 24 – 25 August.
13. Presentation by Farah Ishtiaq at the launch of Region-Specific Dengue Outbreak Prediction and Prevention Modelling program with BeST One Health Partners. May 2024.
14. Dr. Shivranjani Moharir was invited to give a talk at IISc on 'Environmental Surveillance for Pathogens & Antimicrobial Resistance Landscape' at Big Data Bio Meeting. 31 May 2024.
15. Dr. Mansi Malik and team presented a poster at the BD Bio symposium on 'Genomic surveillance of pathogens from clinical samples presenting pyrexia of unknown origin', organised at IISc Bangalore. 1 June 2024.
16. Dr. Sanjay Lamba presented a poster at the Symposium on Big Data Algorithms for Biology 2024, held at the Indian Institute of Science, Bengaluru. Wastewater based Epidemiology as an Early Warning System for SARS-CoV-2 in Hyderabad City. May 31 - June 1, 2024.
17. Dr. Harvinder Kour Khera was invited to a talk at the faculty development program, REVA University, Bengaluru. July 2024.
18. Environmental surveillance for public health action, invited talk by Dr. Farah Ishtiaq in a workshop organized by 5th Karnataka Finance Commission and Institute for Human settlements. August 2024.

19. Dr. Mansi Malik and team presented a poster at the AMR conference on 'Molecular surveillance of invasive fungal infections from clinical samples: A 'Candid'a interplay!' at NCBS 22 August 2024.

20. Dr. Prashali Bansal, member of Dr. Sonia Sen team was selected for platform talk at the Internation Congress of Entomology, Kyoto, Japan. August 2024.

21. Dr. Gayatri Iyer delivered a talk at the Continuation Medical Education talk series organized by MyDNA on 'Importance of Pharmacogenomics and how it would be beneficial in the field of Psychiatric Medicine'. August 2024 (virtual)

22. Dr. Vasanth Thamodaran was invited for a lecture at Workshop on good cell culture practices in stem cells-2024 conducted by BRIC - inStem. September 2024.

23. Dr. Mansi Malik delivered a talk on Clinical surveillance of Vector borne diseases: A molecular approach at the Central University of Tamil Nadu, Thiruvarur. 20 September 2024 (virtual).

24. Talk by Dr. Sresty Tavva on 'Developing improved crop varieties using CRISPR/Cas mediated genome editing approach' delivered at the 'Hands-on training program on Genome editing technologies in crops' organized by IIRR, Hyderabad on 14 - 23 October 2024.

25. Dr. Gayatri Iyer was selected for an early career talk 'Long read sequencing for simultaneous molecular diagnosis and pharmacogenomic profiling for imprinting disorders.' at the 17th Asian Epigenomics Meeting held at JNCASR, Bengaluru. 15 - 16 October 2024.

26. Dr. Mansi Malik gave an oral presentation on clinical surveillance, as part of the workshop 'Decoding Syndromic Infections - The Molecular Diagnostic Workshop' at AFMC, Pune. November 2024.

27. Dr. Mansi Malik gave an Invited talk on 'Simultaneous detection and surveillance of dengue serotypes, chikungunya, and co-infections from clinical samples: A molecular approach' at MICROCON 2024 at BJMC, Pune. 23 November 2024.

28. Dr. Gayatri Iyer and Ms. Sacheta Kulkarni (as genetic counselors) and Mr. Venkatesh Rajendran (as volunteer) participated in the Prader Willi Syndrome Clinic at Aster Hospital, Bengaluru conducted by the Indian Prader Willi Syndrome Association. 16 November 2024.

29. Dr. Mansi Malik presented on 'Molecular surveillance and epidemiology of Leptospirosis and Scrub typhus from clinical samples presenting acute febrile illnesses in Bengaluru, India' at the 3rd International conference on Emerging challenges in prevention and control of vector-borne diseases held at Loyola College, Chennai. She also won the best talk award at the conference. 10 December 2024 (virtual).

