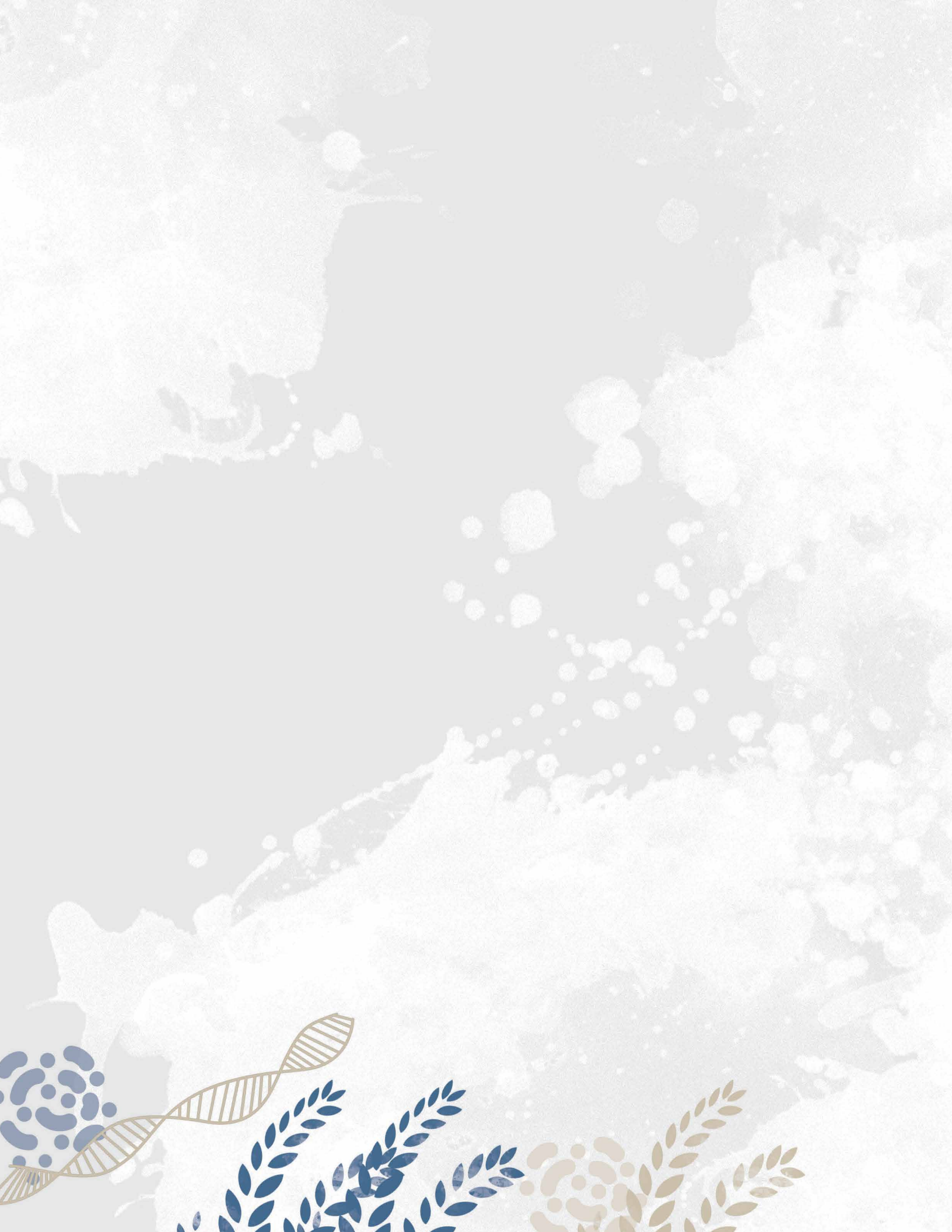
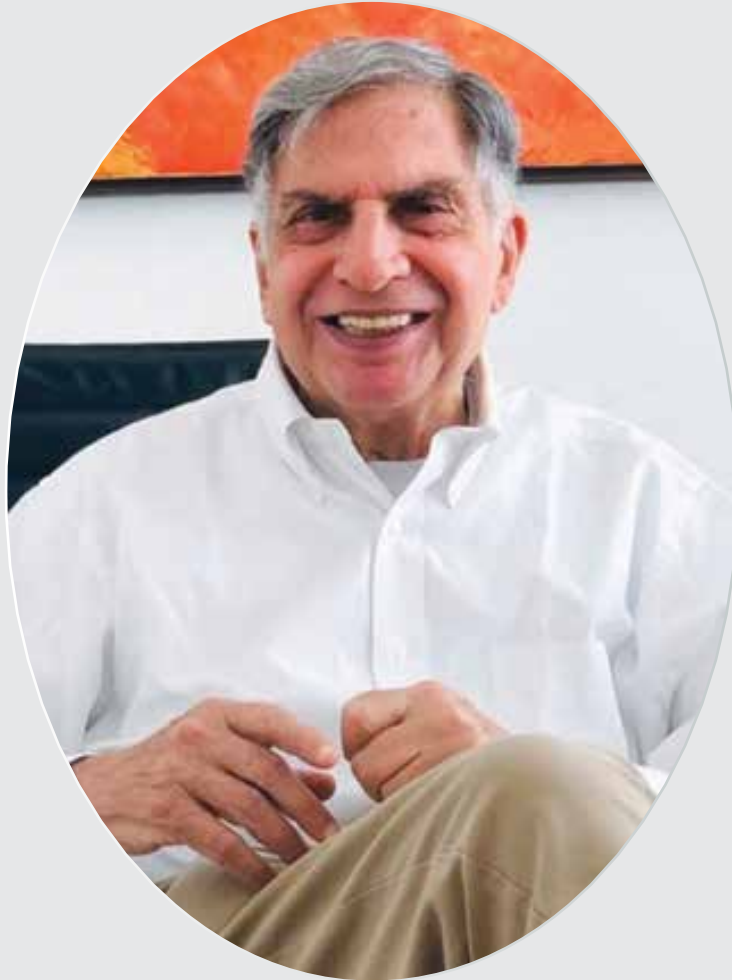


Annual Report

2022







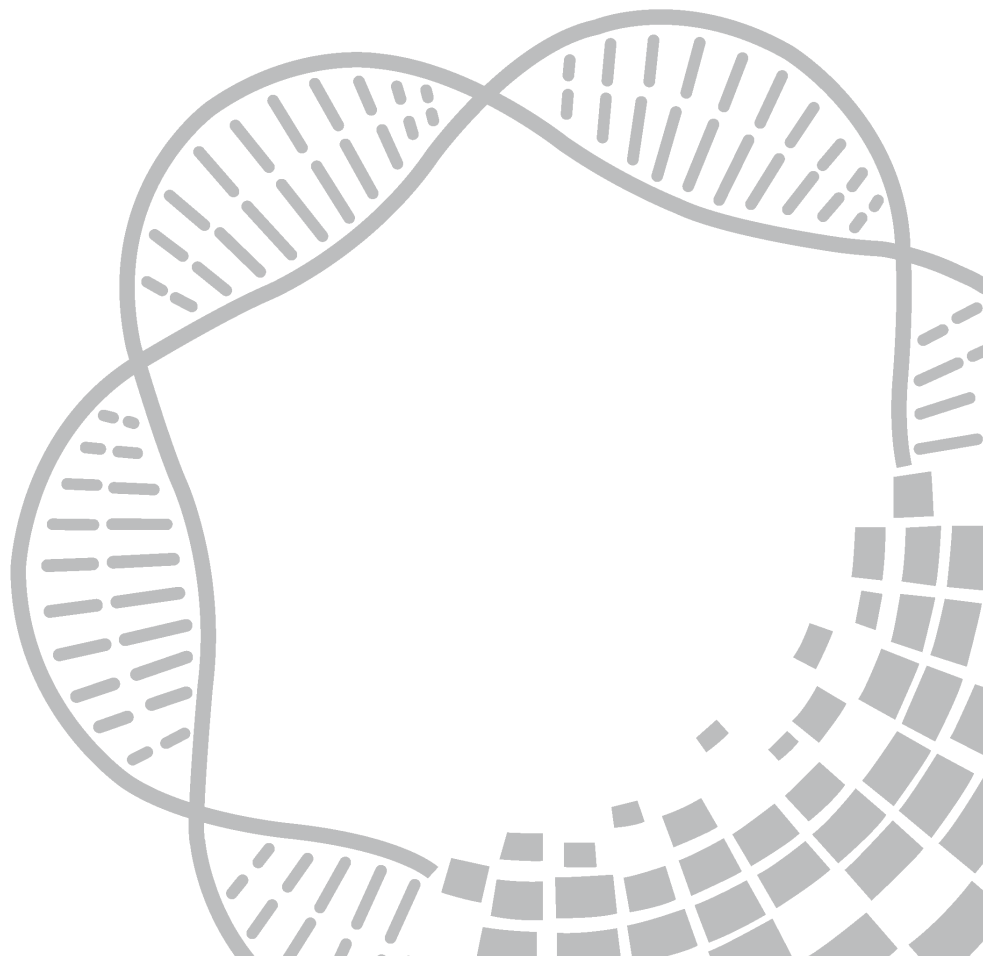
"Recent advancements in genetics and genomics have the potential to solve some of the most complex challenges in agriculture and healthcare and create significant societal value. The Tata Institute for Genetics and Society was established with this vision and I am pleased to note that the institute continues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

Ratan N Tata



Annual Report 2022

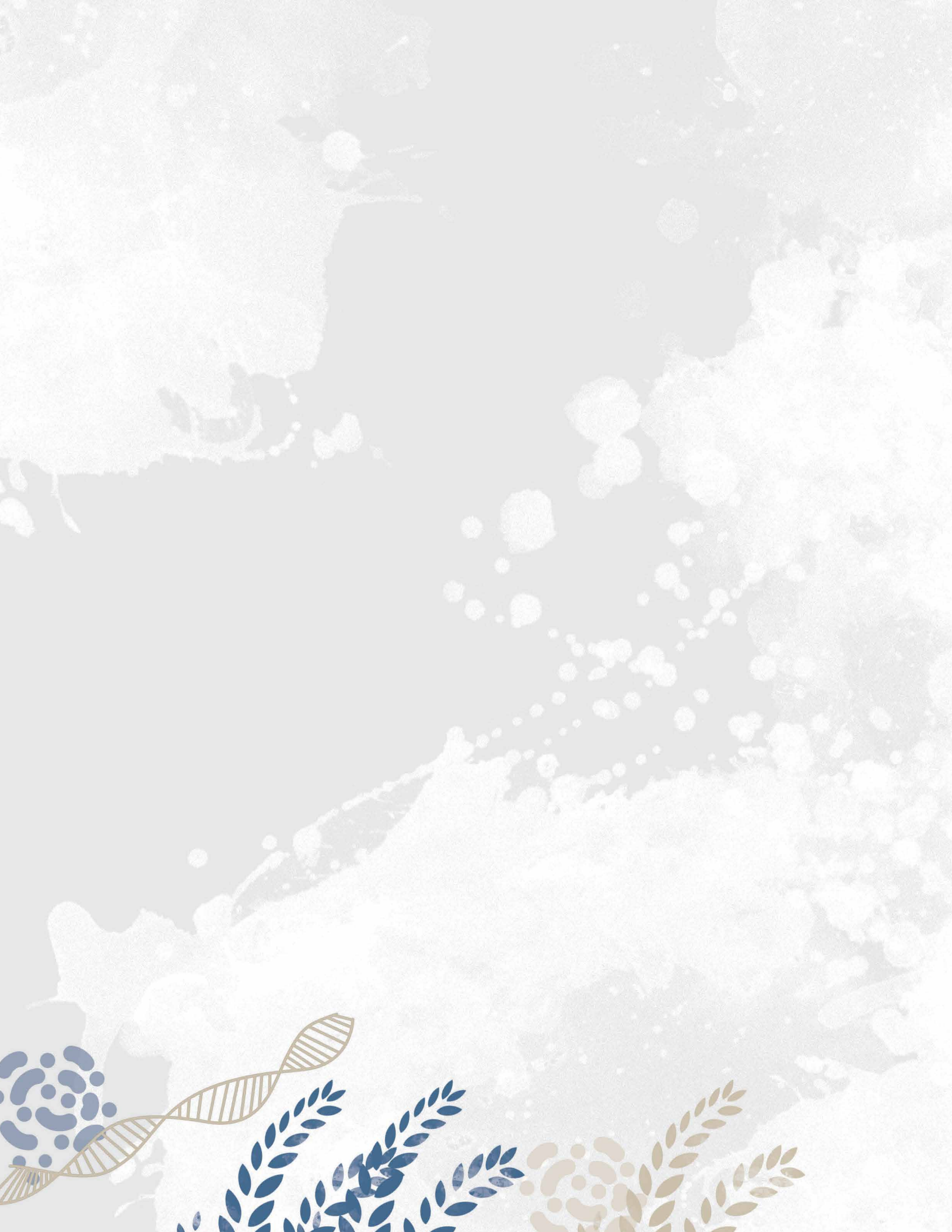
Tata Institute for
Genetics and Society



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Director's Message

The mission of TIGS is to use scientific progress and solve societal challenges. Science, in India as well as globally, is progressing at a tremendous pace towards cutting-edge technologies that have the potential to transform lives. But how can we best channelize and accelerate state-of-the-art scientific developments into cures and effective treatments for debilitating genetic diseases, mitigation strategies for infectious diseases, and the means to ensure food and nutritional security? The Tata Trusts, with its incredible legacy of being a pioneer in supporting social and economic development in India through multiple philanthropic ventures, recognised the significance of this undertaking and generously contributed to establishing TIGS as a conduit between path-breaking scientific and technological research and the societal problems in India.



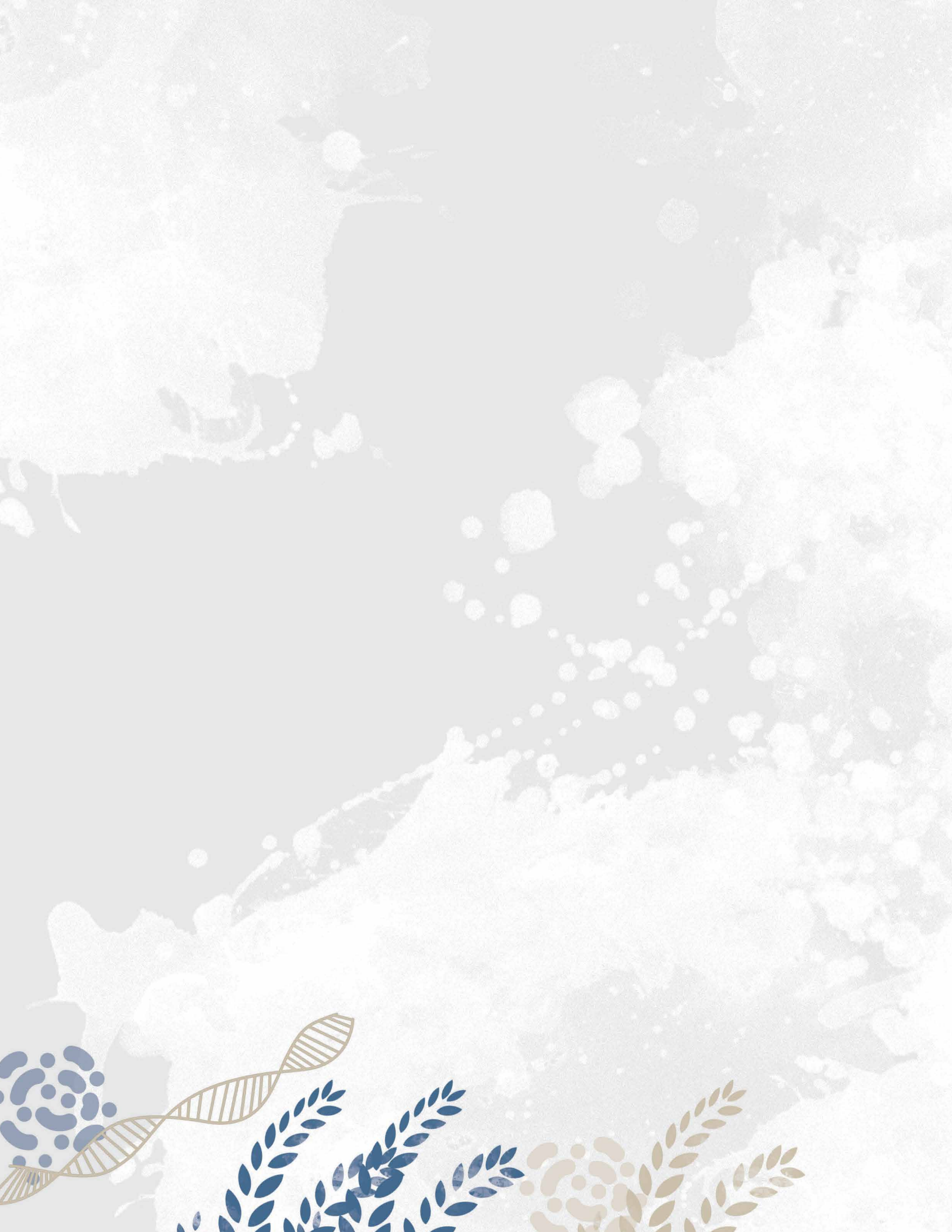
Advances in genomics have not only given us access to the genetic blueprint of all species on the planet but have also made it possible for us to access genomic details at population scale. When put in the perspective of phenotypic correlations, this will pave the way for precision and personalised medicine which is in fact not too far from becoming routine practice. Furthermore, genome editing technologies allow us to modify the genetic code with ultimate precision, which enables cell and gene therapy on the one hand and improvement of crop and livestock on the other.

TIGS is a novel innovative concept that channels philanthropic resources to nurture a much needed connect between science and societal needs. We identify specific societal problems and use the latest science and technological means to provide solutions to these problems. To achieve this in the shortest possible time and be effective, our in-house team collaborates with and involves committed scientists from a variety of organisations across the country, and beyond.

The progress we are making in fundamental and applied research needs the support of a robust policy framework that facilitates the translation of beneficial technologies into societal impact. It is important to work with policy makers and regulators to advocate for the use of safe and efficient technologies that have shown promise in improving health and nutrition. We must ensure that India is not left behind in harnessing the benefits of scientific knowledge. It is also pertinent to create awareness among the public and various stakeholders for broad acceptance of safe technologies that are key to creating a healthy ecosystem for society and environment.

I am very pleased to present this report. As can be seen here, TIGS is marching at a brisk pace to make worthwhile contributions in these directions.

Rakesh K Mishra
Director



TIGS as an Organization



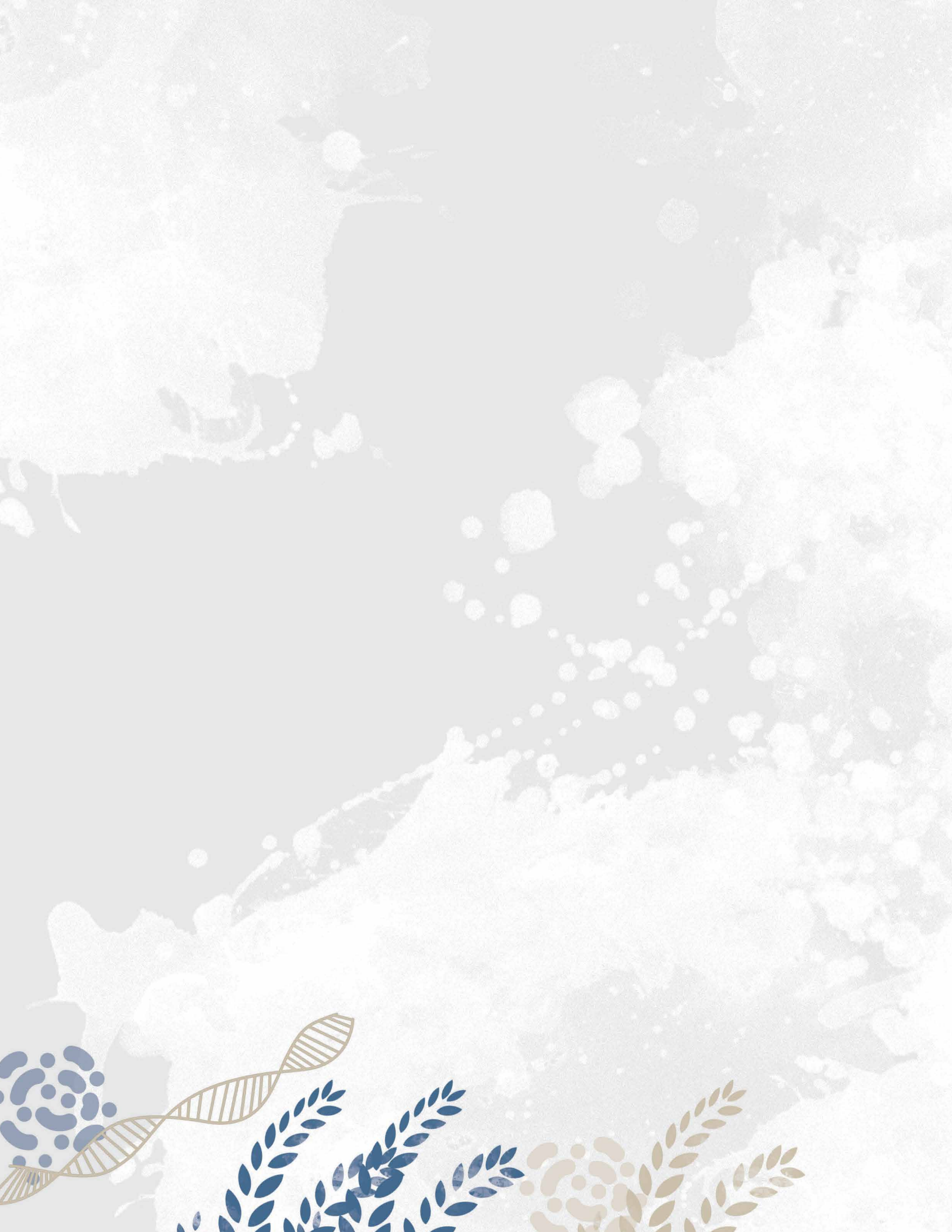
The Tata Institute for Genetics and Society has its inception in the settling and establishment of a Trust in Bangalore in 2017, with Mr Ratan N Tata as the settlor. The objective of the Trust is to support and promote science and technology research in order to find solutions to address some of India's most pressing issues, ranging from healthcare to agriculture.

The most significant challenges that impede the achievement of health equity and nutrition security for all of India's population require systematic evidence-based scientific advancements and technological solutions. TIGS is endowed with funding from the Tata Trust (Tata Education and Development Trust) to create facilities and infrastructure for research and academic activities that can provide such solutions – encompassing the areas of genetics, biological sciences, life and natural sciences, public policy and ethical uses of technology. TIGS is mandated to foster the wide dissemination of its scientific research, policies and best practices and create solutions for the well-being of society.

TIGS has been constituted under a Trust Deed, with Mr Manoj Kumar as the managing trustee. An alumnus of Harvard Business School, Manoj is the Founding Trustee of TIGS and a Senior Advisor to Tata Trusts. He continues to lead the Tata Trusts' engagements with universities and institutions globally and is committed to finding solutions to the most critical social, economic and environmental challenges.



Manoj Kumar
Managing Trustee



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 to support applications of cutting-edge science and technology in genetics and genomics and solve societal problems of the country. We are committed to contributing towards India's accelerated path in emerging as a global power through concerted efforts that use science-based solutions to prevent infectious diseases, improve access to affordable and quality diagnostics and therapeutics for rare genetic disorders, foster health equity, and achieve nutrition security through sustainable models for agriculture. Research programs at TIGS are focused on the following broad areas:

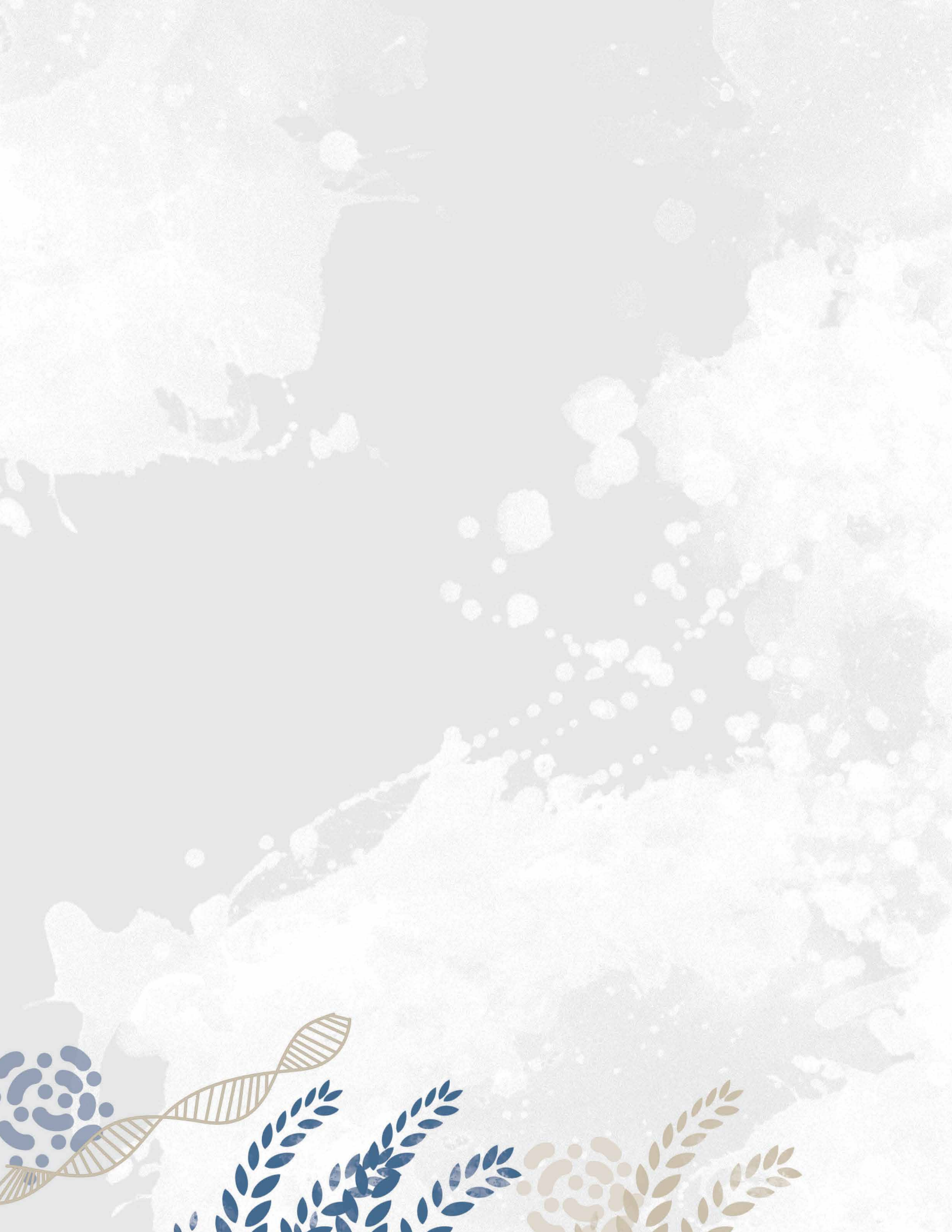
Infectious Diseases: The Infectious Diseases program studies vectors, pathogens, and their relationship to humans and the environment. The program includes development of new diagnostics, devising strategies to control vectors such as mosquitoes, employing environmental surveillance to understand the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

Rare Genetic Disorders: The Rare Genetic Disorders program focuses on genetic diseases that affect a small percentage of the population and do not have sufficient therapeutic or management options. Our efforts are directed towards developing accessible diagnostic assays that can be applicable for screening carriers of particular genetic disease traits as well as cost-effective therapeutic strategies.

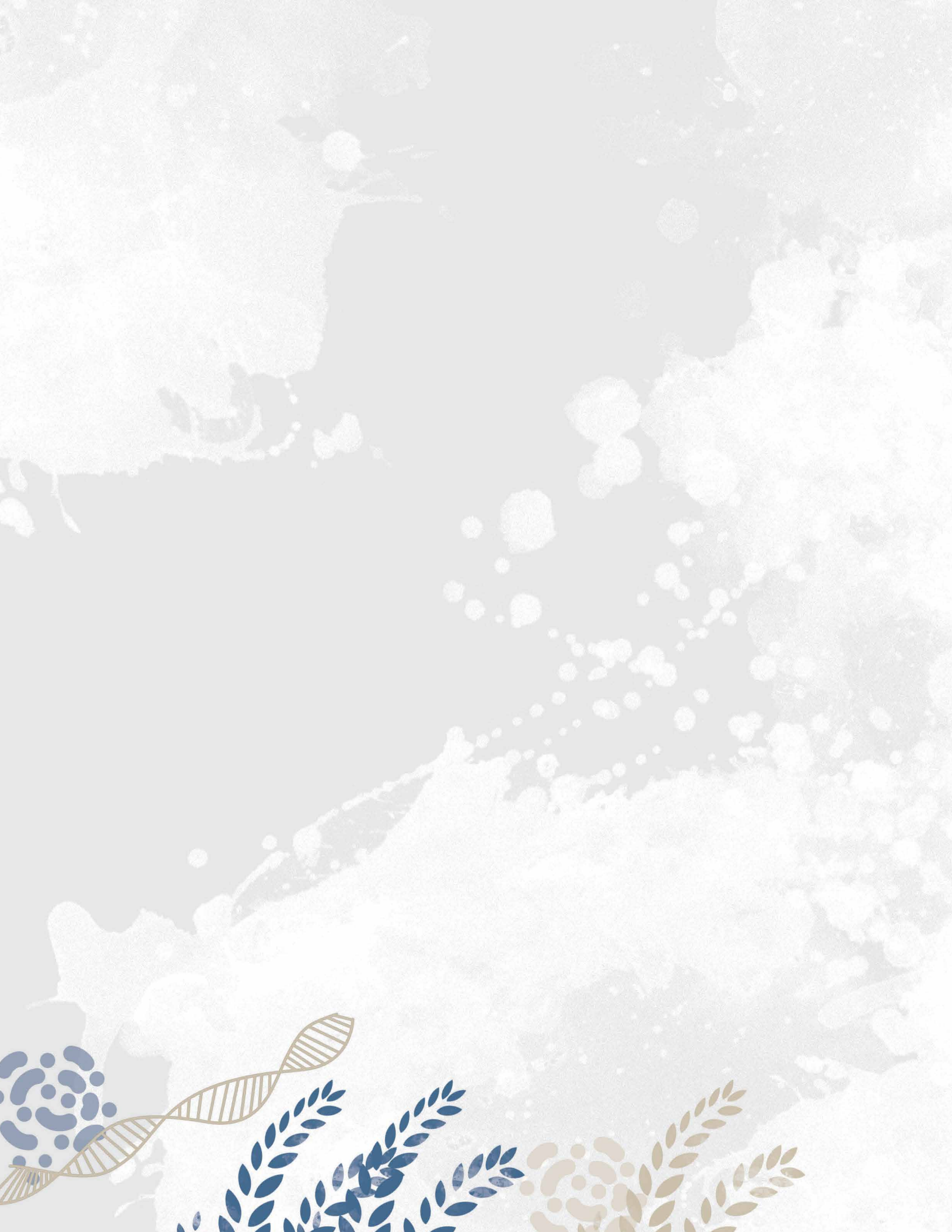
Crop Improvement: The Crop Improvement program is aimed at developing food crop varieties that are nutrient-rich, more resilient to diseases and pests, and drought tolerant. With growing challenges in food production, land availability and climate change, as well as diseases and pests, the agricultural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

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

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

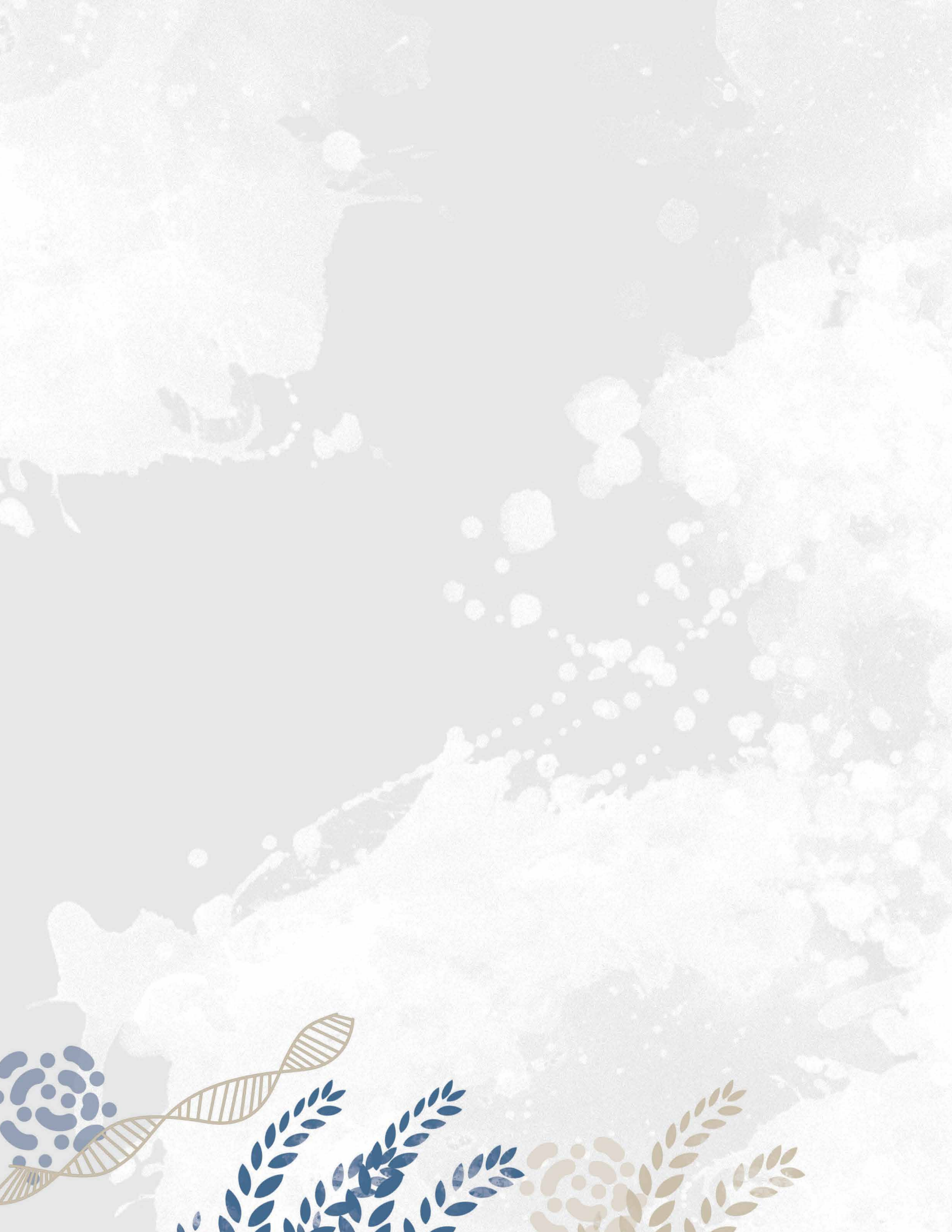


Research Programs



A large, light gray background graphic featuring a stylized DNA double helix on the left and a grid of squares on the right, both arranged in a circular, overlapping fashion.

Infectious Diseases



Infectious Diseases



Farah Ishtiaq



Sonia Sen



Shivranjani C Moharir



Sampath Kumar



Sanjay Lamba



Mansi Malik



Jay Prakash Shukla



Bhagyashree Kaduskar



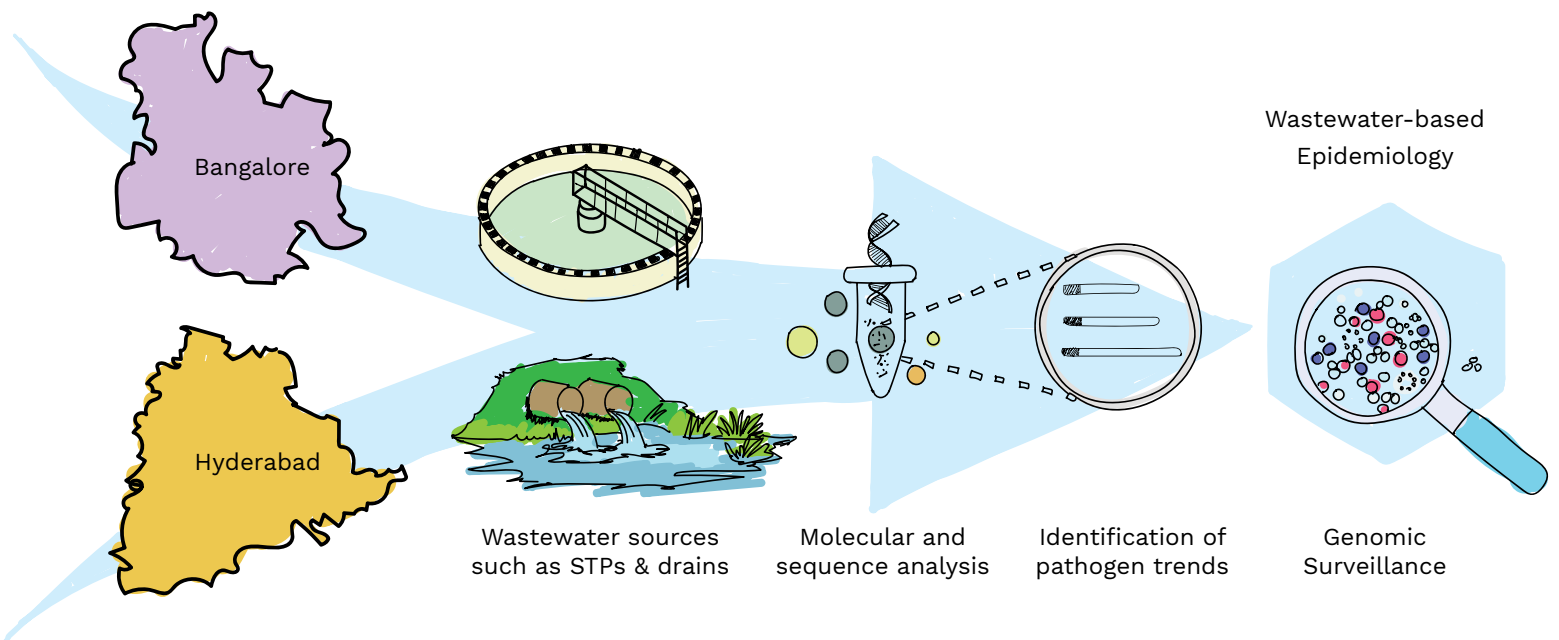
Sunita Swain

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

Environmental Surveillance & Disease Ecology

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

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



Wastewater-based epidemiology and genomic surveillance of SARS-CoV-2 in Bengaluru city

Farah Ishtiaq and Sanjay Lamba

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

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

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

Rockefeller Foundation, Tata Trusts and Indian Council of Medical Research, our WBE approach also includes genomic analysis of emerging viral variants driving the spike in viral load.

Early warning system

We investigated the relationship between SARS-CoV-2 concentrations in wastewater and COVID-19 cases reported on daily basis. Each sewershed site/sewage treatment plant (STP) has a specific catchment area i.e., wards served by the treatment plant. By normalizing the viral load for population size of that catchment, water inflow etc, we could estimate the number of infected individuals in that catchment area which was estimated to be higher than the reported cases in the city. Using Exponentially Weighted Moving Average (EWMA) algorithm (4 days and 7 days -- after adjusting for Omicron and old SARS-CoV-2 lineage incubation period), we observed two major outbreaks in January and June 2022- where the viral load estimated higher number of cases than the number of reported cases by 8-14 days in advance at the citywide level. This further confirmed that the wastewater viral load pattern mirrored the clinical data.

Genomic surveillance

Real-time genomic surveillance is the backbone for understanding and predicting the variants that drive emerging patterns of infection. We monitored viral load and simultaneously sequenced samples in real-time from multiple wastewater sources to identify variant(s) driving the increase in Covid-19 cases in the city. Not every treatment plant showed high viral loads and we were able to identify hotspots in the city; we found that it was BA.2.10 or mixture of BA.2 sub lineages that showed an increase in viral load and this further highlighted that there was no new variant behind the surge, even though BA.4 and BA.5 could be identified in miniscule amounts in a few of the STPs.

Unlike for clinical samples, we developed a specialized method designed to capture the abundance and diversity of lineages in mixed community wastewater samples. Our comparisons with clinical genomic surveillance data from Bangalore (~13000 genomes) on GISAID database showed that while the general trend in Variants of Concern (VOC) remained similar, the wastewater genomic

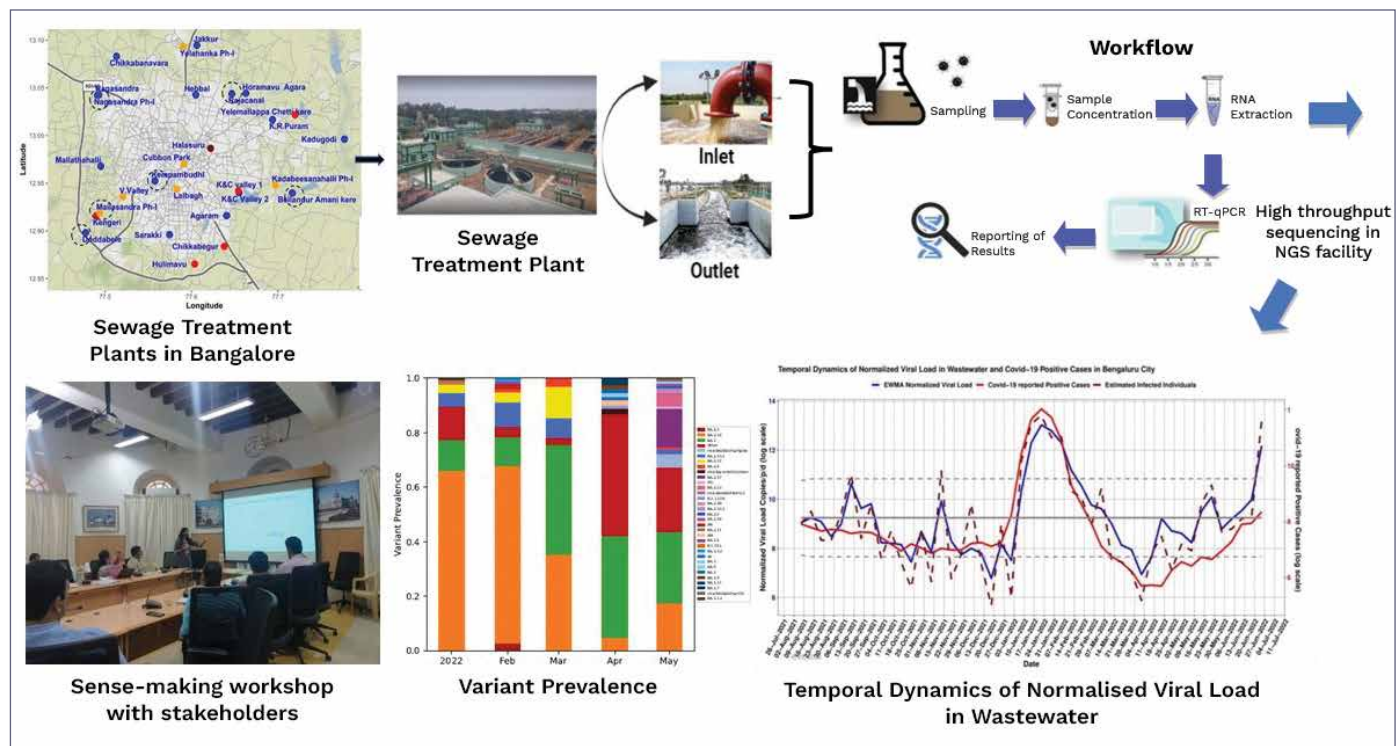
surveillance (~700 samples), recorded a huge diversity in SARS-CoV-2 lineages, dominated by the Omicron family. Specifically, two Omicron lineages, BA.2.10.1, BA.2.12 were detected in wastewater two months earlier (in January 2022) to the first detection of clinical samples in March 2022. The early emergence of a variant in the wastewater implies that a significant proportion of individuals in the community are infected with that variant and shedding the virus and should be used as an affirmative source for variant emergence in a geographical location.

From data to policy

One of the most important aspects of this study is its open access dashboard [<https://storymaps.arcgis.com/stories/c42be68c85634d19a5d92873a10bda66>] (in partnership with Precision Health Pandemic Response-Bangalore initiative), for reporting viral load and citywide positivity rates and a regular discussion with BBMP and BWSSB so that the information can be used for making policy decisions. We have been sharing weekly reports

on viral trend and genomic surveillance with BBMP and how this relates to COVID-19 data in the city.

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



Wastewater-based epidemiology as an early warning system for SARS-CoV-2 in Bengaluru city

Top: Graphical summary of WBE In Bengaluru city, and Bottom: Sense making workshop with stakeholders; Variant prevalence; and Temporal dynamics of normalized viral load in wastewater

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

Shivranjani Moharir

[In collaboration with CSIR-CCMB, Hyderabad]

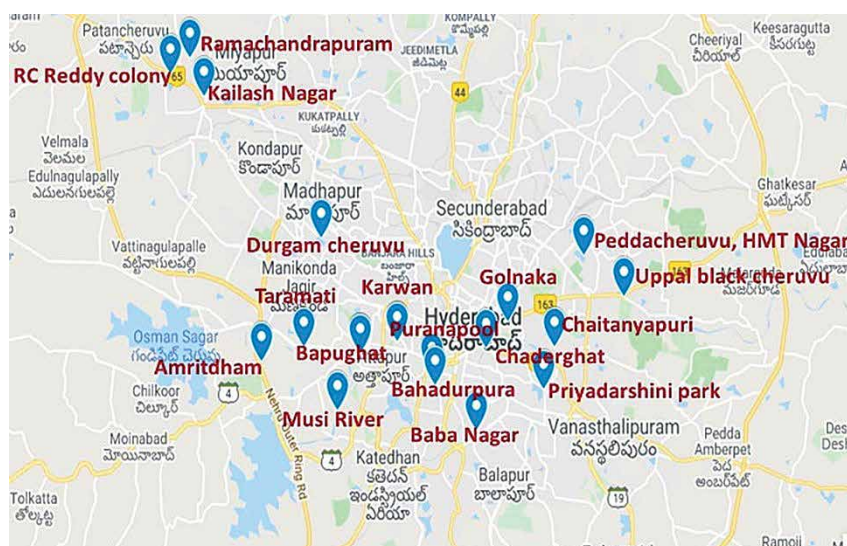
Routine monitoring of public health can help in early detection of emerging or upcoming infectious disease waves in the community and can help in preventing future epidemics. Wastewater is the warehouse of thousands of parasitic, non-parasitic, infectious, non-infectious and saprophytic microorganisms. 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

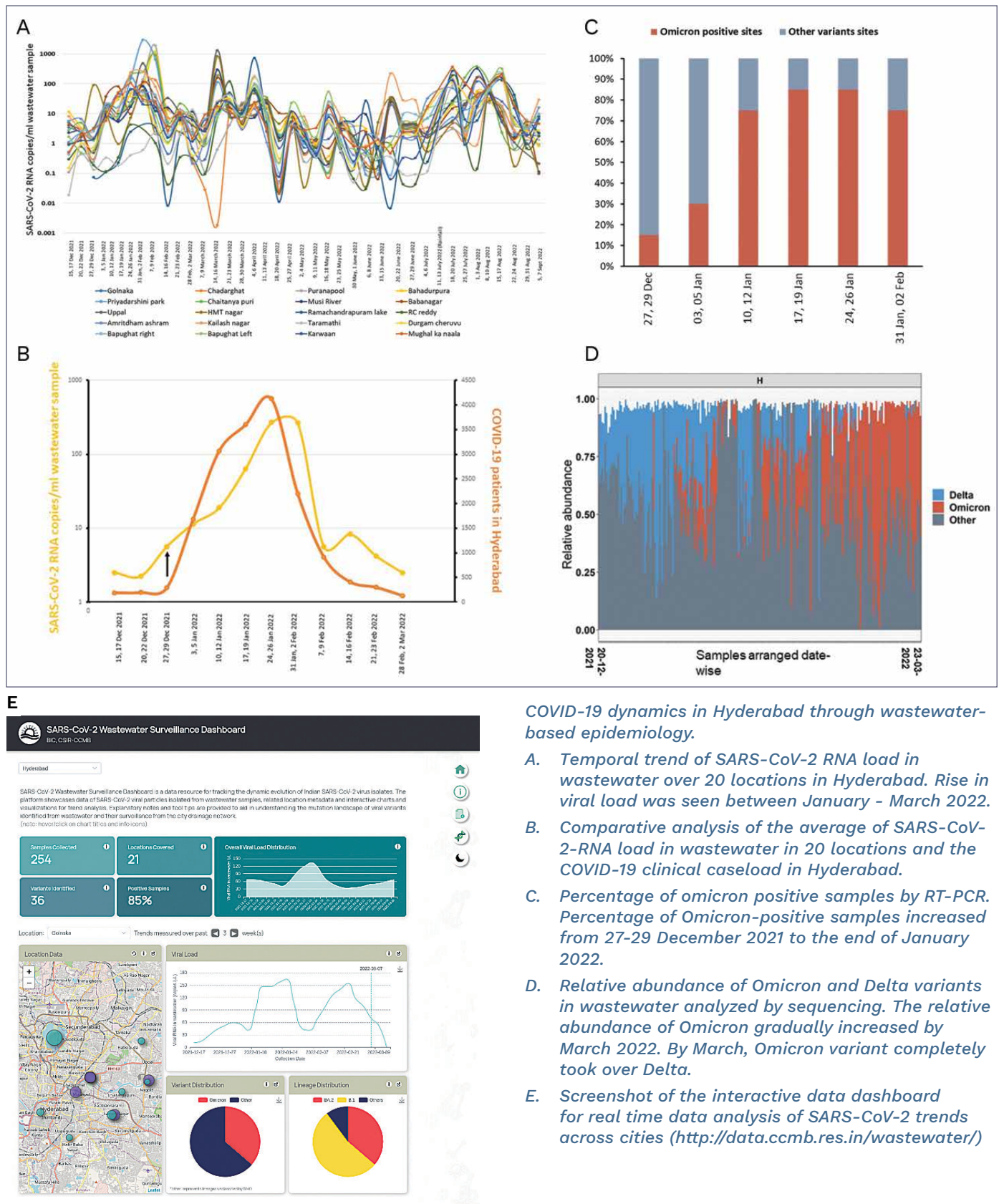
infected individuals in their faeces irrespective of their symptomatic status, wastewater-based epidemiology serves as a tool to monitor even dormant and unreported COVID-19 infections.