Invited talks@ TIGS

4 January 2024
Dr. Puran Singh Sijwali
Senior Principal Scientist,
CSIR – CCMB, Hyderabad

» *Cullin-RING E3 ubiquitin ligases (CRLs) in the human malaria parasite, Plasmodium falciparum*

16 January 2024
Dr. Shiv Grewal [TIGS and NCBS]
NIH Distinguished Investigator,
Laboratory of Biochemistry and Molecular Biology,
National Cancer Institute National Institutes of Health

» *The molecular basis for heterochromatin assembly and epigenetic inheritance*

6 February 2024
Dr. Sujatha Sunil
Group Leader,
Vector Borne Disease Group,
ICGEB, New Delhi

» *CHIK in the Spotlight: Illuminating cellular warfare with the virus*

17 April 2024
Dr. Anirban Ghosh
Principal Investigator,
Ramalingaswami Faculty Fellow,
Indian Institute of Science, Bengaluru

» *Unraveling the molecular insights of cyclic-di-AMP signaling in the context of antibiotic resistance and the development of novel inhibitors to tackle AMR in mycobacteria*

7 May 2024
Dr. Subree Subramanian
Professor,
Dept of Surgery,
University of Minnesota, USA

» *Colorectal Cancer: From Mechanisms of Immune Evasion to Novel Therapeutic Strategies*

15 May 2024
Dr. Karthik Gangavarapu
Institute Researcher,
Scripps Research Institute, San Diego

» *Tracking viral outbreaks using genomic epidemiology*

24 June 2024
Manoj Kumar
Founding trustee of TIGS
Founder & CEO of Social Alpha,
Bengaluru

» *Science and Society: Bridging the Gap*

3 July 2024
Dr. Giriraj Chandak
J C Bose Fellow,
Genomic Research on Complex diseases,
CSIR - CCMB, Hyderabad.

» *Journey of a Physician-Scientist: Bed to Bench and Back to Bed*

26 August 2024
Dr. Lipi Thukral
Principal Scientist,
CSIR – IGIB, New Delhi

» *Bespoke protein recognition properties on the membrane*

17 September 2024
Dr. Ranajit Das
Associate Professor, Division of Data Analytics,
Bioinformatics and Structural Biology,
Yenepoya (Deemed to be University),
Mangalore, Karnataka

» *Integrating Genome-Based Healthcare in Personalized Medicine*

12 November 2024
Dr. Annapoorna P K
Program Officer,
Blockchain for Impact (BFI), Bengaluru

» *Descending the Ivory Tower: From Research to Real-World Impact*

Podcasts

A Deep Dive into GNE Myopathy

March 6 2024

Imagine, as an adult, waking up one day to find out you suddenly can't walk or climb stairs normally anymore. This gait change — called 'foot-drop' — is a characteristic of GNE Myopathy, an adult-onset ultra-rare genetic disease affecting the skeletal muscle caused by a mutation in the GNE gene.

Every Rare Genetic Disease has its unique challenges and stories. In this episode, listen to Dr. Rakesh Mishra, Director of Tata Institute for Genetics and Society, have an in-depth conversation about GNE Myopathy with Prof. Alok Bhattacharya, managing trustee of World Without GNE Myopathy (WWGM), a Patient Advocacy Group. They touch upon developments in science for therapeutics to the mental health of patients with GNE Myopathy.

Prof. Bhattacharya is also a Professor and Head of the Department of Biology at Ashoka University, Sonipat, Haryana. His professional experience, coupled with personal stories, helps him give a well-rounded perspective on the disease itself, challenges in diagnosis, therapeutics, clinical trials and rare disease policies. Additionally, Dr. Mishra and Prof. Bhattacharya discuss how cutting-edge technologies like gene editing and Induced Pluripotent Stem Cells (iPSCs) can aid in understanding the disease better and accelerating #diagnostics and #therapeutics. Finally, Prof. Bhattacharya shares his thoughts on ways forward.

The episode has useful insights for all listeners — individuals affected with GNE Myopathy, researchers or policy-makers interested in Rare Genetic Diseases, or someone who is curious and wants to hear personal stories of rare genetic patients.

Scan to Listen on Spotify

Understanding HD – Science, Support and Management

October 11 2024

Imagine gradually losing control of your movements, speech, and even memory— Huntington's disease (HD) does exactly that. It's a rare, inherited neurodegenerative disorder that usually manifests in mid-adulthood, affecting the brain's ability to function.