Over the last year, routine WBE- based surveillance of SARS-CoV-2 in Hyderabad has been setup at 20 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. A sharp COVID-19 wave was detected in Hyderabad in January 2022 by wastewater surveillance analysis and correlated with the rise in clinical caseloads. In collaboration with the Bioinformatics team at CCMB, and support from the Rockefeller Foundation, we have developed an interactive WBE data analysis dashboard to report on city-wide SARS-CoV-2 trends in real time (<http://data.ccmb.res.in/wastewater/>). This website and interactive dashboard is envisaged as a template for developing a broader platform for environmental surveillance data sharing, real time analytics and public outreach in the future.

We have also been developing systems for identifying the pathogen diversity and antimicrobial resistance genes in wastewater. Samples are collected less frequently, approximately once a month, from some of the locations established for SARS-CoV-2 sampling. The protocols have been optimized and the sequencing data are currently being analysed.



Map showing the wastewater sampling locations in Hyderabad. 20 locations are monitored weekly for the SARS-CoV-2 RNA load in wastewater



COVID-19 dynamics in Hyderabad through wastewater-based epidemiology.

- Temporal trend of SARS-CoV-2 RNA load in wastewater over 20 locations in Hyderabad. Rise in viral load was seen between January - March 2022.
- Comparative analysis of the average of SARS-CoV-2-RNA load in wastewater in 20 locations and the COVID-19 clinical caseload in Hyderabad.
- Percentage of omicron positive samples by RT-PCR. Percentage of Omicron-positive samples increased from 27-29 December 2021 to the end of January 2022.
- Relative abundance of Omicron and Delta variants in wastewater analyzed by sequencing. The relative abundance of Omicron gradually increased by March 2022. By March, Omicron variant completely took over Delta.
- Screenshot of the interactive data dashboard for real time data analysis of SARS-CoV-2 trends across cities (<http://data.ccmb.res.in/wastewater/>)

Identification of inhibitors of non-structural proteins for the treatment of Kyasanur Forest Disease

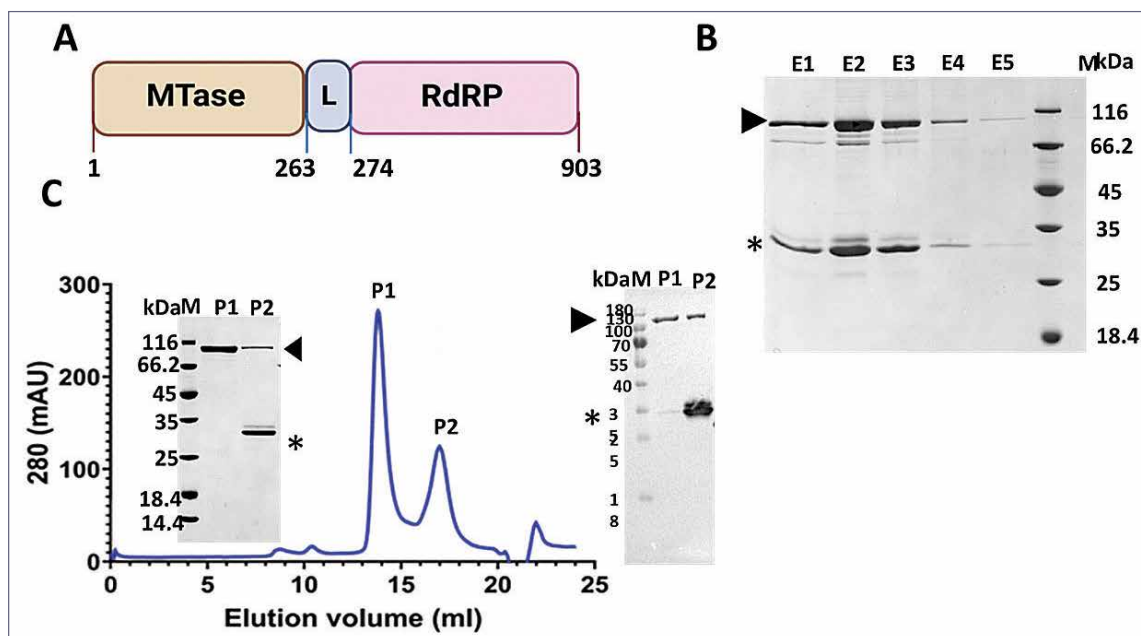
Anirudha Lakshminarasimhan and Mansi Malik

Kyasanur Forest Disease (KFD) is a zoonotic disease restricted to the Western Ghats and surrounding regions of south India. It is a viral disease with an incidence of about 500 cases every year, transmitted via infected ticks that bite intermediate mammalian hosts such as rodents and monkeys. Humans in contact with infected animals risk contracting the disease, although it may also directly spread via tick-bites. The absence of any treatment regimen for this neglected disease

underscores the need to develop effective and targeted therapeutic strategies. Till date, there are no drug discovery programs that address KFD.

We have identified two non-structural proteins, NS3 and NS5 from Kyasanur forest disease virus (KFDV), as promising targets for small molecule intervention. The identification of drug-like molecules for one or both target proteins can help shortlist drug candidates useful for the treatment of Kyasanur Forest Disease.

Towards this goal, we have successfully expressed and purified KFDV NS5 protein, and determined its purity by size exclusion chromatography and SDS-PAGE analysis. The RNA dependent RNA polymerase (RdRP) activity of KFDV NS5 protein was determined using nucleotide extension assay, and the inhibition of this activity was tested using Sofosbuvir and its triphosphate metabolite (an FDA approved drug for the treatment of Hepatitis C). We successfully observed and recorded inhibition of the RdRp activity of the in-house purified KFDV NS5 protein by Sofosbuvir and its triphosphate metabolite, making this a strong candidate for the treatment of KFD.



Expression and purification of NS5 protein A. Domain organization, B. Affinity chromatography and C. NS5 Protein Purification & WB

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

Mansi Malik and Farah Ishtiaq

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

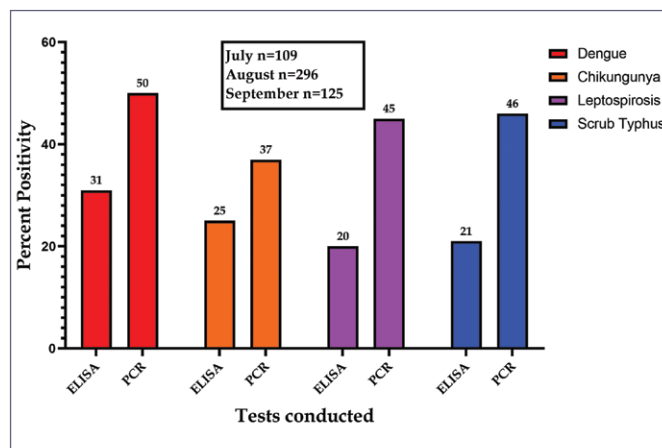
Communicable diseases need continuous surveillance activities to track, predict and control emerging, re-emerging, and novel infections that are potential threats to human health and wellbeing. Dengue and chikungunya are the two common vector borne diseases in India transmitted by the *Aedes* spp. mosquitoes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

Bengaluru, located in the state of Karnataka in Southern India, is the third most populous city in India. It has an area of 709 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.

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

1. 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.
2. 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/sero types 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. Going ahead, we will be working towards developing accurate quantification of pathogen (viral/parasite/bacterial) load from clinical samples. We are also keen on establishing SOPs and initiating clinical surveillance for Hepatitis A & E.

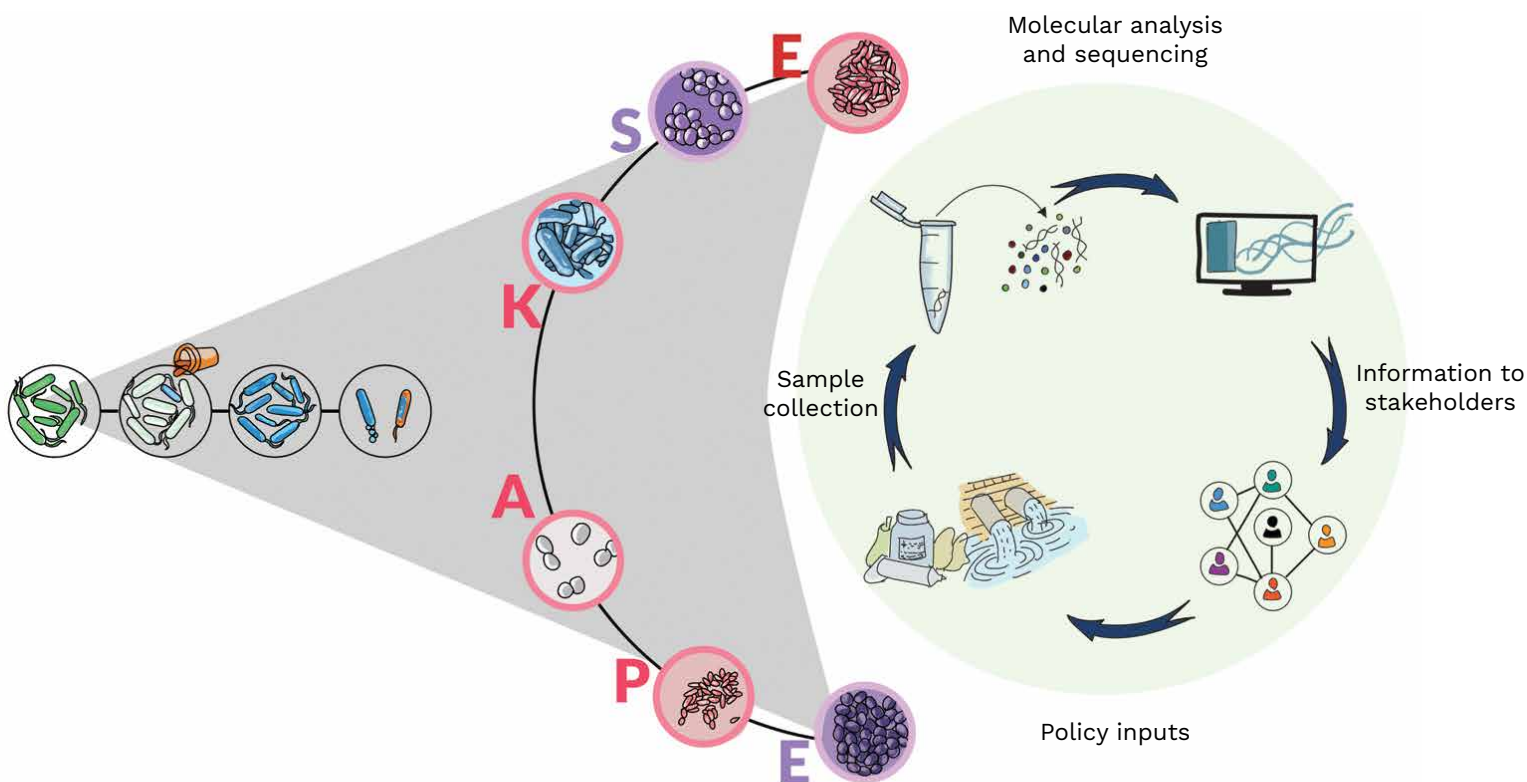


Disease trends in Bengaluru city: Vector borne disease incidence-2022

Antimicrobial Resistance

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

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



Reversal of antimicrobial resistance in ESKAPE pathogens

Farah Ishtiaq

[In collaboration with Amrita University]

To date, there has been no successful strategy to ensure that MDR strains can be reverted to an antibiotic sensitive phenotype. In our research plan, we will explore alternate strategies to combat AMR using Natural Products, bacteriophages specific to the pathogenic bacteria and also utilize CRISPR-based genome editing strategies with plasmids and/or lysogenic phage for sensitizing critical priority Gram

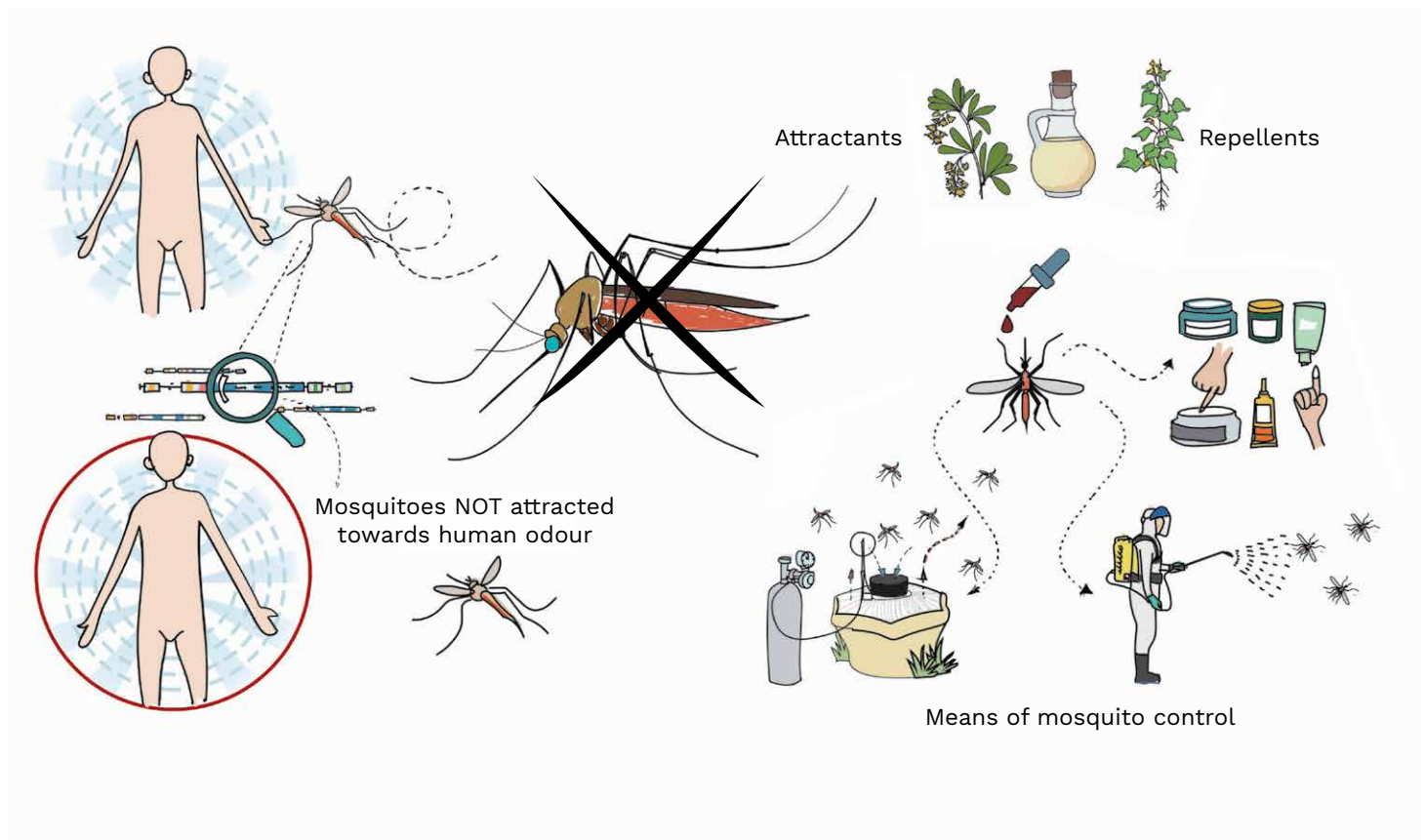
negative ESKAPE pathogens such as MDR *Pseudomonas aeruginosa* to antibiotics. Additionally, these approaches can also be applied to other multi-drug resistant nosocomial pathogens such as *Klebsiella pneumoniae*, *Acinetobacter baumannii* as well.

In order to address some these aspects, we have identified novel or partially characterized antibiotic resistance genes by mutation analysis to be targeted in *Pseudomonas aeruginosa*. We have also explored bacteriophage resistance and innate immune susceptibility in *Pseudomonas aeruginosa*. PAO1 was treated with AM.P2 phage and phage resistant mutants were successfully isolated. Different strategies were explored to design a plasmid that could be used to create an integrating base editing system in *Pseudomonas aeruginosa* for reversal of drug resistance. A Tn7 transposon-based integrated CRISPR Base editing system was developed to target *ampC/ampR* in *Pseudomonas aeruginosa* PAO1.

Vector Control

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

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



Genome assembly, annotation and genome comparison of *Anopheles stephensi*

Sunita Swain

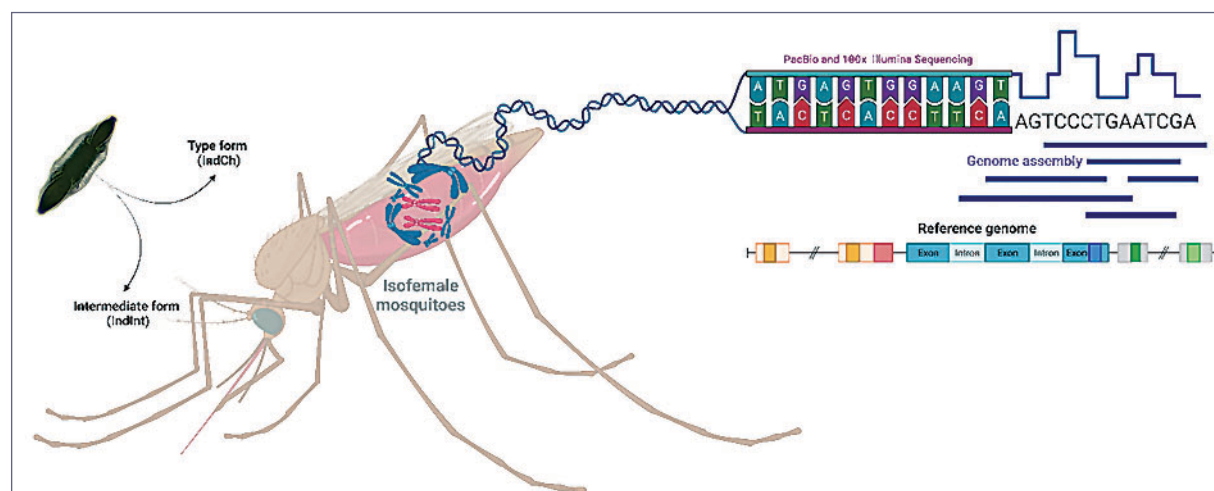
[In collaboration with IBAB, Bengaluru]

Chromosomal inversions play an important role in vector evolution. *Anopheles stephensi*, with its three distinctly identifiable forms at the egg stage correlating with varying vector competence, offers an ideal species to discover functional mosquito genes implicated in Plasmodium resistance. However, there was no quality reference genome available for these ecological forms. We collaborated with IBAB to develop high-quality genomes of two isofemale lines of *An. stephensi*, IndCh of type-form (PMID: 35246568), and IndINT (PMID: 36351999) Intermediate-form with varying vectorial capacity.

Unlike the earlier reported genomes of two other type form strains, STE2 (2R+b/2Rb) and UCI (2Rb/2Rb), IndCh

was found to be homozygous for the standard form (2R+b/2R+b). Comparative genome analysis revealed base-level details of the breakpoints and allowed extraction of 22,650 segregating SNPs for typing this inversion in populations. The large number of SNPs were tailored to 1740 exonic SNPs enabling genotyping directly from transcriptome sequencing.

Further, the chromosomal-level assembly of an intermediate form of *An. stephensi* strain (IndInt), shows a heterozygous paracentric inversion, 3Li, involving 8 Mbp, which is syntenic to the extensively studied 2La inversion implicated in Plasmodium resistance in *An. gambiae* involving 21 Mbp. Deep annotation of genes within the 3Li region in the IndInt assembly reveals the presence of a tumor necrosis factor-alpha (TNF-alpha) like gene, which is the homolog of the Eiger gene in *Drosophila*. We have identified all the genes in IndInt required for Eiger-mediated signaling by analogy to the TNFalpha system, suggesting the presence of a functionally active Eiger signaling pathway in IndInt. Comparative genomics of type-forms with that of IndInt, reveals structurally disruptive mutations in Eiger gene in all three strains of the type-form, suggesting compromised innate immunity in the type-form as the likely cause of high vectorial capacity in these strains.



Anopheles stephensi genome assembly and analysis

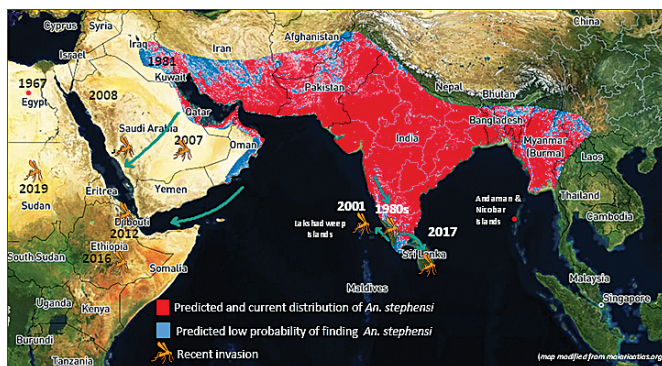
An. stephensi in Lakshadweep Islands: Comparison between mainland & island populations

Farah Ishtiaq

[In collaboration with University of Jaffna, Sri Lanka and IBAB, Bengaluru]

Anopheles stephensi originated in Southeast Asia and the Arabian Peninsula. It has recently emerged as an efficient and invasive urban vector for transmission of malaria. *An. stephensi* transmits *Plasmodium vivax* and *Plasmodium falciparum* parasites. There are three known forms, “type”, “intermediate” and “mysorensis”, of which the type and intermediate forms are efficient vectors in both rural and urban environments. Typical breeding sites are artificial containers, such as domestic wells, cisterns, overhead water tanks and roof gutters, with clean and unpolluted water allowing rapid expansion to urban environments.

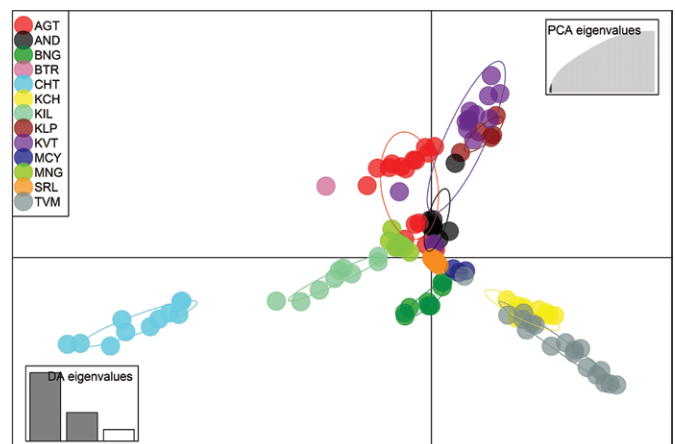
An. stephensi has rapidly extended its geographical range, with the type form being reported in Lakshadweep Islands (2001), in countries in the Horn of Africa (2012), Sri Lanka (2017), and most recently in the Republic of Sudan



(2019). The introduced *An. stephensi* exhibits resistance to several classes of insecticides, posing challenges in controlling its spread to new areas.

Using fine-scale landscape genomics, we have undertaken a biogeographic study of *An. stephensi* populations from the Indian mainland and Lakshadweep to shed light on the possible colonization route to nearby islands (including Sri Lanka), genetic diversity and effective population size that might have helped its establishment in new locations.

Our macroecological analysis of Lakshadweep islands revealed that *Aedes albopictus* is the dominant species, with entomological indices significantly above the epidemic threshold (as per the World Health Organization), indicating high risk of dengue virus transmission (Nihad et al. Sci Rep,12: 8060; <https://doi.org/10.1038/s41598-022-11898-y>). To understand gene flow, admixture between populations, effective population size and colonization time to the island populations, we analysed 168 *An. stephensi* samples from 14 populations using 15 X next-generation sequencing data. We found significant genetic clustering between the island populations. However, among the mainland populations, samples from the city of Mangalore showed signatures of gene flow.



Discriminant analysis of Principal Component showing genetic clustering between mainland (KCH=Kochi, MNG=Mangalore, TVM=Trivandrum, BNG=Bangalore) and islands populations- AGT=Agatti, AND=Androth, BTR=Bitra, CHT=Chetlat, KIL=Kiltan, KP=Kalpani, KVT=Kavaratti, MCY=Minicoy, SRL=Sri Lanka).

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

Farah Ishtiaq

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

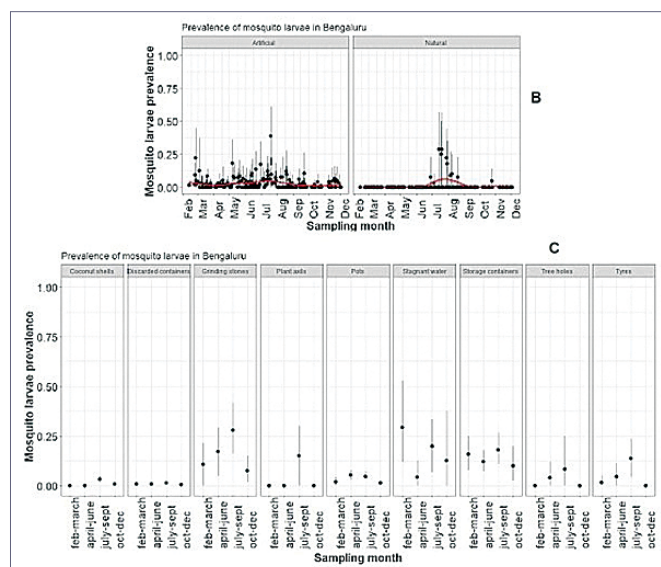
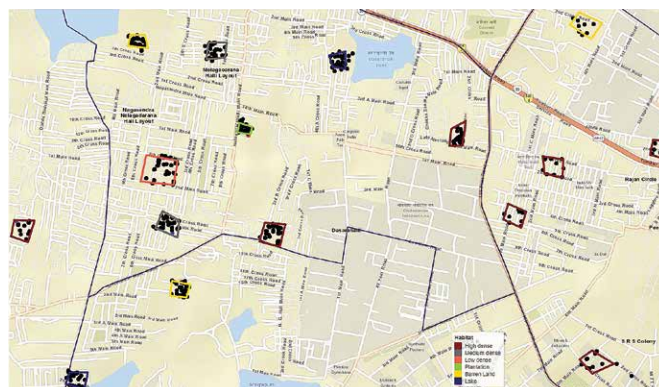
Vector surveillance is an essential component of vector-borne disease prevention. Dengue is the most common mosquito-borne viral infection, mainly transmitted by Aedes mosquitoes. Dengue has been associated with an increase in urbanisation and availability of larval habitat. Using evidence-based approach, our goal is to understand the role of urbanisation in driving the prevalence and abundance in Aedes mosquito larval habitats and their relationship with dengue incidence.

Urbanisation, land use patterns and climate are constantly changing the diversity and distribution of mosquito species. Recent studies emphasize how incorporating vector ecology into disease transmission models can greatly enhance their predictive ability. We continue to lack studies examining the links between vector ecology, pathogen transmission, and control strategies. Hence there is an urgent need to focus on the ecology and behaviour of commensal species in an urban landscape.

The disease ecology approach is also important from the perspective of emerging infectious diseases. The goal is to understand the role of vector ecology and genetics in the pathogen transmission dynamics. We use a combination of field and molecular techniques to answer questions related to how mosquito ecology, species richness, and niche overlap drive the emergence of a disease.

Our longitudinal study on Aedes species larval habitat across Bangalore city is designed to capture mosquito larval diversity with focus on Aedes sp habitat across 48 Index wards and 40 random grids. We mapped the Aedes species larval habitat and its overlap with other mosquito species. Our data show high larval presence in artificial or man-made habitat like storage containers, grinding stones and stagnant water. We are generating spatial clustering of dengue cases to strategize removal of larval sites with BBMP.

A



- A. Map showing distribution of grids across various habitat types in Bangalore.
- B. Prevalence of mosquito larvae across months;
- C. Seasonal prevalence of mosquito larvae by microhabitats

Screening for novel mosquito attractants and repellents

Jay Prakash Shukla and Bhagyashree Kaduskar

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

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

Designing and making of dual choice olfactometer (Y maze)

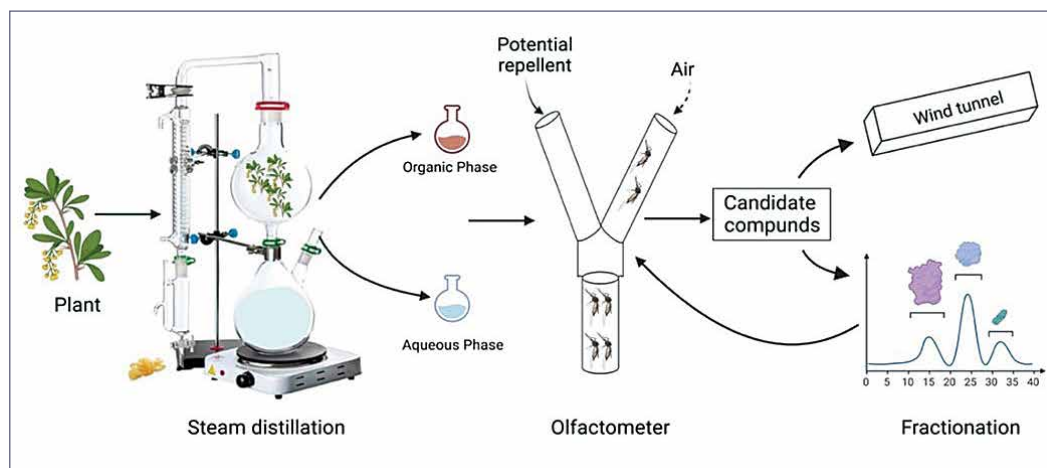
We are adopting our olfactometer design from a recently published olfactometer from Leal et al. 2017. Since its inception, dual choice olfactometer has evolved over time. This design offers controlled, clean laminar air flow and, decision making chamber advantage to avoid odour mixing before behavioural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

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

Plant essential oil procurement

Plant identification and compound isolation is a crucial part of this project, and we are collaborating with Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow and Society for Research and Initiatives for Sustainable Technologies and Institutions (SRISTI), Ahmedabad, to procure plant essential oil.

In the next phase, we will evaluate the olfactometer by using known mosquito attractants and repellents such as DEET, eugenol, citronellal, acetone, hexane, etc. After evaluation, we will incorporate necessary modifications in the olfactometer to improve sensitivity.



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

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

Sonia Sen

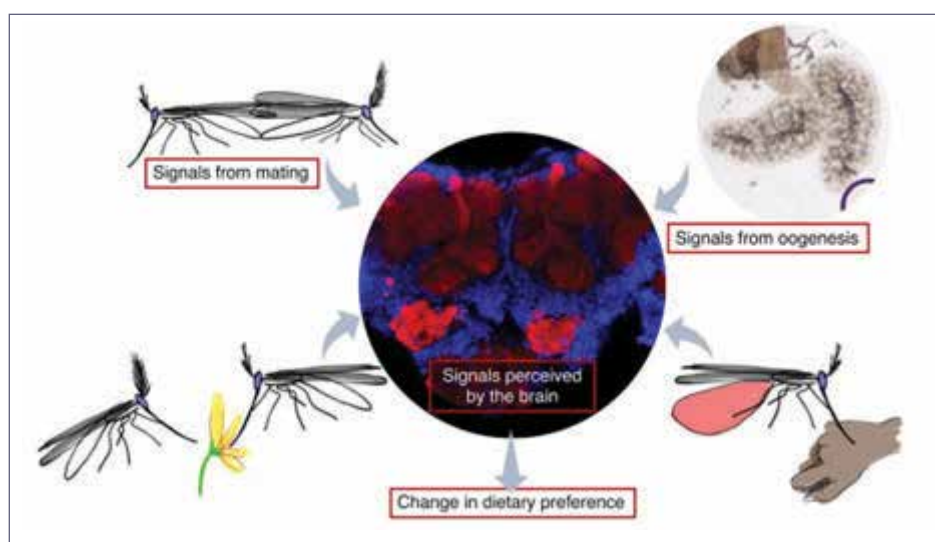
Mosquitoes, both male and female, usually feed on carbohydrate-rich sources of nectar or sap. Occasionally, the female switches to taking a blood meal. This dramatic change in dietary preference is essential for the development of her eggs. Because of this, female mosquitoes of some species have become 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. We are also developing cheaper alternatives to single cell transcriptomics for the Indian research and biomedical community, and have standardised methods that enable single cell transcriptomics to be performed on fixed tissue samples.

We have promising candidates that are now being validated through RNA interference. These will be useful targets for developing small molecule interventions for blood-feeding.



Summary of feeding behaviour in *Anopheles stephensi*

Infectious Diseases Team



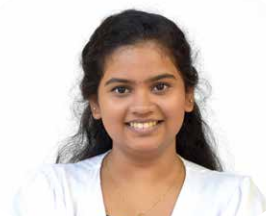
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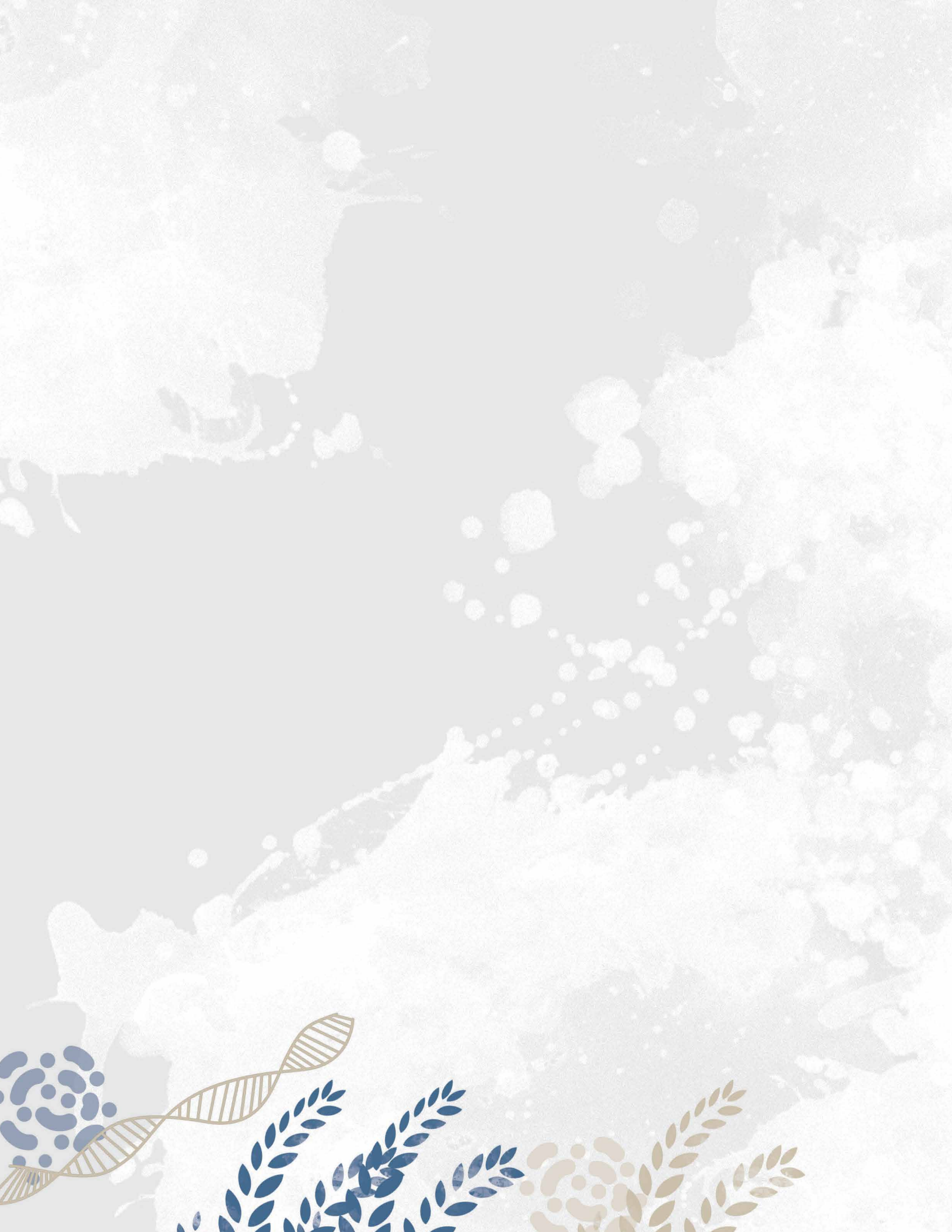
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Rare Genetic Disorders

Rare Genetic Disorders



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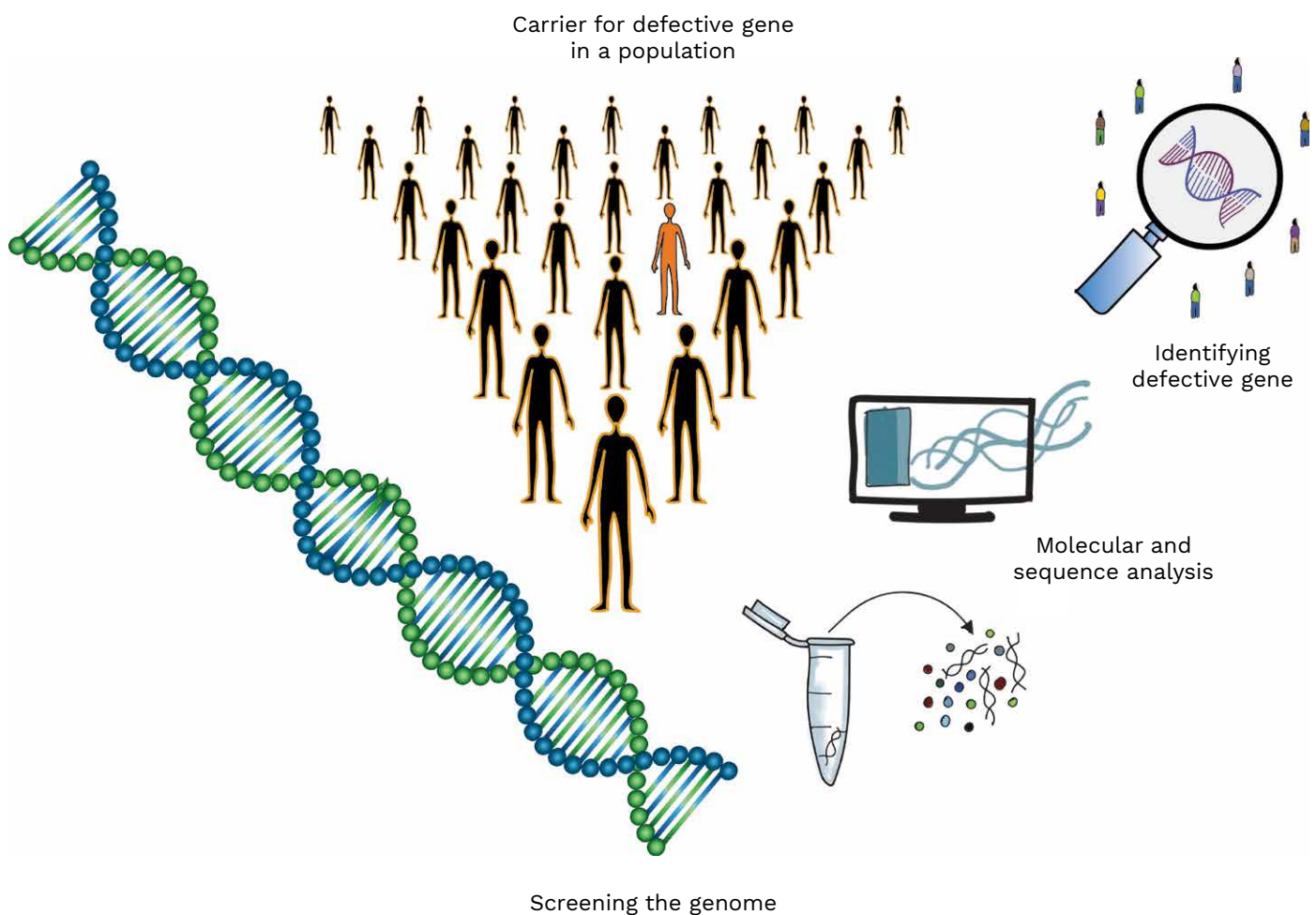
Genetic disorders are far from rare in India, owing to the high population density in the country, which translates to a very high disease burden. 5000-8000 rare genetic diseases have been identified globally, 450 of which have been reported in India. Mostly affecting children, they carry a huge socio-economic,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

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

Diagnostics and Screening

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

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



Development of diagnostic kits for rare genetic disorders

Shivranjani C Moharir and Harvinder Kour Khera

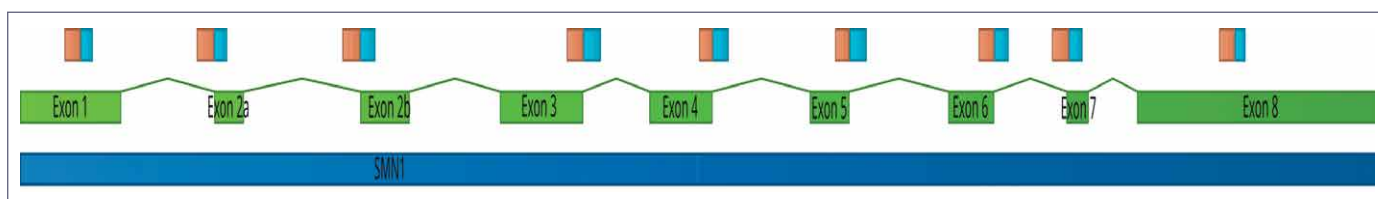
[In collaboration with CSIR-CCMB, Hyderabad]

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

Multiplex ligation-dependent probe amplification (MLPA)

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

We designed an MLPA-NGS assay to detect the SNPs responsible for SMN1 to SMN2 gene conversion as well as to identify the presence or absence of all other exons in SMN1/2 giving a complete diagnosis of gene conversion and copy number of the SMN genes. The development of the MLPA-NGS technique as a diagnostic kit for SMA is currently under progress. Probes identifying the exon 7/8 deletions in SMN1 gene (exon 7/8 deletion is the causative factor in more than 95% of SMA cases) and other exon deletions are included, along with reference probes. We are validating the assay with other approaches, and developing a digital PCR-based approach for identifying exon 7/8 deletion in parallel.



MLPA-NGS assay to detect SNPs involved in SMA

Developing a rare genetic diseases database - GenTIGS

Illyas Rashid and Shivranjani C Moharir

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

The database would include a wide variety of information related to RGDs from sources such as OMIM and Orphanet and will include local prevalence, affected genes, pathogenic variants, gene regulatory factors, the role of non-coding RNAs, along with patient information. Clinical data (primary source) will be sourced from our partner hospitals and research organizations. Gene

annotations and sequences, reports and information on local trends will be obtained from online databases such as Ensembl and NCBI-gene databases (secondary sources) to perform a comparative analysis. The datasets will be managed and stored using a relational database management system (RDBMS).

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

GenTIGS A Gene Database on Rare Genetic Disorders

Home Gene Information Sequence Analysis Patient Data Archive Contact

Home / Gene Information / Functional stage

RGD List **Functional Genes**

Batten Diseases Palmitoyl-protein thioesterase 1 PPT1 Search

S.No.	Name/GeneID	Location	Gene Length	Exons	Details
0	PPT1 5538	000001.11 52, complement)	25792 nt	9	more...

Tripeptidyl peptidase 1 TPP1
CLN3 lysosomal/endosomal transmembrane protein, battenin CLN3
DnaJ heat shock protein family (Hsp40) member C5 DNAJC5
CLN5 intracellular trafficking protein CLN5
CLN6 transmembrane ER protein CLN6
Major facilitator superfamily domain containing 8 MFSD8
CLN8 transmembrane ER and ERGIC protein CLN8
Neuronal 9 CLN9
Cathepsin D CTSD
Granulin precursor GRN
ATPase cation transporting 13A2 ATP13A2
Cathepsin F CTSF
Potassium channel tetramerization domain containing 7 KCTD7

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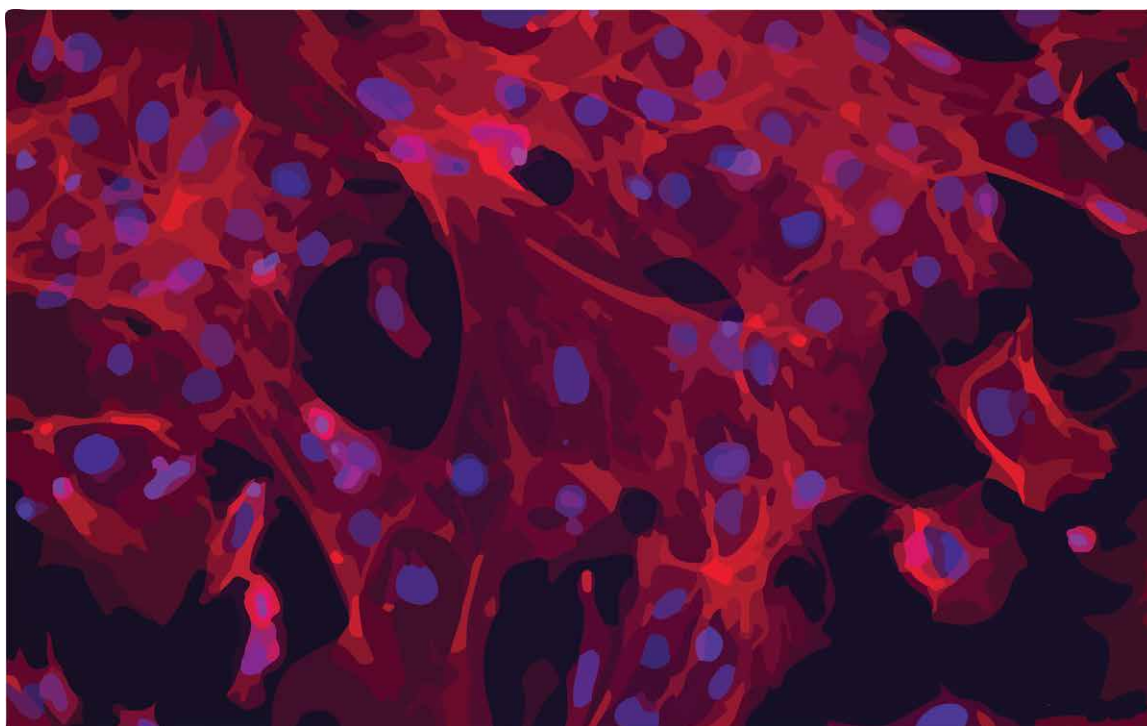
Screenshot of the GenTIGS collection viewer

Therapeutics

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

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

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



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

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

Vasanth Thamodoran and
Anirudha Lakshminarasimhan

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 U.S 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 neighbouring states. Based on this report, and the prevalence of consanguineous marriages, the incidence of SMA in India is speculated to be higher than in US and Europe.

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

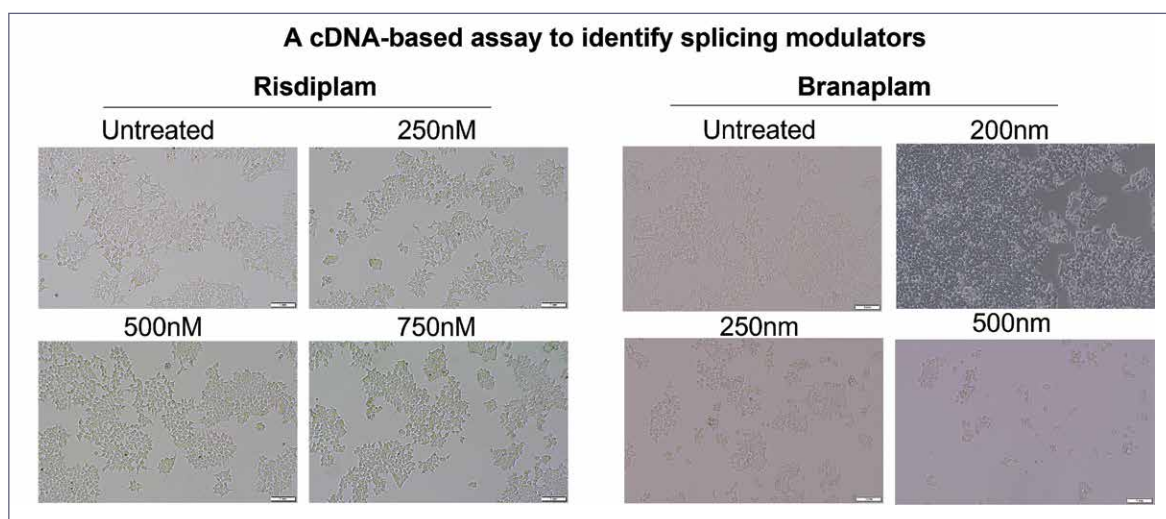
gene do not exhibit any symptoms of the disease and can therefore act as carriers.