In this episode, Dr. Meera Purushottam, a leading expert from National Institute of Mental Health and Neurosciences is in conversation with Dr. Rakesh Mishra, the director of Tata Institute for Genetics and Society, India exploring various aspects of Huntington's disease from the genetic origins of the disease to the current treatment landscape. Listen in, to learn about the challenges in diagnosis, how the disease impacts mental health and the role of early interventions.

Dr. Purushottam sheds light on the challenges of diagnosing HD in India, its prevalence among the population, and the critical role of early intervention. The conversation also delves into the emotional and psychological impact of HD on patients and their families, and how Patient Advocacy Groups (PAGs) play a vital role in supporting the HD community.

Whether you're a researcher, a clinician, someone living with Huntington's disease, or simply curious about neurodegenerative disorders, this episode is packed with knowledge, personal insights, and future-forward discussions.

Scan to Listen on Spotify

Epidermolysis Bullosa (EB)

6 December 2024

Listen into the fascinating world of genetics in a conversation between Dr. Rakesh Mishra and Dr. K Thangaraj on our latest podcast episode, where we explore the groundbreaking research on epidermolysis bullosa (EB), a rare genetic skin disorder that has significant implications for the Indian population.

With over three decades of expertise in human genome variation, Dr. Thangaraj shares his journey into the discovery of population-specific genetic mutations and how these findings can transform societal health. Through engaging discussions, we uncover the challenges and triumphs of conducting fieldwork in diverse communities, the role of whole genome sequencing in identifying novel mutations, and the critical importance of genetic counseling and public health strategies in mitigating the burden of genetic disorders.

Join us for a compelling conversation that bridges the gap between basic research and real-world applications, paving the way for a healthier future.

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Publications

1. Khera, Harvinder Kour, Ashwathi Valiyaparambil, Deepak K. Jagannath, Vysakh K. Viswanath, Naveen Kumar, Jay Prakash Shukla, Sabyasachi Pradhan, and Anirudha Lakshminarasimhan. 'Nano-differential scanning fluorimetry as a tool for the assessment of refolded antibody fragments: A case study for anti-Pfs25 single-chain antibodies.' *Biochemical Engineering Journal* 206: 109287 June 2024 DOI: https://doi.org/10.1016/j.bej.2024.109287

2. Annamalai Nataraj, Divya Mondhe, Vishwananth Srikantaiah, Farah Ishtiaq 'Metagenomic analysis reveals differential effects of sewage treatment on the microbiome and antibiotic resistome in Bengaluru, India.' Water Reuse. June 2024 DOI: https://doi.org/10.2166/wrd.2024.032

3. Madhukar MK, Singh N, Iyer VR, Sowpati DT, Tallapaka KB, Mishra RK, Moharir SC. Antimicrobial resistance landscape in a metropolitan city context using open drain wastewater-based metagenomic analysis. Environ Res. 19;252(Pt 1):118556. March 2024 DOI: 10.1016/j.envres.2024.118556

4. Bhattacharya, A., Bhattacharya, S. & Mishra, R. Current status of research in rare genetic disorders and drug discovery in India. J Biosci 49, 39 February 2024. DOI: https://doi.org/10.1007/s12038-024-00434-x

5. Aasdev, A., Sreelekshmi, R.S., Iyer, V.R. et al. Spinal muscular atrophy: Molecular mechanism of pathogenesis, diagnosis, therapeutics, and clinical trials in the Indian context. J Biosci 49, 36, February 2024. DOI: https://doi.org/10.1007/s12038-023-00412-9

6. Iyer, V.R., Praveen, P., Kaduskar, B.D. et al. mRNA biotherapeutics landscape for rare genetic disorders. J Biosci 49, 33, February 2024. DOI: https://doi.org/10.1007/s12038-023-00415-6

7. 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, January 2024, DOI: https://doi.org/10.1016/j.heliyon.2023.e23693