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 is inversely related to the age of onset of disease. The median survival is 7 months, with 95% chances 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 increase in the levels of full length SMN transcript.



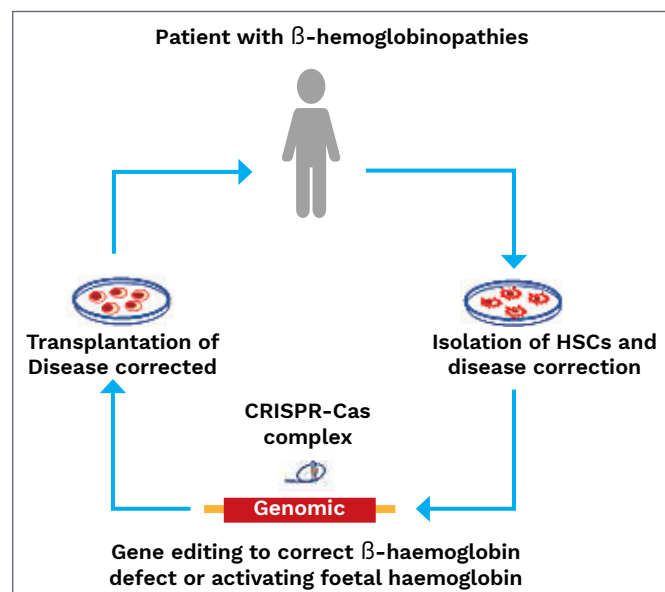
RT-PCR based assay for splice variants. HEK293T cells were exposed to splicing modulators Evrysdi (Risdiplam) and Branaplam and the highest concentration with low toxicity was identified.

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). In recent times, gene editing based strategies have been found to be 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 found to be successful in clinical trials.

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



Flowchart outlining the key steps in gene editing-based gene therapy.

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 γ -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):

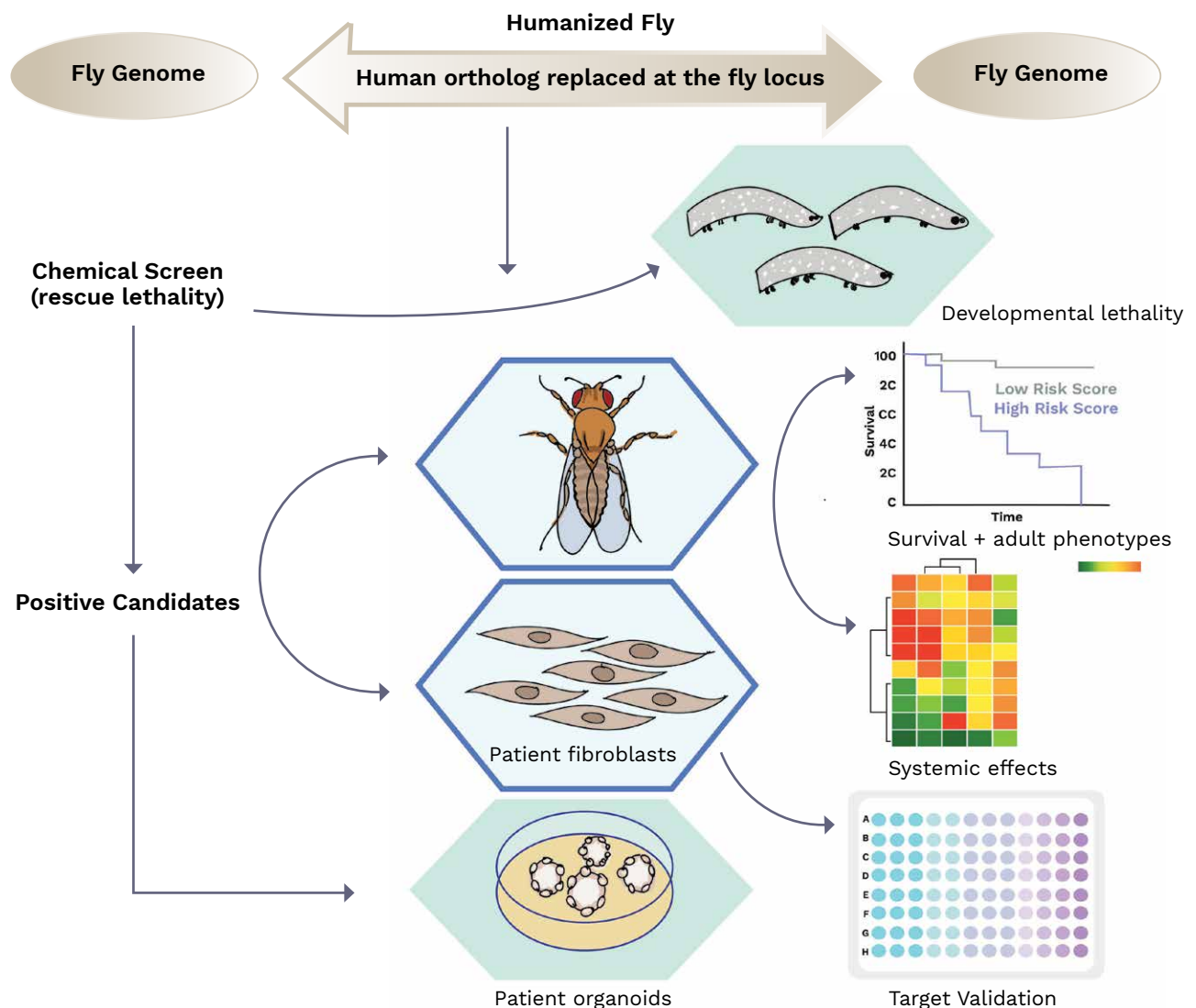
We plan on working further with the crRNA that gives highest activation of γ -globin. Synthetic crRNA will be complexed with enAsCas12a protein (RNP) or co-transfected with mRNA expressing enAsCas12a in human adult/umbilical cord derived CD34+ cells (HSCs). After culturing the cells for 48-hrs ex-vivo, the percentage of editing will be validated. The cells will also be analysed for off-target effect using NGS. A collaboration with JSS medical college, Mysore has already been initiated to obtain umbilical cord blood to derive HSCs.

Disease Modelling & Novel Interventions

Screening for novel drugs is one of the costliest steps in drug development. Modelling rare genetic disorders using *Drosophila* and cell culture allows for fast, cost-effective screening of novel therapeutic interventions. This also reduces the animal burden in drug development.

We use a cost-effective *Drosophila* model for screening small molecules, mRNA therapy and anti-sense oligos (ASOs) against less explored diseases and rare genetic disorders. *Drosophila* shows more than 80% conservation with human genes and pathways. Over the last hundred years, *Drosophila* researchers have developed excellent genetic tools and behavioural assays useful for testing the effect of drugs and for evaluating their impact on key pathways, behaviours and lifespan.

At TIGS we are developing a model of primary screening in flies, followed by testing of potential candidates in cell culture and animal models. Developing *in vitro* models using stem cells and induced pluripotent stem cells (iPSCs) provides a ready 'disease-in-a-dish' model for studying the effect of interventions on the target cell type. This will make it possible to develop low cost and effective treatments for rare genetic disorders.

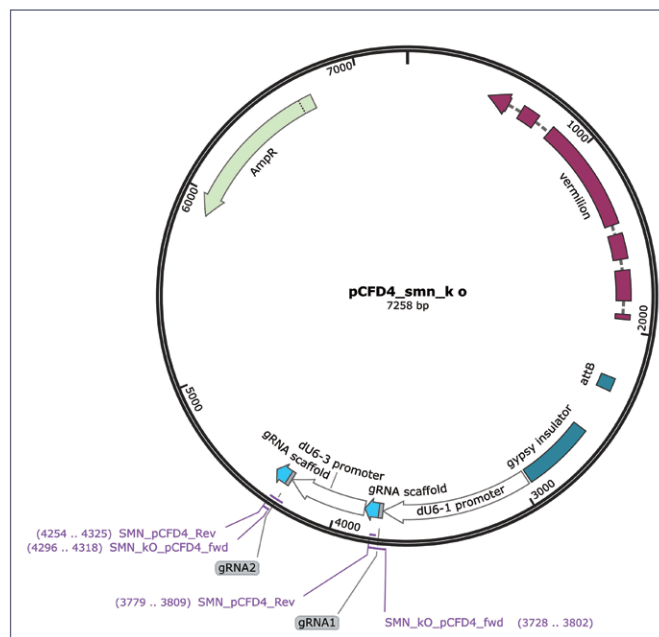


Drug screen using *Drosophila melanogaster* SMA model

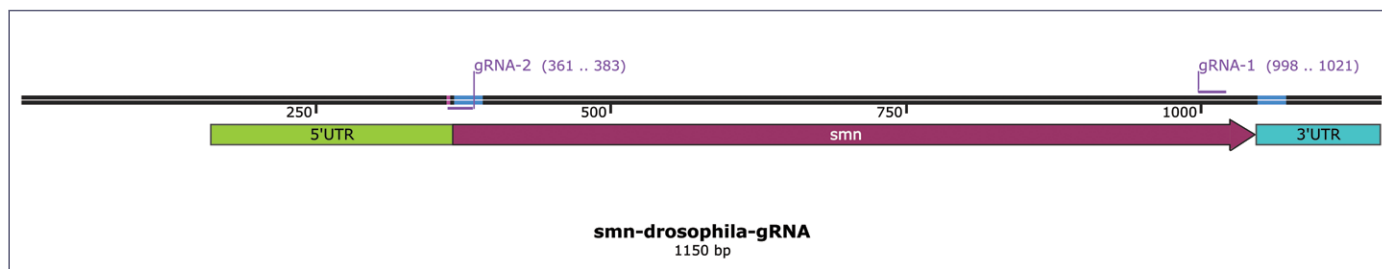
Bhagyashree Kaduskar and Jay Prakash Shukla

Spinal muscular atrophy (SMA) is caused by defects in survival motor neuron 1 (SMN1) gene. Currently, there are small molecular drug screens established in cell culture and animal models worldwide to increase functional SMN protein. However, performing such screening in cell lines or animal models is very costly and time consuming. Additionally, cell line-based screens are limited in assessing systemic effects of the drug while the animal model cannot be used for high throughput screens. *Drosophila* disease models can successfully bridge this gap. Drug screen in flies can be done on a large scale, help assess systemic effects and are comparatively cheap. This can help reduce the overall price of the drug development process and develop cost-effective treatments for SMA. We have initiated the following goals at TIGS:

1. To establish humanized *Drosophila* SMA model.
2. To design, synthesize and test small molecular drugs on the SMA fly model.



The two gRNAs are cloned in *Drosophila* expression vector pCFD4. This plasmid will be injected in flies to generate a stable fly line ubiquitously expressing the two gRNAs.



Generating donor plasmid with human SMN2

Design of gRNAs for clean deletion of fly smn. The two gRNAs would target the Cas9 nuclease to the target sites and cleave the endogenous smn gene. This then will be replaced by a shorter Human SMN2 gene.

Human pluripotent stem cell-based disease models for testing biotherapeutics

Vasanth Thamodaran and Anirudha Lakshminarasimhan

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

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

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

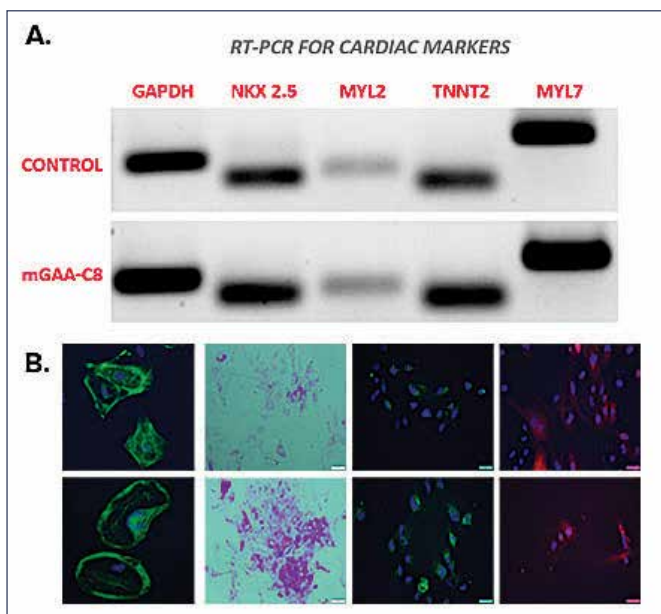
The Organisation for Rare Diseases India (ORDI), has listed about 250 rare genetic disorders (RGDs) that are prevalent in the Indian context. The lack of stem cell models for a majority of these RGDs has hindered the generation of insights on them. Thus, establishment of pluripotent stem cell lines carrying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

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

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

A. Lysosomal storage disorders (LSDs)

- » **Optimization of gene editing in iPSCs:** The optimal nucleofection condition that provides efficient gene editing in iPSC/ESC was identified using guide RNAs that target the OCLN gene.
- » **Generation of Pompe-iPSC:** Using the identified optimal nucleofection condition, the GAA gene which is defective in Pompe patients was targeted in hESC (hem20). Successful gene editing was validated by Sanger sequencing and the cells were single cell cloned to isolate a cell line that carries homozygous mutation.
- » **Establishment of differentiation protocols:** As cardiac and skeletal muscles are defective in Pompe's disorder, the differentiation procedures were successfully established to mimic the same (Figure 1).



Cardiac cells displaying Pompe pathologies.

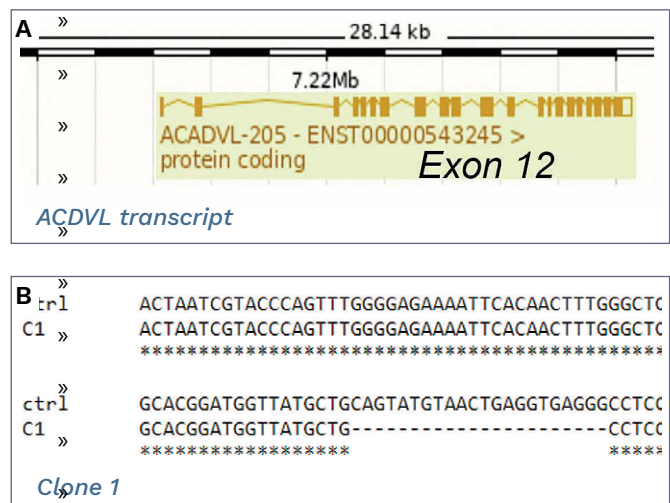
- A. The cells expressed all the cardiac markers and
- B. The cardiac cells showed signs of hypertrophy, glycogen accumulation and Lysosome dysregulation.

B. Skeletal myopathies

[in collaboration with DBT-inStem]

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

- » **Gene editing of ACADVL gene:** To generate iPSC-based disease model for VLCADD, the exon 12 of ACADVL gene was targeted using CRISPR-Cas9 and one of the clones was identified as carrying a homozygous 21 bp deletion. The clone was karyotypically normal and also confirmed to be pluripotent (Figure 2).
- » **Investigating VLCADD in cardiac and skeletal muscle:** Differentiation of VLCADD iPSC to cardiac and skeletal muscle lineages showed hypertrophy.



Gene editing to generate VLCADD iPSC.

- A. Transcript image showing the binding of sgRNA at exon 12.
- B. Sanger sequencing showed 21bp deletion in the C1 clone.

Rare Genetic Disorders team



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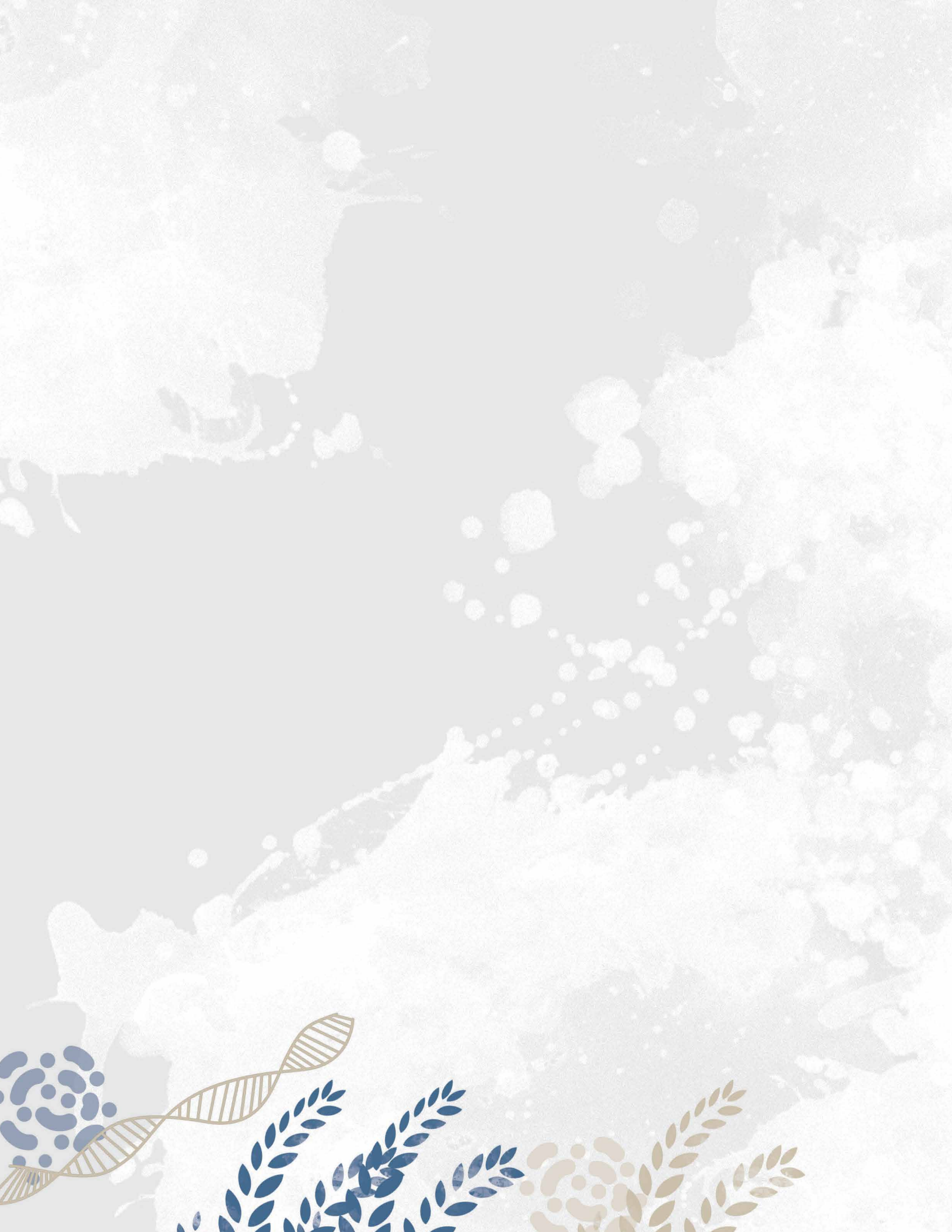
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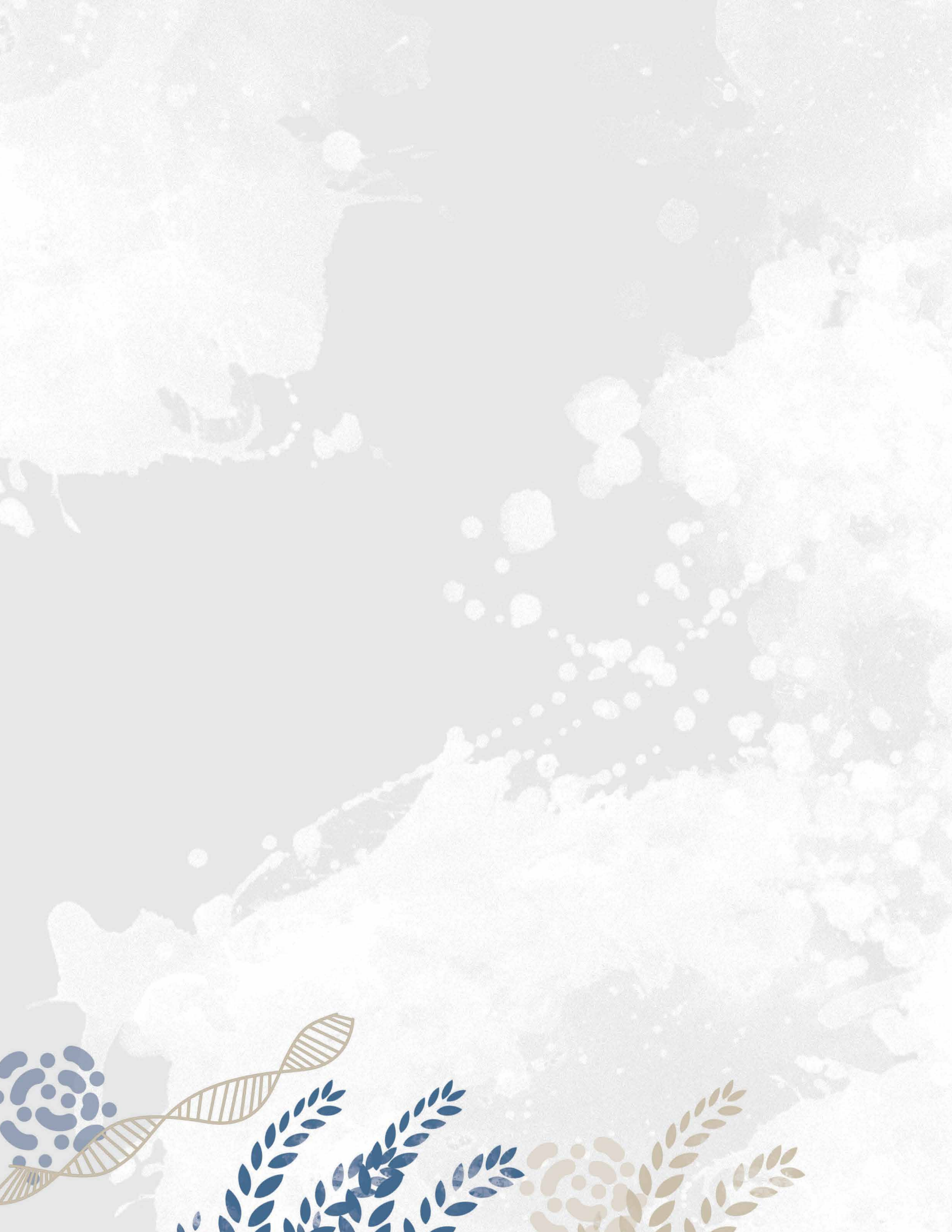


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Crop Improvement



Crop Improvement



VS Sresty Tavva



Rambabu Ratnala



Sampath Kumar



Shivranjani C Moharir

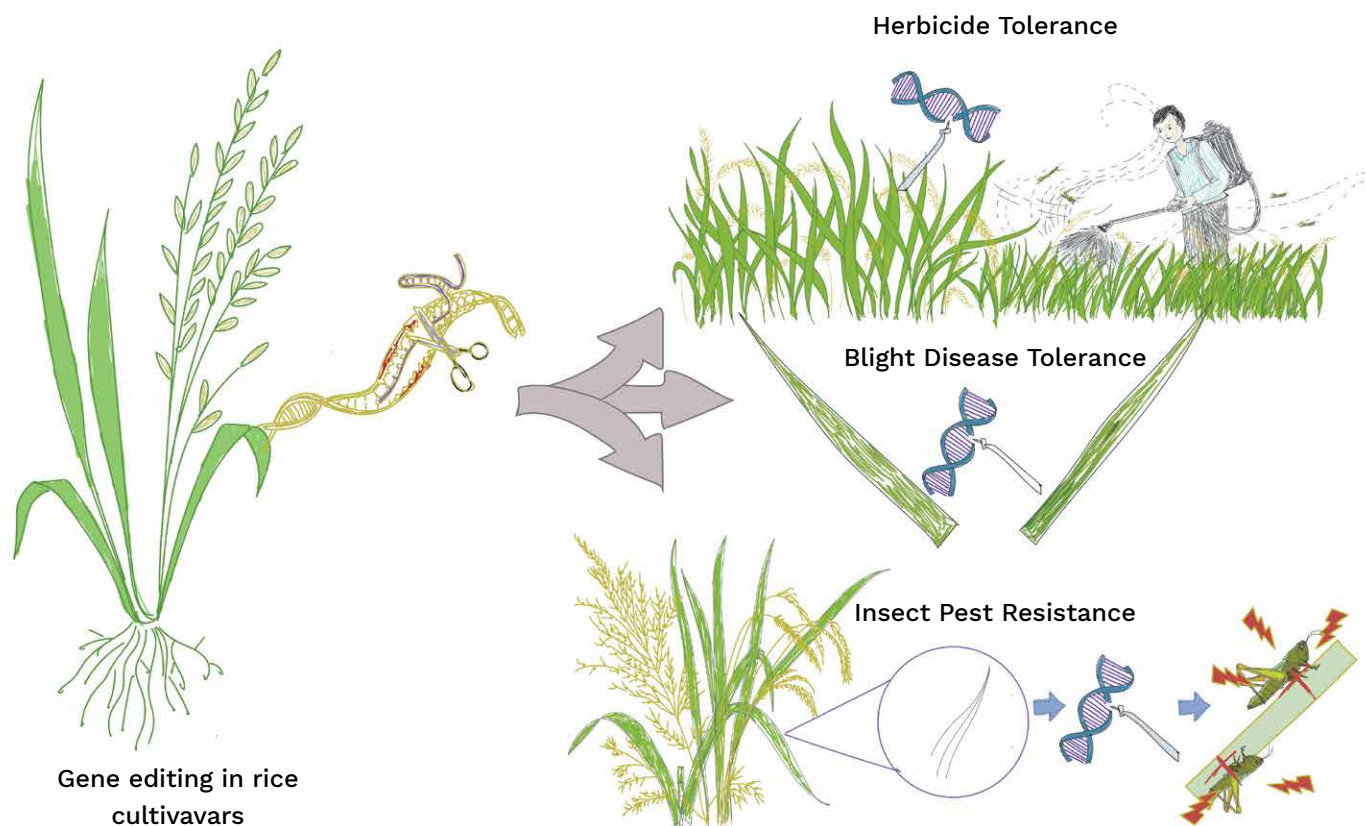
In the face of climate change and an increasing global population, food security and nutrition have become some of the biggest challenges of the day. We need to innovate and implement different approaches to improve nutritional quality of food grains, reduce crop losses due to diseases and pests, and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

Genome Editing

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

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

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



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

V S Sresty Tavva

It is hypothesized that when biotic stress tolerance traits are introgressed into the genetic background of elite rice cultivars, it can sustain rice yields and improve crop productivity. We are working towards developing bacterial leaf blight resistance through genome editing of appropriate alleles in the background of aerobic rice cultivar (KMP175) and a mega variety (MTU1010). Bacterial leaf blight (BLB) caused by *Xanthomonas oryzae* pv. *oryzae* is one of the most devastating diseases restricting rice production. It spreads systematically through the leaf xylem tissue and infection leads to significant yield losses. More than 38 BLB genes have been identified so far in rice and the recessive *sweet11*, *sweet13* and *sweet14* genes provide broad-spectrum resistance genes to BLB (Chu et al., 2006; Oliva et al., 2019). Suppressing the expression of SWEET genes can result in the development of resistance to BLB isolates, PthXo1, PthXo2, PthXo3 and AvrXa7 (Oliva et al., 2019).

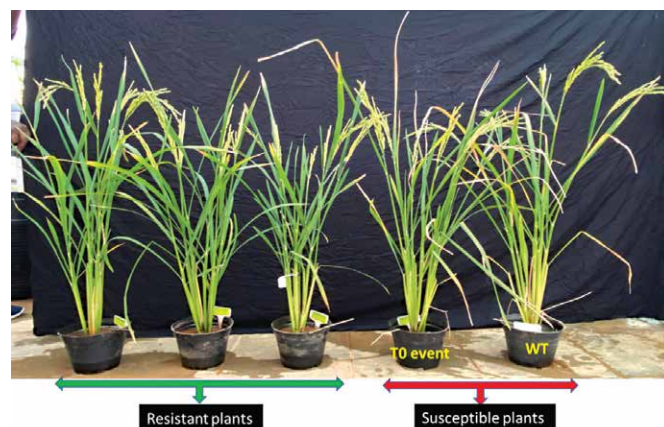
Vector construction and rice transformation: RNA guided site-specific DNA double strand break (DSB) through CRISPR/Cas9 system was used to create mutations in the target region. We have designed SDN1 strategy to edit target genes selected for developing BLB disease resistance. The binary vectors containing guide RNA (gRNA), SpCas9 (codon optimized for rice) and plant selectable marker expression cassettes were constructed. Rice transformation experiments were carried out through particle bombardment using either seed-derived calli or immature embryos as explants. Stable rice events generated were sent to greenhouse to perform both genotypic and phenotypic studies.

Molecular characterization and phenotyping: T0 rice genome edited lines generated using MTU1010 and KMP175 varieties were screened by PCR amplification of the target region followed by restriction digestion and Sangers sequencing to check for the insertions and/

or deletions in the target region (Figure 1). Appropriate phenotyping methods for rice bacterial leaf blight were developed using *Xanthomonas oryzae* pv. *oryzae* (strain IXO631) under greenhouse conditions. Fully expanded boot leaves of rice events were inoculated by adopting a leaf clipping method. The lesion lengths were measured 14 days after inoculation. Lesion length measurements = up to 3 cm will be scored as resistant, 4–10 cm as moderately resistant/susceptible, 11 cm and above as susceptible. The most appropriate dilution of the inoculum that caused adequate disease reaction with MTU1010 and KMP175 wild-type plants was used for screening the edited lines.

We have screened all T0 plants by inoculating with Xoo strain (IXO631) that secretes PthXo1 TALE to identify BLB resistant and susceptible lines (Figures 1 and 2). Based on the phenotypic and genotypic data, we have identified a total of 55 BLB T0 plants with either monoallelic or biallelic deletions or insertions in the effector binding element of the target promoter of both MTU1010 and KMP175 varieties.

Backcrossing of edited lines to segregate out transgenes: The edited T0 lines selected based on molecular and phenotypic data were backcrossed with their respective wild-type parent plant (MTU1010 or KMP175) to segregate out the Cas9 and antibiotic marker genes. Appropriate screening methods will be performed to ensure that the backcross seed (BC0F1) collected from selected T0 lines of both MTU1010 and KMP175 varieties should not carry any transgenic cassettes. The selected events (BC0F2) with no transgenic cassette and having bi-allelic homozygous mutation will be advanced.



Phenotype of T0 genome edited rice events inoculated with IXO631 (PthXo1) strain.



Leaf clipping assay of T0 genome edited rice events showing susceptible/resistance reaction to Xoo strain, IXO631 (PthXo1) 14-days after inoculation. 1 to 7 showed resistant reaction; 8 and 9 showed susceptible reaction; 10 - wild-type parent control

Genotypic and phenotypic data collected from selected T0 edited lines generated using MTU1010 (top) and KMP175 (bottom) varieties, respectively.

T0 Event ID	Germplasm	Deletions(-)/insertions (+) in the target region		Mutation status	Disease symptoms 14 DAI with IXO631 strain
		Allele 1	Allele 2		
003	MTU1010	WT	+G	Mono-allelic	Susceptible (10.7 cm)
012	MTU1010	-G	+G	Bi-allelic	Susceptible (10.5 cm)
013	MTU1010	+T	-CTGT	Bi-allelic	Moderate resistant (4.5 cm)
017	MTU1010	-G	+G	Bi-allelic	Susceptible (9.2 cm)
019	MTU1010	WT	-TACTGTACACC (-11bp)	Mono-allelic	Resistant (0.5 cm)
020	MTU1010	WT	+T	Mono-allelic	Moderate resistant (4.5 cm)
026	MTU1010	WT	-AATATGCATCTCC CCCTACTGTA (-23 bp)	Mono-allelic	Susceptible (11.2 cm)

T0 Event ID	Germplasm	Deletions (-)/insertions (+) in the target region		Mutation status	Disease symptoms 14 DAI with IXO631 strain
		Allele 1	Allele 2		
001	KMP175	-GTACACCA (8bp)	+A	Bi-allelic	Moderate (3 cm)
008	KMP175	-TAC (3bp)	WT	Mono-allelic	Moderate (4.1 cm)
010	KMP175	-CCTACTGT (8bp)	WT	Mono-allelic	Moderate (2.9 cm)
021	KMP175	-TACTGTACAC (10bp)	-GTA (3bp)	Bi-allelic	Resistant (1.6 cm)

Genome editing of rice cultivars to develop insect pest resistance

Rambabu Ratnala

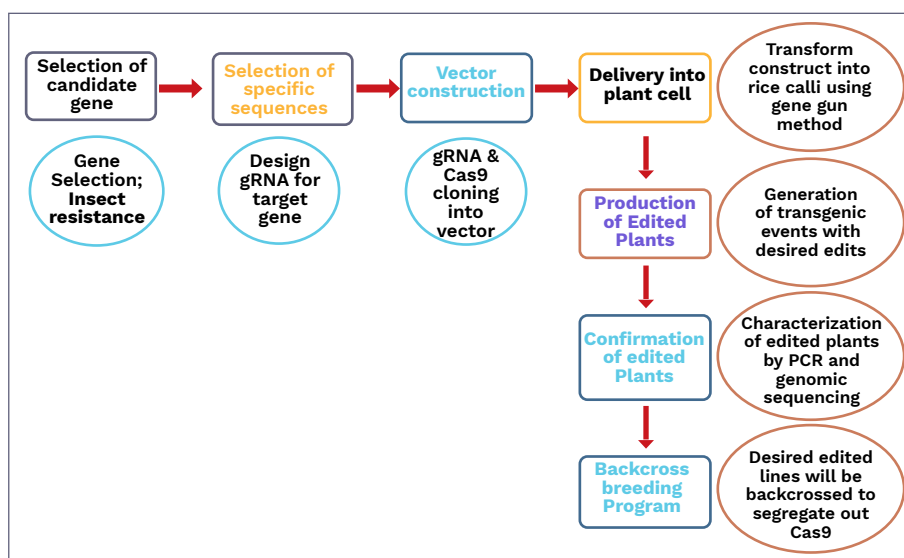
To ensure global food security for continuing population growth, it is vital to control the various insect pests that damage rice. The brown planthopper (BPH) and stem borer are two of the most serious pests in rice production.

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

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

We have used the gene gun method to create 50 putative transgenic events in the background of MTU1010 by seed-derived callus with CYP gene editing constructs. Out of 50 events, none of them have the target mutations. T1 seeds were collected from these 50 events, and the event 16-3 was identified with Ds red fluorescence and 30 seeds were selected and carried forward. Sequencing analysis reveals the presence of the indel mutation in 7 of the 30 T1 plants at the target site in the gene. These T1 plants are now in the greenhouse. Using the immature embryo callus-derived method, 800 calluses were transformed in eight batches. Nearly 90 Ds red calluses were selected and regenerated; now they are in the root hardening stage.

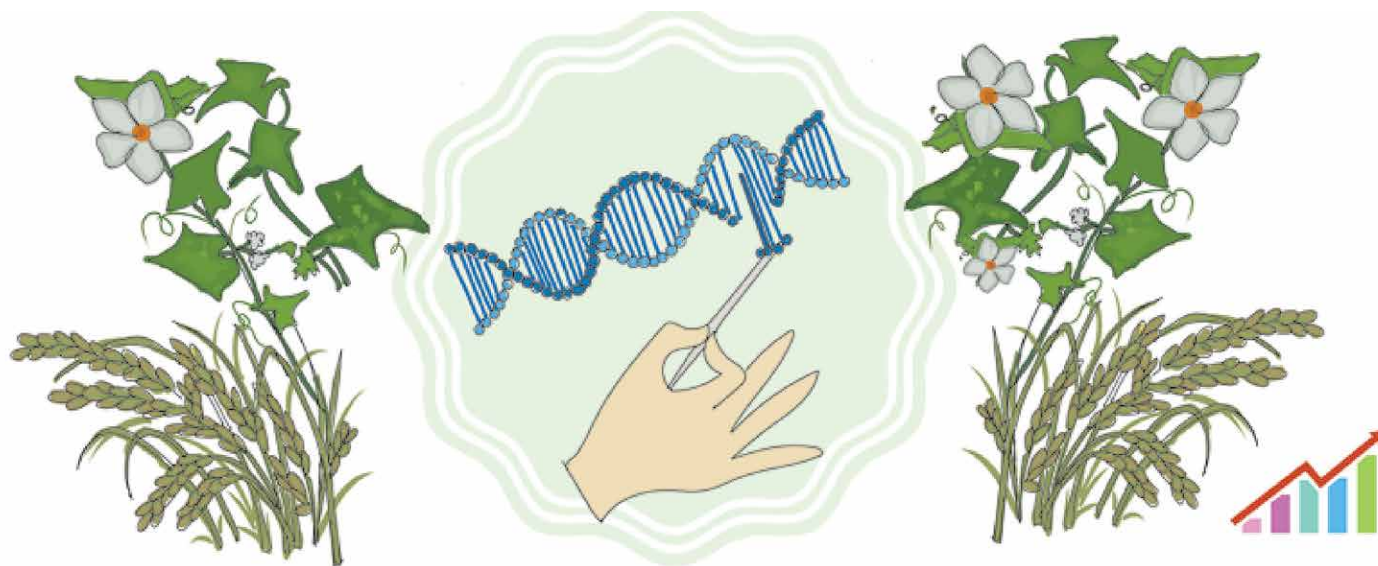
We aim to develop resistance against both brown plant hopper (BPH) and striped stem borer (SSB) in popular indica rice cultivars. The final product generated will be a rice variety that will be helpful to farmers who face huge yield losses due to these pests. It will also contribute to a reduction in the massive use of pesticides and chemicals to control insect pests in order to provide environmentally friendly and chemical-free rice to society. Insect-resistant Indica lines created in this project will serve as an excellent source of germplasm and will be transmitted to a popular background.



Experimental design and workflow for generating genome edited lines

Mutation Breeding

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



Enhancing crop traits and yields via genetic approaches

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

V S Sresty Tavva

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

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

carryout field experiments and to generate and evaluate hermaphrodite parwal plants. We have set the following objectives:

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



Pointed gourd lines that are being assessed for hermaphrodite trait

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

Shivranjani C Moharir

[in collaboration with CSIR-CCMB]

Most of the traditionally grown varieties of rice are rich in carbohydrates but do not provide adequate amounts of micronutrients such as iron, zinc and proteins.

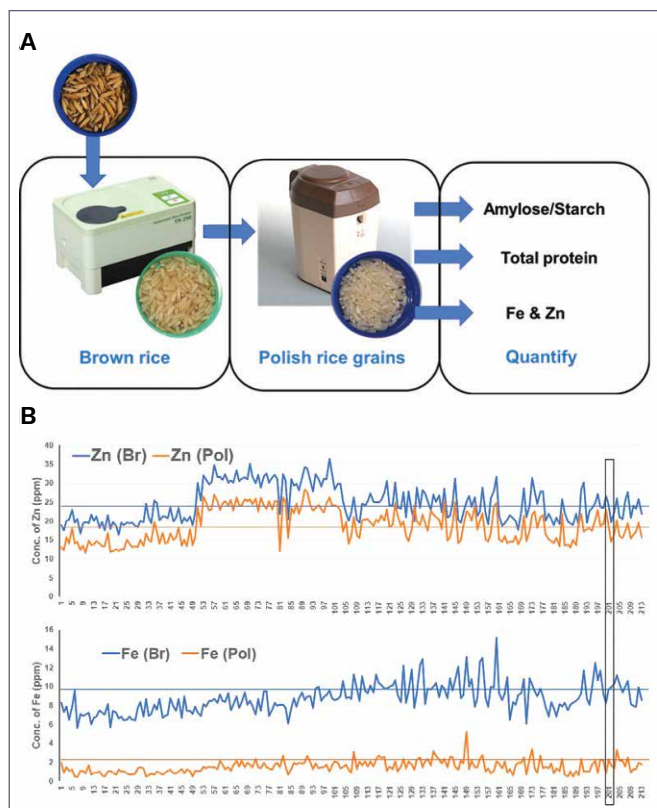
We aim to screen rice lines generated by mutagenesis for beneficial traits like low glycemic index, and high iron, zinc and protein content. We are testing rice mutant lines previously developed by CSIR-CCMB in collaboration with ICAR-IIRR as well as freshly mutagenized rice lines.

We have screened over 200 mutant lines for iron and zinc concentration in the grains. In the initial screening, some mutants show higher zinc and iron concentrations in the grains than their parents. We will quantify the same in another batch of the same lines and in the next generation of the same lines. The lines that consistently show higher zinc and iron will be used for the quantification of all the elements in the grains by other approaches.

As part of the collaborative work, we have also generated a new mutagenized population in the background of Improved Samba Mahsuri (ISM), the bacterial blight tolerant, low GI rice variety. The grains of these plants will soon be screened for various nutritional parameters.

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

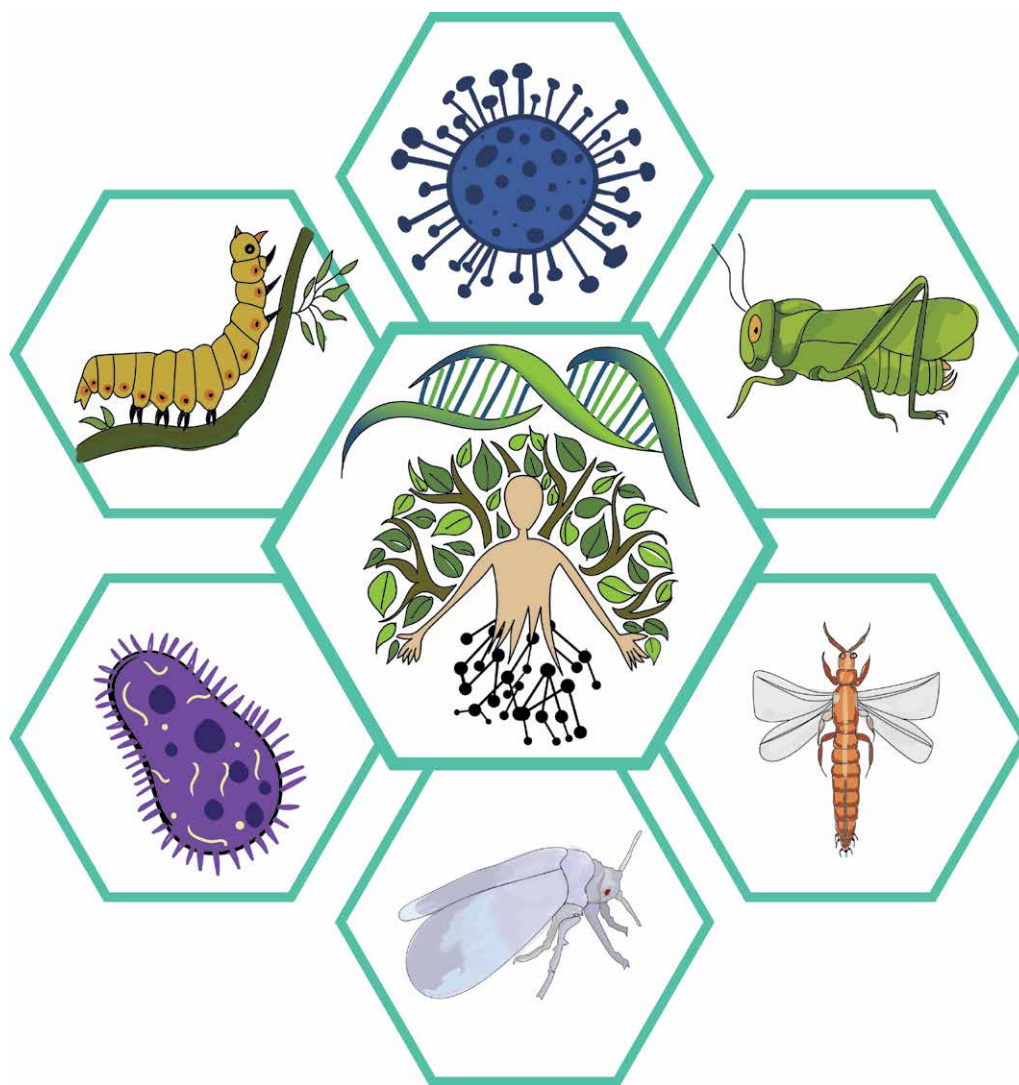
Rice varieties tested for zinc and iron content.



A. Workflow for nutrient estimation.
B. Zinc and iron content in brown and polished rice lines.

Disease and Pest Management

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



Integrated pest management programs can
improve nutrition security

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

Sampath Kumar

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

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

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

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

Our preliminary studies suggest that a high voltage, low amperage electric shock given through a non-invasive method is able to kill the neonate stage of the borer (the neonate is present just beneath the bark). Further studies are in progress to change the frequencies and pulse duration to reach the borers present in the central core regions of the coffee stem.



Coffee stem borer infested plant and an adult coffee stem borer

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 the farmers in mitigating the threat posed by FAW.

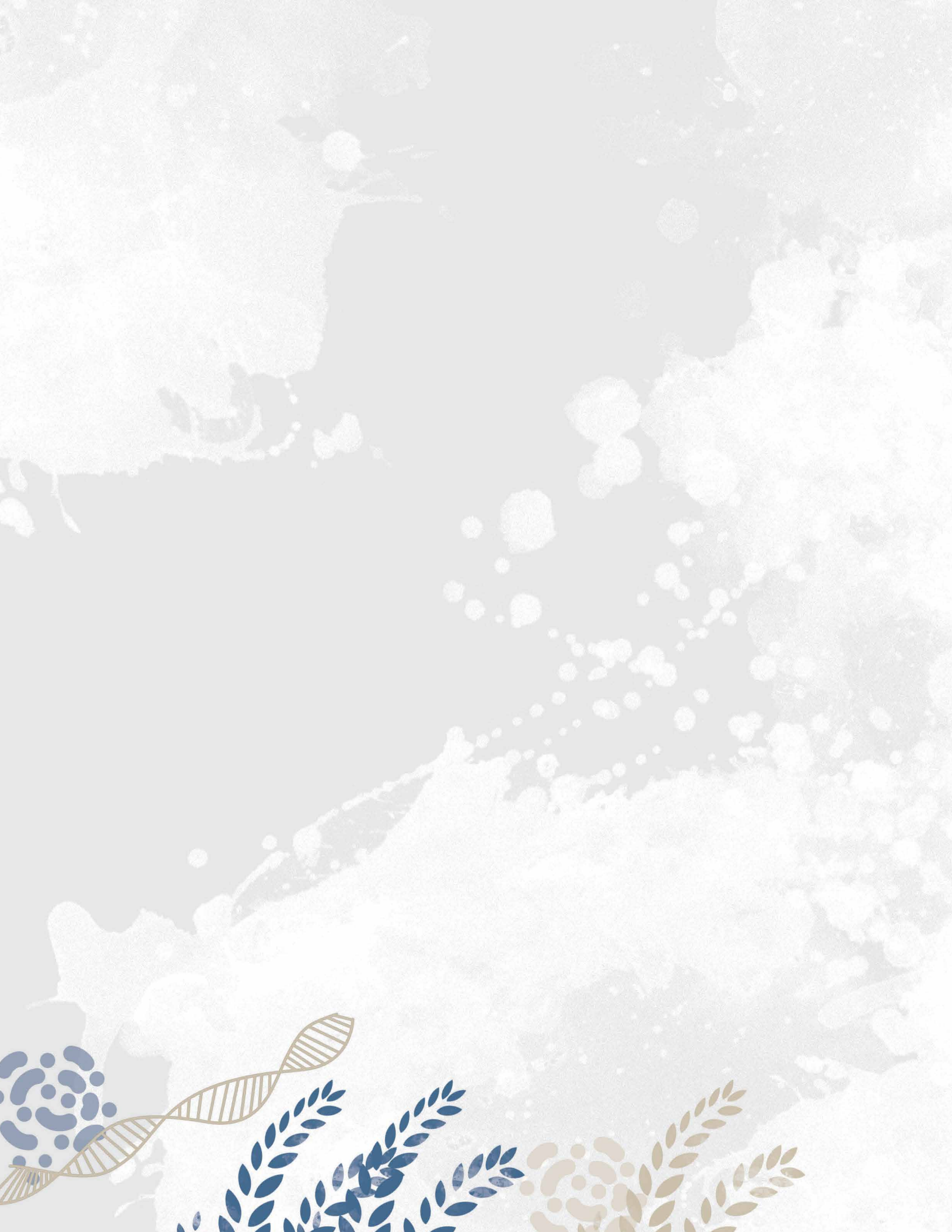
Since the fall season this year, we have developed protocols for conducting field surveys related to assessment of damage, yield loss and insecticide usage patterns. Our approach includes surveillance in major

corn growing areas of Karnataka and assessing the rate of infestation and crop loss due to FAW. We have set-up the infrastructure and are developing protocols for maintaining field-collected FAW under lab conditions for conducting bioassay studies. We will culture FAW to evaluate various combinations of insecticides and finally devise insecticide resistance management strategies.

The findings of our study would provide valuable inputs in identifying key insecticides (rather than broad spectrum insecticides) that can aid in the management of FAW. Based on the insecticide resistance/ susceptibility data, a roadmap can be laid for region specific application of pesticides in Karnataka and elsewhere in India.