Grants

	Project	Agency	Period
1	Centre for Advanced Research for Neuromuscular Genetic Disorders (CAR-NMGDs): Clinical data-based disease modelling, molecular diagnostics, and mRNA-based biotherapeutic technology platform	**Indian Council of Medical Research (ICMR)**	2024 - 2029
2	Environmental Surveillance of avian influenza in and around Bengaluru to develop an early warning system (in collaboration with NCBS)	**Bill and Melinda Gates Foundation**	2024 - 2027
3	Disorders with altered genomic imprinting: aetiology, molecular diagnosis and counselling	**DST INSPIRE (Faculty Fellowship)**	2024 - 2029
4	Part of the grant 'Prospective Natural History Study of GNE Myopathy Patients from India' with NIMHANS	**Tata Endowment Fund**	2024 - 2026
5	Development of mRNA-based biotherapeutic candidate for GNE myopathy	**World Without GNE Myopathy**	2024 - 2025
6	Establishing iPSC-based disease models for lysosomal storage disorders by gene editing - A platform with an applicability for a diverse range of genetic disorders	**BIRAC**	2024 - 2026
8	Friedreich's Ataxia: Diagnosis to therapeutics	**DBT India Alliance**	2024 – 2029
9	Antimicrobial Resistance (AMR) Monitoring at the ICMR VRDL Centers through Hospital Wastewater Surveillance and Customization of Indigenous AMR Detection Assays	**ICMR**	2024 – 2025

Patents filed with the Indian Patent Office

	Title	Inventors
1	Lamp coupled CRISPR detection kit for malaria	**Harvinder Kour Khera, Rakesh Mishra**
2	Lamp coupled CRISPR kit for detection of m. Tuberculosis	**Harvinder Kour Khera, Rakesh Mishra**
3	Multiplex quantitative RT-PCR assay for detection of dengue and chikungunya viruses	**Mansi Malik**
4	Kit for simultaneous detection of hepatitis A and hepatitis E viruses	**Mansi Malik**
5	Kit for simultaneous detection of scrub typhus and leptospirosis	**Mansi Malik**
6	Duplex quantitative molecular assay for simultaneous detection of hepatitis B and hepatitis C viruses	**Mansi Malik**
7	Fuvirbap: A q RT-PCR Assay for detection of fungi, virus, bacteria, and plasmodium	**Mansi Malik**
8	Bfcas12a associated detection assays and kits	**Harvinder Kour Khera, Rakesh Mishra**
9	Multiplex real time RT-PCR assay for detection of influenza, RSV and Sars-Cov-2 viruses	**Satyaprakash Pandey, Pooja Dhanya Babu**

#TIGS in the News

Silent wave of JN.1 COVID virus in Hyderabad, Secunderabad

The new virus strain has transmitted to a majority of population in the twin cities, as per an analysis from waste water sampling by scientists

Updated - January 01, 2024 12:58 pm IST - HYDERABAD

एम्स भोपाल और टीआईजीएस बेंगलूरु के बीच समझौता ज्ञापन पर हस्ताक्षर ...

AIIMS Bhopal partners with Tata Institute for Genetics and Society for research & innovation

29 May 2024 | News

NEWS FEATURE | 17 April 2024 | Correction 24 April 2024 | Correction 23 October 2024

What toilets can reveal about COVID, cancer and other health threats

Wastewater testing grew tremendously during the pandemic. But is it ready to tackle the opioid crisis, air pollution and antibiotic resistance?

By Betsy Ladyzhets

Urban Agenda | Get your hands dirty: Sewage surveillance is critical for public health in India

By Soumya Chatterjee

DH
DECCAN HERALD

Citizen scientist programme launched to intensify dengue awareness

Columns | Indian Scenario

One Health Bengaluru: A united approach to tackle health and environmental concerns

Debraj Manna & Mohit Nikalje

Posted on Jun 28, 2024 in SCIENCE, POLICY, RESEARCH and ENTREPRENEURSHIP

One Health Bengaluru Initiative, led by the Bengaluru Science and Technology Cluster (BeST), aims to minimise the spread of infectious diseases and benefit the environment by collaborating across several organisations. This multi-sectoral approach will help policymakers make informed decisions to control the spread of diseases and tackle environmental challenges. This article explores how the One Health approach paves the way for a healthier future.

Technical Advisory Committee recommends sewage surveillance for early detection of Mpox in Karnataka

While recommending that one isolation facility should be readied for Mpox cases in Bengaluru and Mangaluru, the STAC has advised that rapid response teams (RRTs) should be trained and readied for surveillance.

Updated - August 26, 2024 12:57 pm IST - Bengaluru

Bangalore Life Science Cluster condoles death of Ratan Tata

Ratan Tata was instrumental in the establishment of the Tata Institute for Genetics and Society (TIGS)

Updated - October 10, 2024 04:29 pm IST - Bengaluru

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