Fifth instar Fall Armyworm (Spodoptera frugiperda) and Pest infestation on maize leaf and leaf whorl



Crop Improvement team



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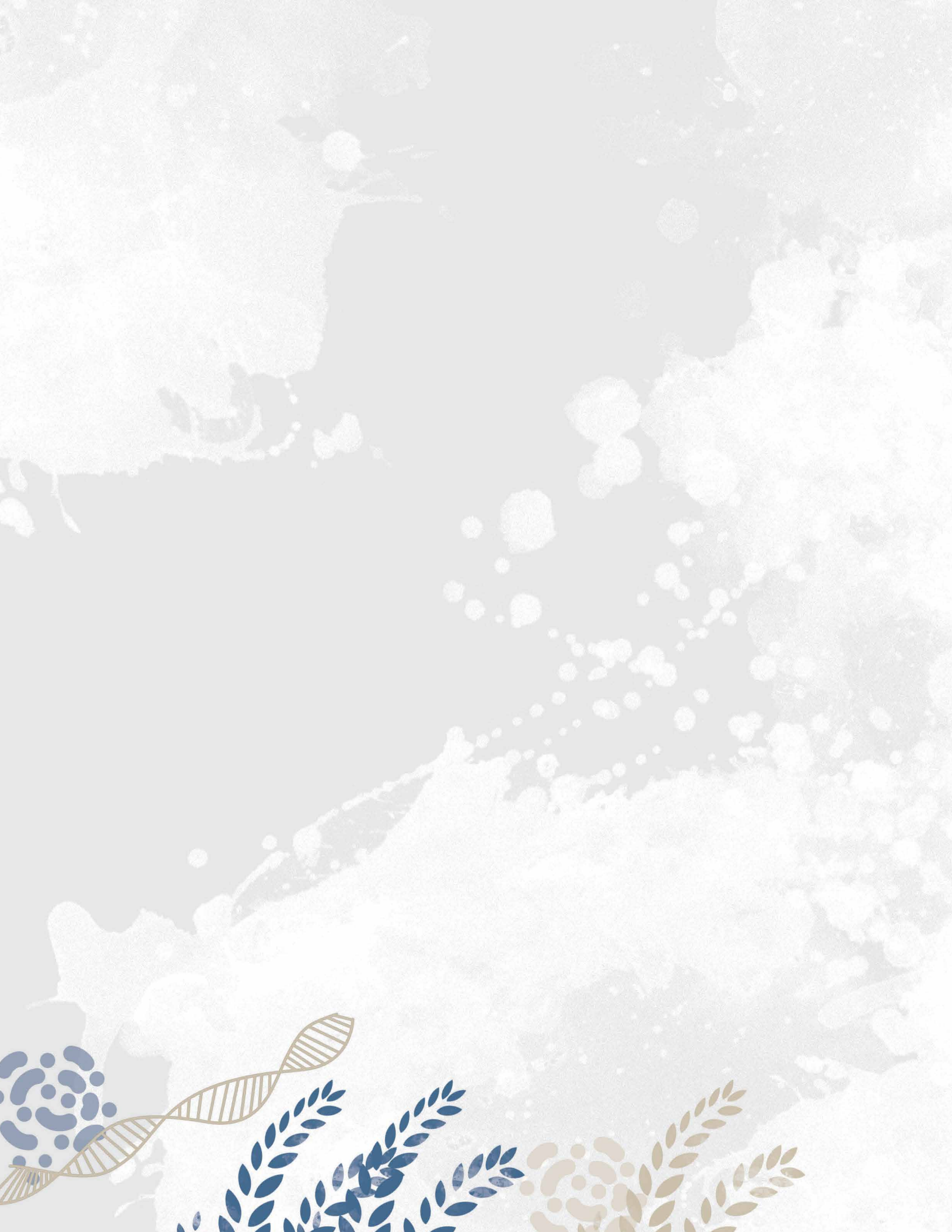
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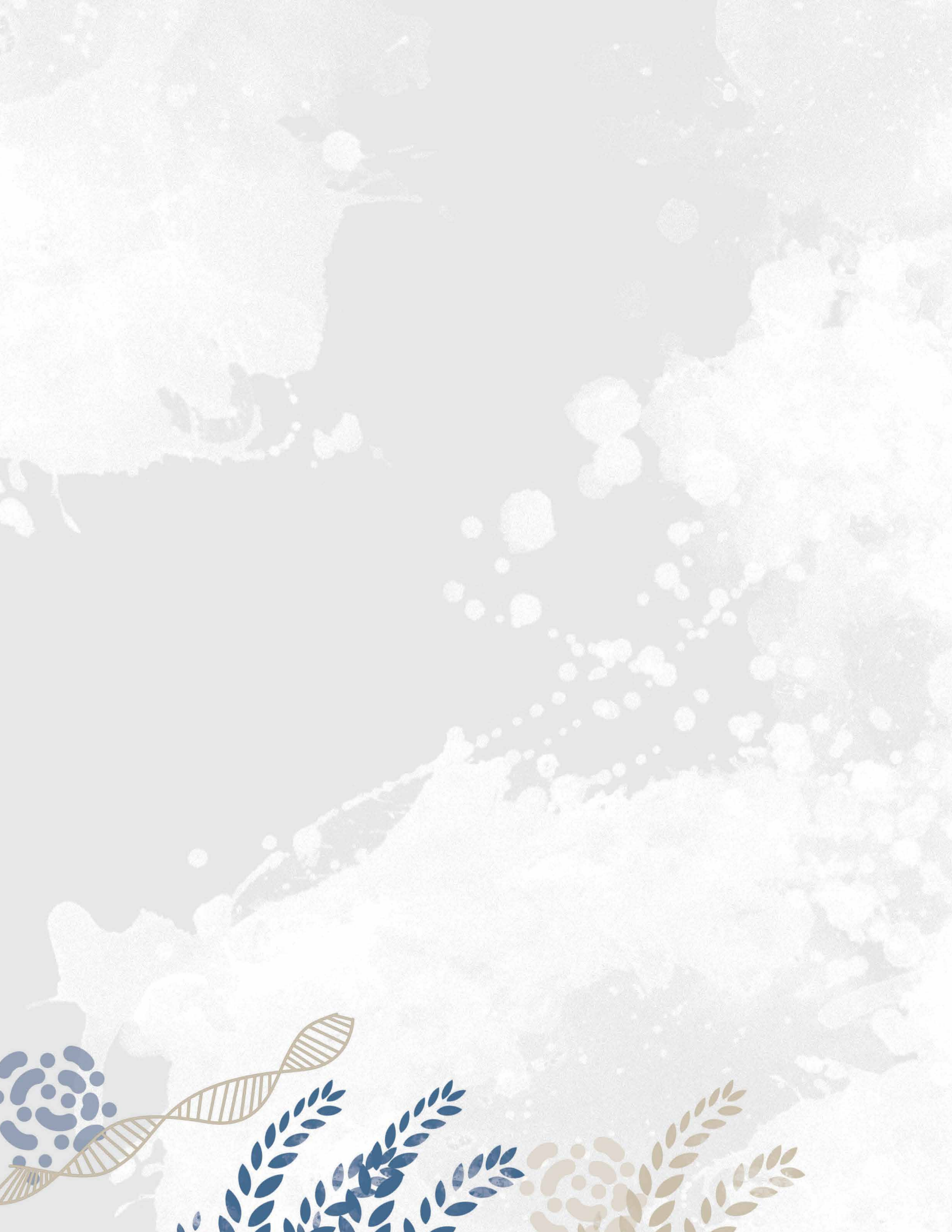
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Technology Platforms



Technology Platforms



Bhagyashree Kaduskar



Harvinder Kour Khera



Rajesh V Iyer



Vasanth Thamodaran

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

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

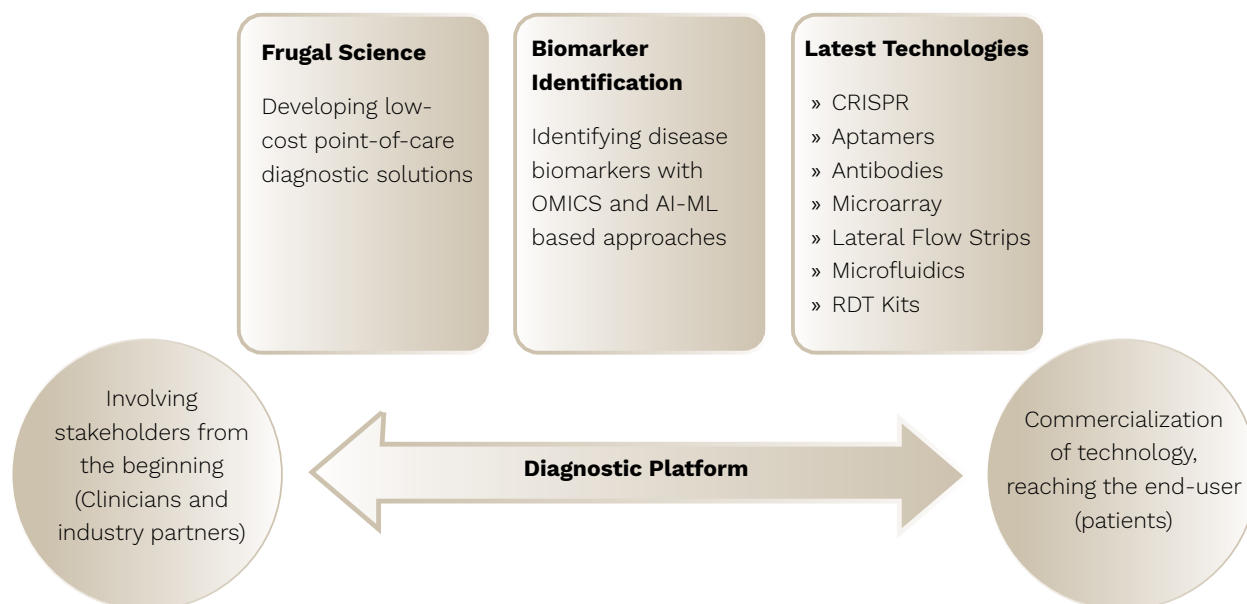
TIGS is working to develop multiple platforms, that include instrumentation and knowledge expertise, in order to accelerate early research for quick transition to the development of a treatment modality. Once developed, these platforms will be open and available as a shared resource for multiple stakeholders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

Diagnostics Development Platform

Molecular diagnostics provides powerful tools for early and more accurate diagnosis of diseases, paving the path towards personalized medicine. Accurate diagnosis is the key to the right treatment, and early diagnosis of a disease is critical for saving lives. Absence of cost-effective diagnostic methods and delayed or

inaccurate diagnosis remain a health care challenge in our country. To address the existing diagnostics gap, we are developing a platform for diagnostic solutions for various infectious and rare diseases using the latest cutting-edge technologies like CRISPR.

Our diagnostics platform is focused on developing novel, low-cost, point-of-care diagnostic solutions suitable for field application in India using the latest cutting-edge technologies such as CRISPR, digital PCR, isothermal amplifications (LAMP and RPA) as well as NGS panels. The aim is to provide innovative solutions for early diagnostics that are rapid, robust, affordable, and accessible to the remotest part of the country.



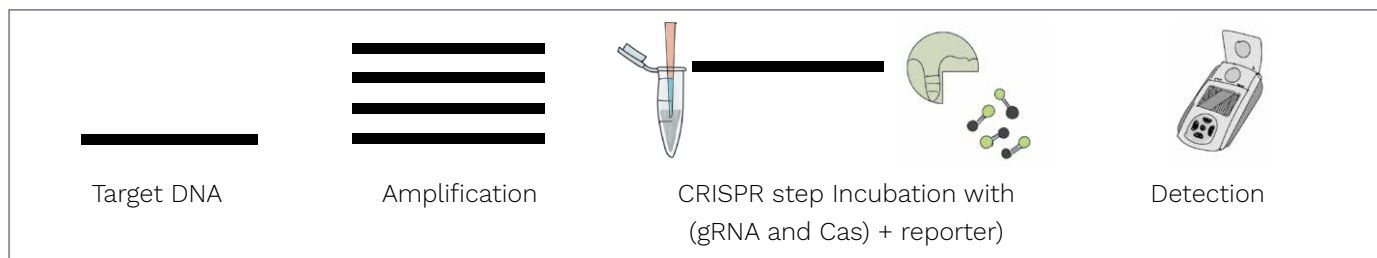
Indigenous point-of-care CRISPR/CAS based diagnostics for infectious and rare diseases

Harvinder Kour Khera

India accounts for 27% of global tuberculosis cases, one fourth of which are drug resistant, and 3% of global malaria cases. There are several disadvantages to the current rapid diagnostic test-based detection of malaria, and drug-resistant tuberculosis detection takes several weeks. At TIGS, we are developing CRISPR-based diagnostic solutions for malaria and tuberculosis.

We have standardized the amplification of target regions for CRISPR-based detection of Malaria and Mycobacterium tuberculosis. We are now working towards improving the sensitivity of the assays in order to detect low parasite loads/copies.

In the case of rare genetic diseases, diagnosis using sequencing or multiplex ligation-dependent probe amplification (MLPA) after the observation of symptoms is quite expensive and requires infrastructure and expertise. Low-cost targeted nucleic acid-based panels would be the approach to overcome this problem. We are currently optimizing CRISPR-based assays developed for the detection of SMA (Spinal muscular atrophy). We are also working towards indigenization of resources to reduce the cost. In this context, we have optimized expression and purification methods to develop in-house generated Cas enzymes.

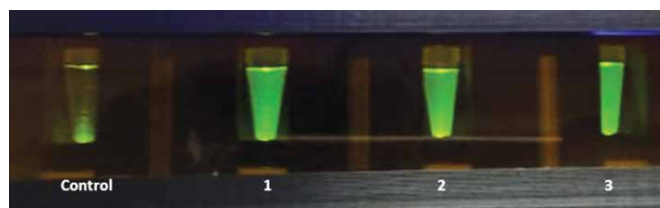


Cas 12a based detection. DNA is extracted from the samples followed by targeted amplification. The amplified DNA is incubated with Cas 12a and single stranded reporter DNA and detected via measurement of the fluorescence released.

Device for rapid visual detection of COVID-19 infection

Harvinder Kour Khera

In a collaborative effort with Enhanced Innovation Pvt limited and BARC, we optimised CRISPR Cas 12a based Covid 19 detection using a low cost CRISPR cube device which can rapidly show a visually detectable color change in infected samples. The device is portable and can run on battery for 24 hours upon single charge. Once approved by the ICMR, the device can be used in low-resource settings for Covid detection.



COVID-19 diagnostic device. A) CRISPR cube device. The device has an isothermal block which can house 12 tubes at a time and a view finder to observe the fluorescence. B) Naked eye detection of SARS-CoV2 using CRISPR cube.

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. As the cells differentiated from patient iPSCs also show the disease phenotype, they are very valuable in drug screening and testing. However, obtaining patient samples has issues of ethical concerns and accessibility. Further, the mutation from a specific patient may not represent the most prevalent disease variant.

Using genome editing, it is now possible to disrupt a gene function by introducing the mutation of interest and to correct a disease associated mutation. Therefore, to study a specific genetic disorder, the mutation of interest can be introduced in the target gene in a pluripotent stem cell derived from a normal donor. Once generated, the cell line can be differentiated to lineages to study disease pathogenesis or drug screening.

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

Vasanth Thamodaran

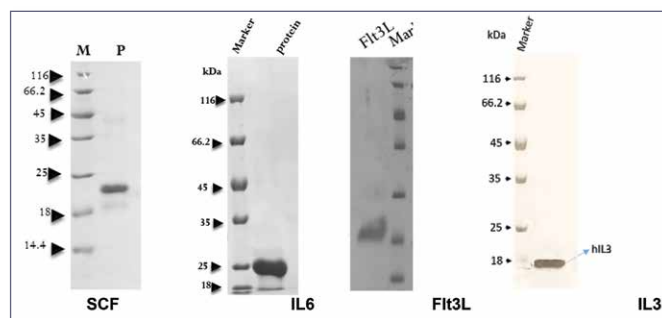
We aim to generate pluripotent stem cell models for lysosomal disorders. Using the CRISPR-Cas gene editing tool, mutations that are widely prevalent in India will be introduced in pluripotent stem cells derived from normal donors. The cell lines carrying the disease associated mutation will then be differentiated to lineages affected by this disorder to study the disease pathogenesis. These disease models

can also be used for testing biotherapeutics and drug screening.

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

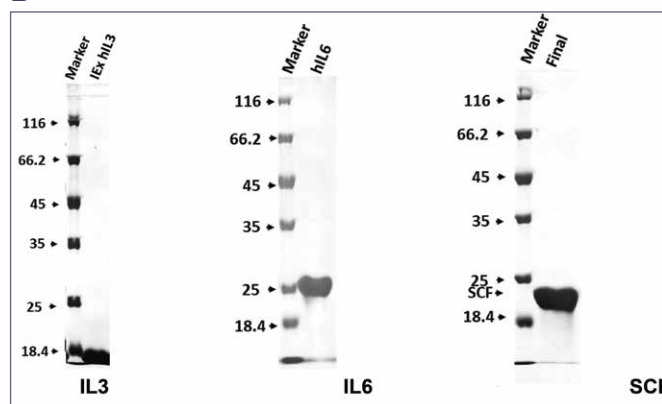
In collaboration with Anirudha Lakshminarasimhan and JSS Medical college (that provides a ready source of cord blood cells from which HSCs are produced), we have successfully expressed the growth factors IL3, IL6, SCF and FLT3L in bacteria, refolded and purified. In addition, three growth factors, IL3, IL6 and SCF, were overexpressed in cytoplasm and purified.

A



Human recombinant growth factors expressed and purified from E.coli. A) Micrographs showing gel images of refolded and purified growth factors, SCF, IL6, FLT3L and IL3.

B



B) Micrographs showing gel images of purified proteins, IL3, IL6 and SCF, that are overexpressed in cytoplasm.

mRNA Therapeutics Platform

Messenger RNAs (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.

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

mRNA-based therapies for the prevention and treatment of infectious diseases

Bhagyashree Kaduskar and Rajesh Iyer

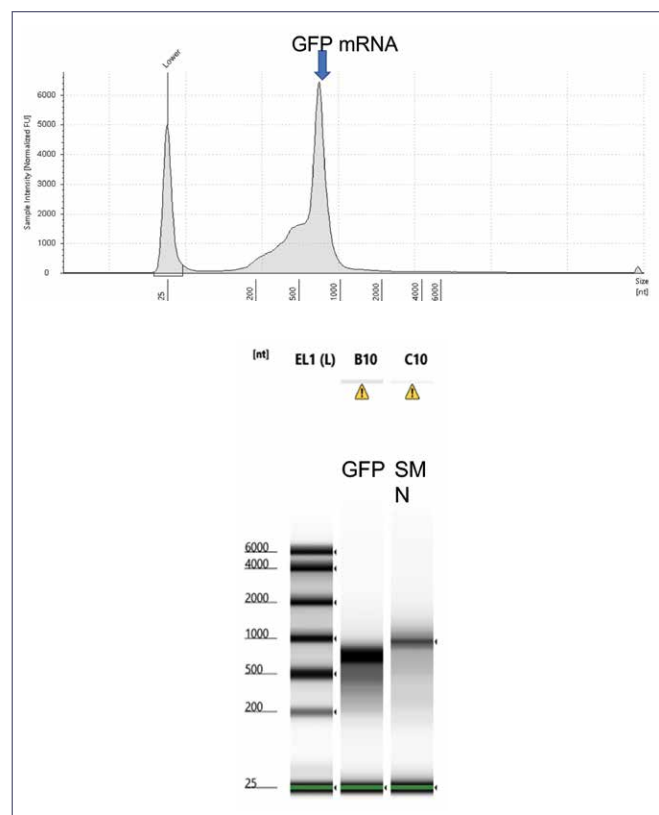
Monogenic rare genetic disorders are a result of loss of protein function. In a few such diseases, intravenous biweekly administration of therapeutic protein has been found to rescue disease symptoms and improve the patient's life. Though effective to a certain degree, these therapies are costly. This cost is primarily due to the cost intensive purification methods to produce therapeutic proteins.

We reasoned that, as an alternative to protein therapy, mRNA encoding therapeutic proteins can be utilized to produce the therapeutic proteins *in vivo*. mRNA production, owing to its synthetic nature, is highly scalable with a relatively smaller footprint which ultimately leads

to affordable therapeutic solution for many diseases.

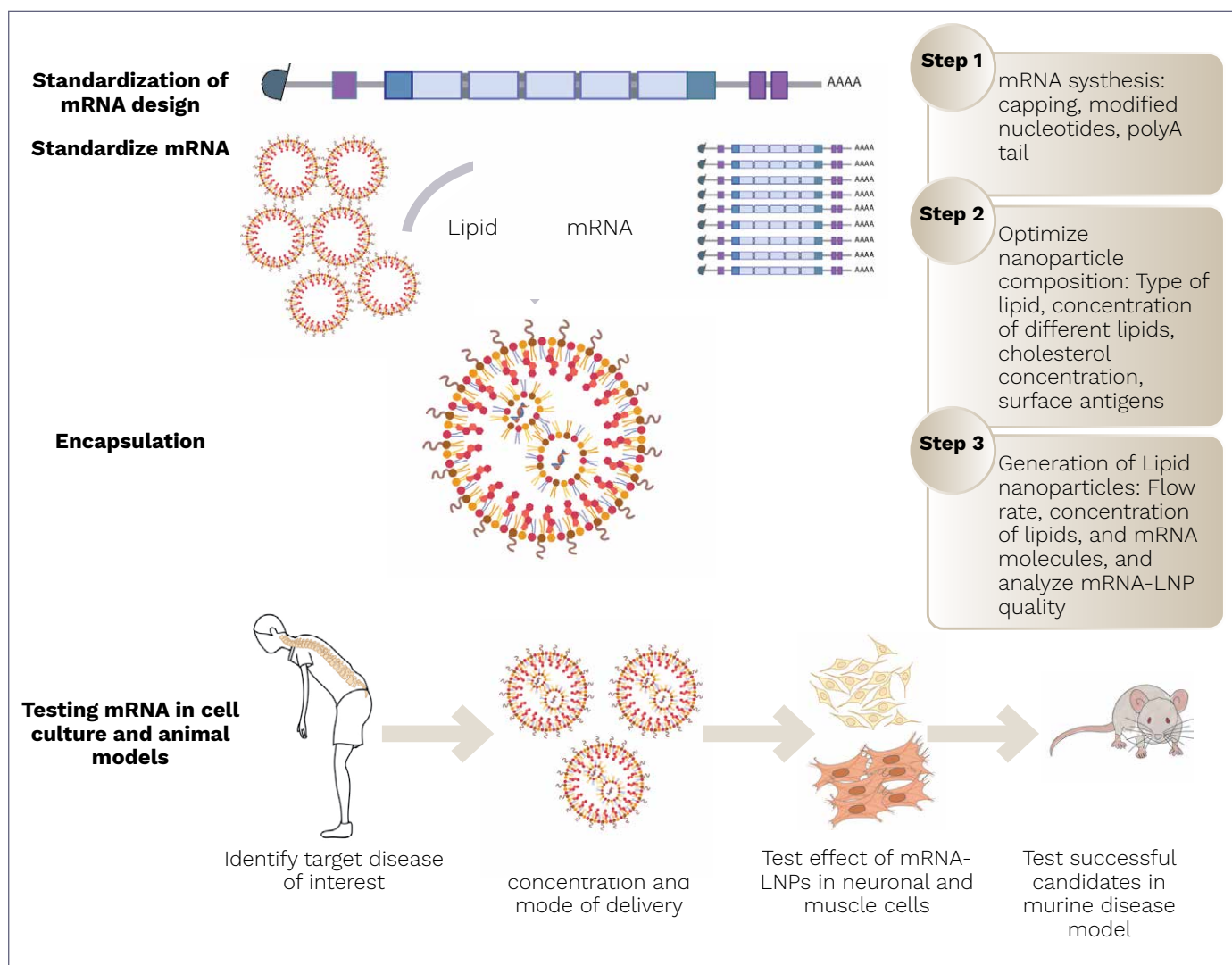
We will begin with the mRNA-LNP particle production and test it on relevant disease models available at TIGS such as SMA patient cell lines.

We have already standardized the mRNA synthesis, purification of mRNA using different kits, capping and polyA tailing.



mRNA: IVT+ Capped+ polyA tailed

This will be followed by setting up a complete mRNA therapy lab including nanoparticle synthesis equipment and particle analyzer as well as the cell culture, mRNA transfections and expression analysis systems needed.



Stepwise process of mRNA lipid nanoparticle synthesis. Also describes the different steps planned for synthesis and testing the novel formulations in cell lines and relevant mouse models.

Technology Platforms team



Ashwathi V
Research Associate



Deepak K J
Research Assistant



Swetha Mariam Stanley
Research Assistant



Sabari Kannan G
Research Assistant



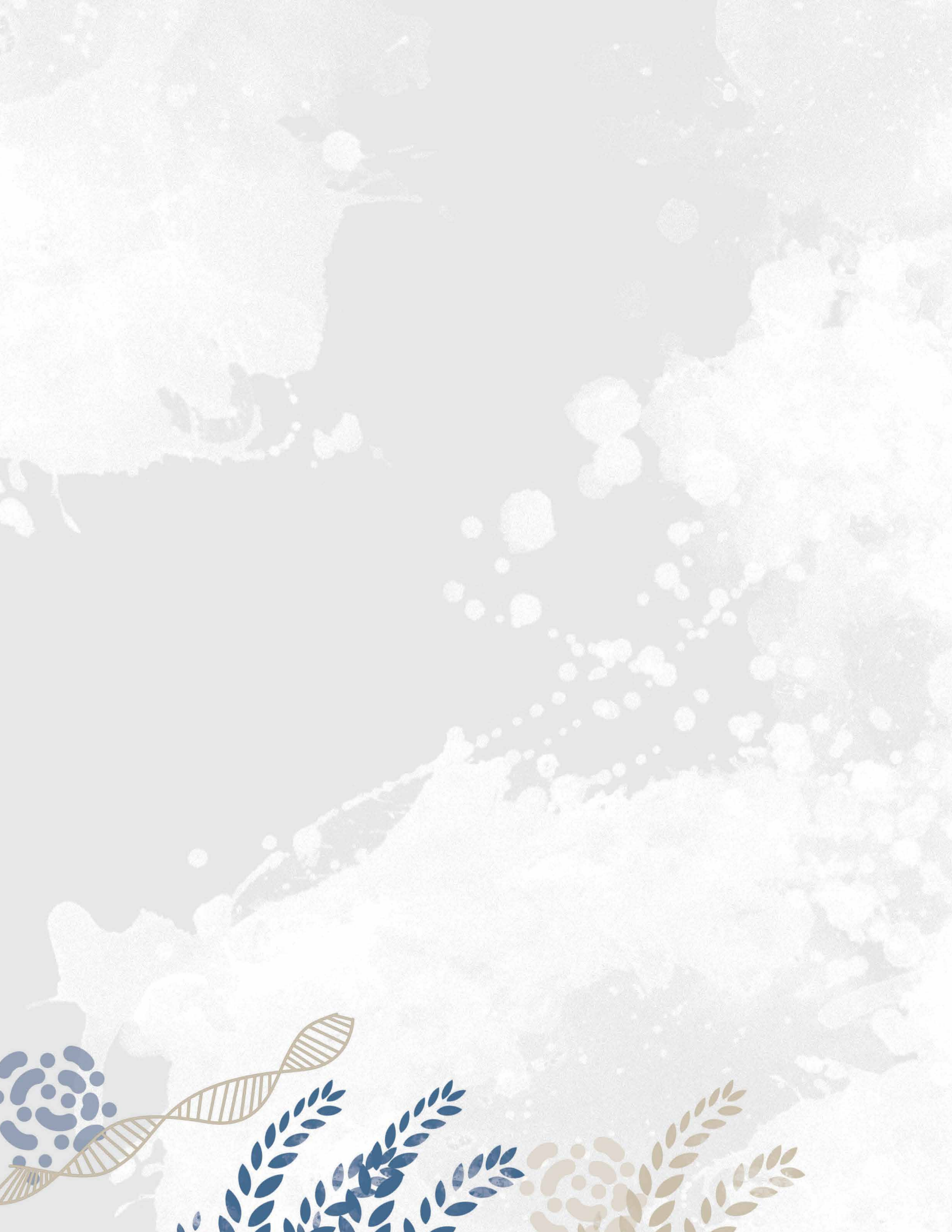
Lenifer Helen D Souza
Research Assistant



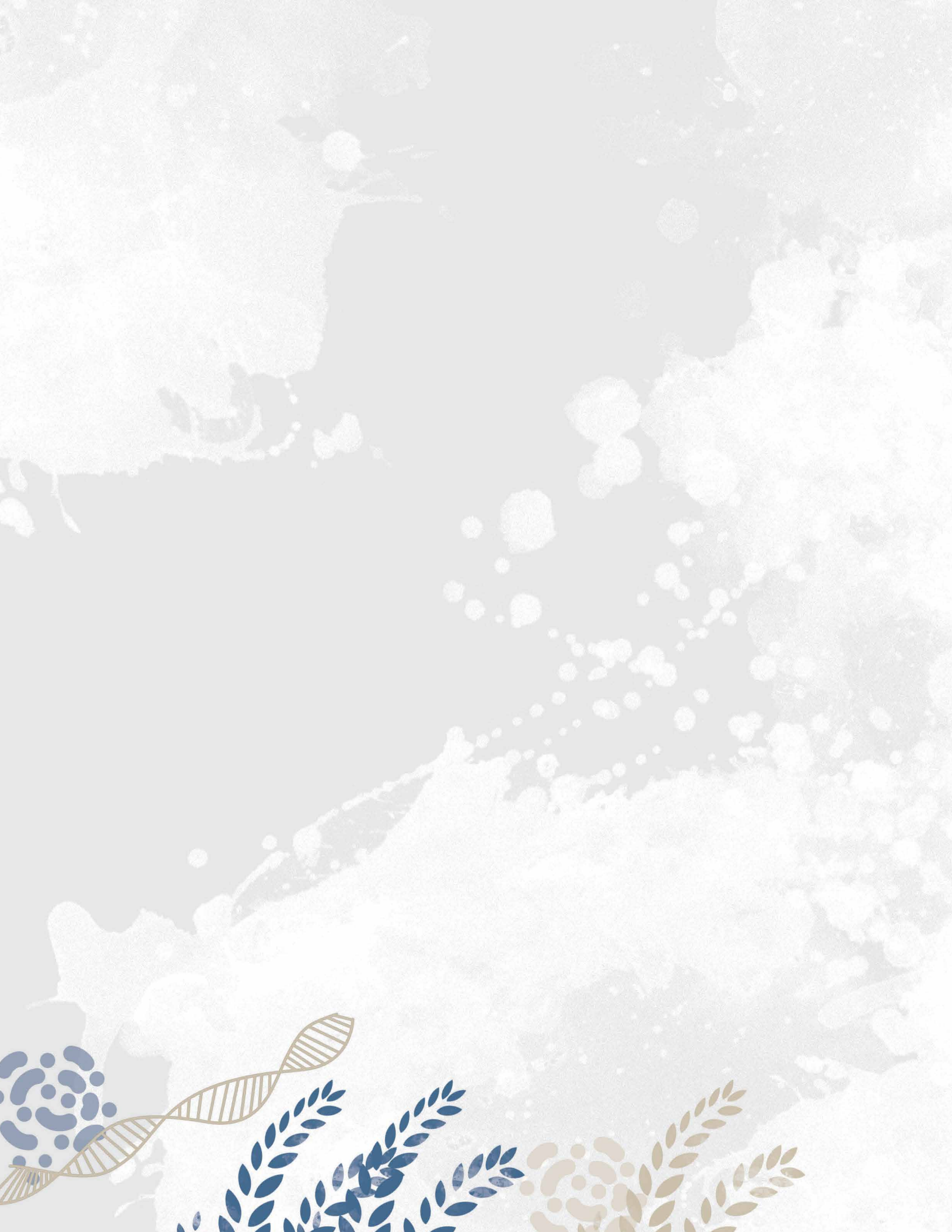
Praveen P
Research Assistant



Lakshmy Venugopal
Research Assistant



Facilities



Facilities



Sunita Swain
Insectary Manager



V S Sresty Tavva
Greenhouse In-charge

Mosquito Insectary

Sunita Swain

Mosquito-borne diseases such as malaria, dengue, Chikungunya, Japanese encephalitis (JE), lymphatic filariasis, and Zika have a significant impact on public health. The development of strategies to control mosquito vectors requires a thorough understanding of their biology, ecology, behaviour, and vector bionomics. TIGS has developed a state-of-the-art Insect Bio-safety Level 2 (IBSL-2) containment facility to support contemporary research on insecticides, repellents, attractants, vector development and physiology, disease transmission, host-parasite/pathogen interactions, life histories studies, population dynamics, behavioural genetics, ecological interactions, and related subjects.

The Insectary is managed by a team of skilled vector biologists. The team provides different services for mosquito-related work, facilitating online interaction of rapid resolution of insectary related queries, requirements and services. Periodic orientation programs as well as trainings and hands-on workshops are planned to allow an expanding network of users to access the Insectary.



Mosquito larval room to rear larvae (aquatic phase of the life cycle)

Mosquito colony maintenance and regular operations

Ten populations of *Anopheles stephensi* and two *Aedes aegypti* are being maintained in the facility.

Aedes albopictus, and a new population of *Anopheles stephensi* from Bangalore were established in Mar-April 2022.

Plasmodium falciparum *in vitro* culture

We successfully completed *P. falciparum* vectorial capacity of 10 populations along with 2 isofemale lines with two duplicates.

Immunofluorescence assay protocols of *Plasmodium falciparum* ookinete stages were standardized using different antibodies.



Standard operations in mosquito adult room, including blood-feeding

Greenhouse Facility

V S Sresty Tavva

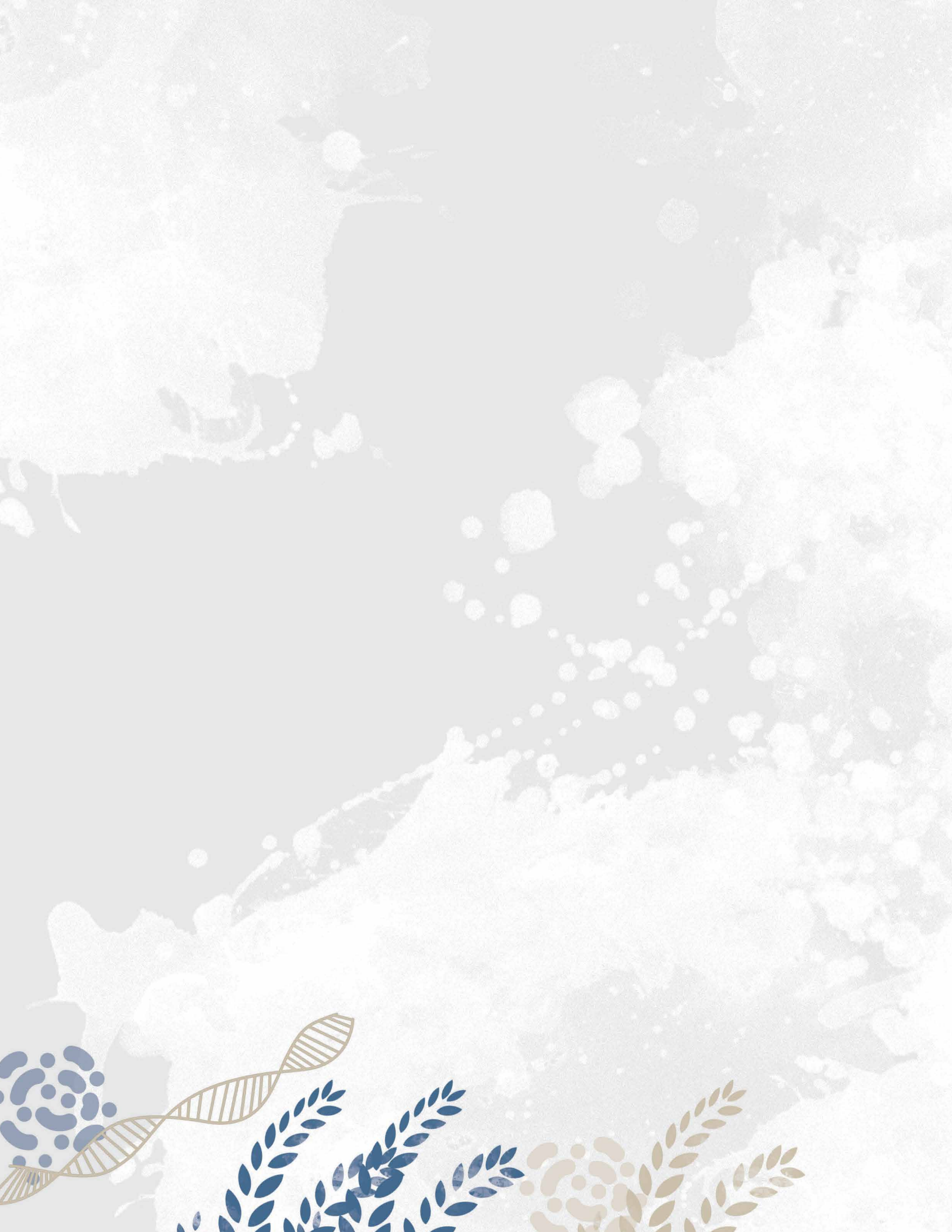
TIGS has a state-of-the-art greenhouse facility for growing transgenic and non-transgenic plants under controlled conditions. The greenhouse is carefully designed to avoid any unintentional transmission of recombinant or synthetic nucleic acid molecules through plant pollen and to avoid any escape and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

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

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



Greenhouse facility with modified plant lines



Facilities Team

Chaitali Ghosh
Assistant Insectary
Manager



Naveen Kumar
Research Associate



Soumya Mogaveerthi
Research Assistant



Chethan Kumar R
Research Assistant



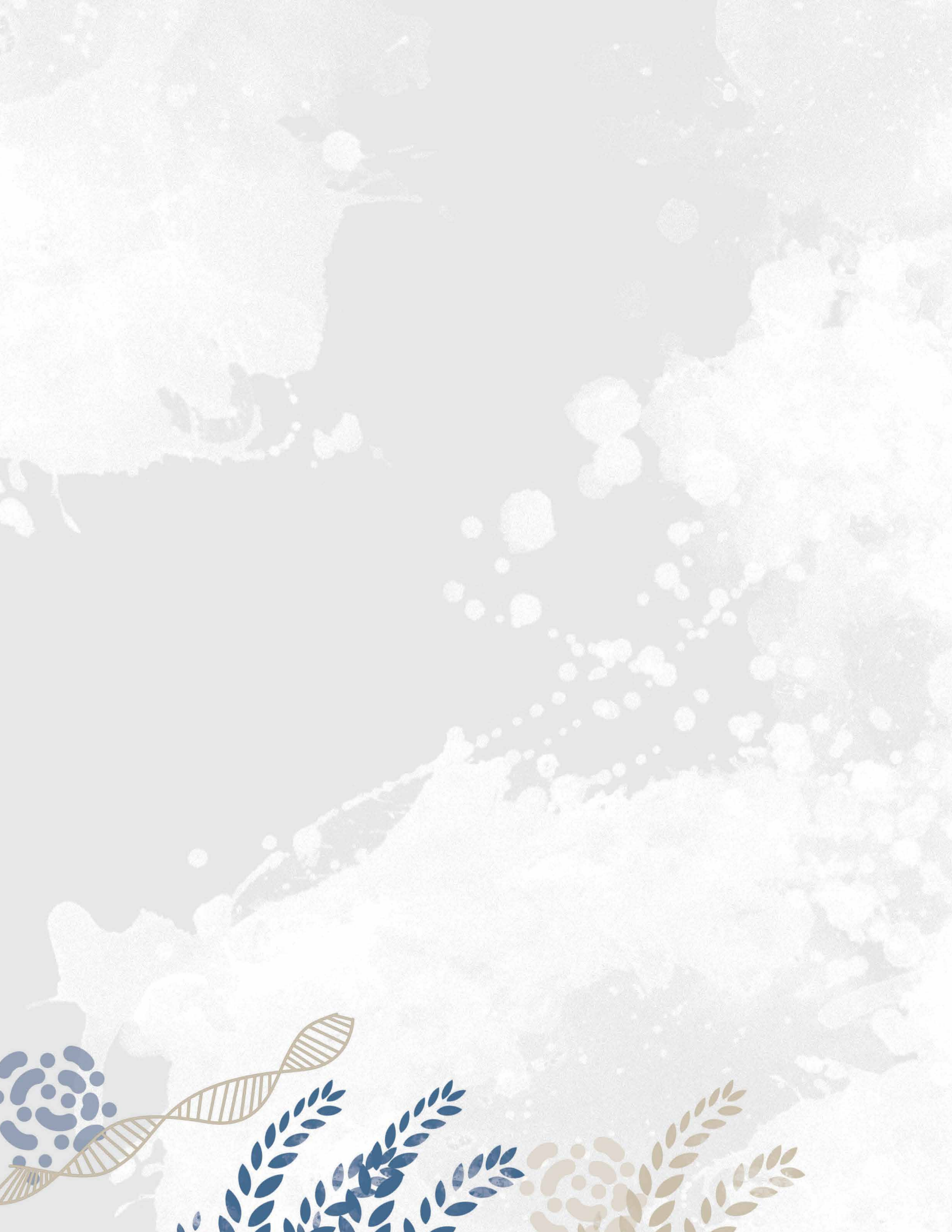
Soumya Gopal Joshi
Research Assistant



Joydeep Roy
Laboratory Assistant



Sanjay M
Green House Assistant



Community Engagement and Outreach

Community Engagement and Outreach



Saveetha Meganathan

The Community Engagement program is central to TIGS' journey in serving the most vulnerable and disadvantaged populations of India using cutting-edge science innovations in the fields of agriculture and health. It is our goal to optimize scientific advancements to the contextual needs through a robust Community Engagement program that entails the development of Information, Education and Communication (IEC) materials for societal outreach, as well as science communication and policy research to create a seamless path towards accessible, low-cost, highly efficient humanitarian technological solutions.

Community engagement for the promotion of humanitarian technology

Saveetha Meganathan

TIGS is driven by a goal to integrate scientific advancements with a holistically developed community engagement program to engage with local communities for achieving health equity and nutrition security. We build socially conscious and ethically bound research programs to develop humanitarian technologies that will systematically benefit, strengthen and serve the Indian society. In this pursuit, we have created a proactive community engagement program that entails amplifying, addressing and allaying community concerns through consistent and clear science communication and engagement with stakeholders at the societal interface. Exploratory and action research projects lead to policy advocacy and better funding opportunities which will have a positive impact on peoples' lives.

TIGS is committed to the dissemination of scientific knowledge to differently literate communities using innovative tools, thereby attaining social inclusion to processes of scientific advancements. We build trust with communities, network with humanitarian groups, develop coalitions and networks to create communication channels to share resources, and enable efficient technology transfer to stakeholders. It is evident from global scientific research practices that community engagement is a very relevant process and reinforces positive impact when there is a need to address complex societal challenges. Such dynamic and socially serving scientific research can become a model for scaling technological solutions to address issues faced by developing countries

TIGS is a unique and pioneering research institute in India that serves as a catalyst to bring forth pathbreaking developments that impact people's lives in the following areas:

i) epidemiological surveillance and development of affordable and efficient health care technologies for infectious diseases, ii) cost efficient precision diagnostics and therapeutic treatments for rare genetic diseases, and iii) developing nutrient rich local food crop varieties that can be a solution to impending threats of droughts and famines.



Webinars and lectures

TIGS is mandated to enable cutting edge science to solve societal challenges. In our efforts to develop a science-based environment for societal benefit, we have created a monthly webinar series that brings together stakeholders and experts to engage in knowledge sharing and to discuss evidence-based science of direct value to society.

14,000+
Engagement
5,200+
Attended

In the past year we have organised several webinars on a variety of topics.

1. Rare Disease Day, 28th Feb 2022

About 5000-8000 types of rare diseases have been documented all over the world, and 450 of them are identified in India. Most of these diseases have a genetic origin. Almost 95% of them have no approved treatments, and less than 1 in 10 patients receive treatments that are disease-specific. These are some of the challenges that 72-96 million people who are likely affected by rare diseases in India need to navigate. A webinar highlighting the rare diseases scenario in India was held on 28th February 2022



L - R. Dr. Meenakshi Bhat, Associate Director, Centre for Human Genetics, Bengaluru; Dr. Sanjeeva GN, Associate Professor, Indira Gandhi Institute for Child Health, Bengaluru; Dr. Rakesh Mishra, Director TIGS

Rare Disease Day Webinar

The International Rare Diseases day is observed on the last day of February each year to raise awareness about 5000-8000 types of rare diseases that have been documented globally, and around 450 of these are the most commonly described. 80% of these disorders are genetic in etiology and at least half of them affect children. Less than 5% of these disorders have a definitive treatment. In India, many strides have been taken to look for innovative methods of diagnosis and treatment.

Join our webinar to hear from the experts.

Feb 28 2022 6.30 PM

Speakers:
 Dr. Meenakshi Bhat, Associate Director, CHG
 Dr. Sanjeeva GN, Associate Professor, IGCH
 Dr. Rakesh Mishra, Director TIGS

Moderated by:
 Dr. Rakesh Mishra, Director TIGS

Scan QR Code to register

The aim of the webinar was to create awareness regarding recent developments in the field, and the panel of experts discussed the challenges and new strategies for the diagnosis and treatment of rare diseases.

2. TB - The Silent Killer - Understanding Disease dynamics, Diagnostics and Treatment, 31st Mar 2022

TIGS
Tata Institute for Genetics and Society

Webinar on
TB - The Silent Killer
 Understanding Disease dynamics, Diagnostics and Treatment

Dr. Vinay Nandicoori
 Director, CSIR - CCMB
 Transcriptional regulation in M. tb

Dr. Sadhna Sharma
 Professor & Head, Biochemistry, PGIMER, Chandigarh
 Implications of nanomedicine-based therapy against Tuberculosis

Dr. Varadharajan Sundaramurthy
 Faculty, NCBS
 Cellular determinants of M. tuberculosis entry and intracellular survival pathways

Dr. Urvashi Singh
 Professor, Department of Microbiology, AIIMS Delhi
 Diagnostic Challenges for TB Treatment Decisions

Dr. Rakesh Mishra
 Director, TIGS
 Welcome Address

March 31 2022 3 PM

Scan to Register

24th March (World Tuberculosis Day) marks the discovery of Mycobacterium tuberculosis (M.tb), that causes the deadly disease Tuberculosis (TB), by Dr. Robert Koch in 1882. According to the World Health Organization (WHO), each day about 28,000 people are infected with TB and 4100 lose their lives to this deadly disease. India accounts for a majority of the TB burden across the globe. Increasing drug resistance is a major challenge for TB elimination. This year the theme of TB Day was 'Invest to End TB. Save Lives,' and our panel of experts discussed the need, ways and means to invest more in TB research, diagnostics, and treatment.



L - R. Dr. Rakesh Mishra, Director TIGS; Dr. Sadhna Sharma, Professor & Head, Biochemistry, PGIMER, Chandigarh; Dr. Urvashi Singh, Professor, Department of Microbiology, AIIMS, New Delhi; Dr. Varadharajan Sundaramurthy, Faculty, NCBS, Bengaluru; Dr. Vinay Nandicoori, Director, CSIR - CCMB, Hyderabad

3. Haematological Disorders: Therapeutics and Disease Modelling, 19th April 2022



According to the National Health Mission India, 7% of the world's population has an abnormal manifestation in haemoglobin with 70% of it constituting sickle cell anaemia. In India, sickle cell anaemia has a high prevalence, reaching up to 48% in certain indigenous (Adivasi) communities. Access to diagnosis and treatment for the afflicted population has been a challenge, thereby increasing their vulnerability and impacting their health.

Therapeutic options to manage blood disorders range from administering therapeutic drugs to gene therapy. The panel of experts discussed how not all patients respond to treatment equally and disease models can offer insights on varying disease pathogenesis that can enable the development of better treatment/therapeutic options.



L - R. Dr. Dipty Jain, Retd. Professor and HOD, Department of Paediatrics, Government Medical College, Nagpur, and Nodal Officer, CSIR Sickle Cell Mission Mode Project ; Dr. Rakesh Mishra, Director TIGS; Dr. R V Shaji, Professor, Department of Haematology, CMC, Vellore and Adjunct scientist, Centre for Stem cell Research (a unit of DBT - inStem)

4. Huntington's Disease: From bedside to bench and back, 30th May 2022



HD is a brain disorder that affects all parts of brain function, and thus leads to physical, cognitive, and emotional symptoms. There is gradual loss of brain cells in certain parts of the brain, specifically the basal ganglia and the cerebral cortex. All the important domains of brain function such as cognitive abilities (thinking, judgement, and memory), physical abilities and emotion control get affected, although in a staggered and unpredictable manner during the course of the disease. These symptoms, typically, begin between the ages of 35 and 55 by which time most persons have already had children and so the disease continues to be transferred to the next generation. Besides, the symptoms can first occur in children (Juvenile HD, which is often more severe), or the elderly as well.



L - R. Dr. Sonia Sen, Senior Scientist, TIGS; Dr. Meera Purushottam, Senior Scientific Officer, Molecular genetics laboratory, Department of Psychiatry, NIMHANS Bengaluru and Joint Secretary, Huntington's Disease Society India; Dr. Sheeba Vasu, Associate Professor, Neuroscience Unit, JNCASR Bengaluru; Dr. Sanjeev Jain, Professor, Department of Psychiatry, NIMHANS and Co-chair, Huntington's Disease Society India with Dr. Rakesh Mishra, Director TIGS

5. Wastewater-based epidemiology (WBE): SARS-CoV-2 & beyond, 31st May 2022



Wastewater-based epidemiology (WBE) is an important tool to understand infectious disease prevalence in a particular geographical area or community. During the COVID-19 pandemic, WBE has been extensively used by health authorities and researchers from several countries, including India, to keep a track on the progression of SARS-CoV-2 infection. It is found that both symptomatic and asymptomatic patients shed viral fragments through the faeces. The viral RNA load in the human waste, which is collected as sewage or wastewater, can be used as a readout to estimate the prevalence of the disease in the community.

The panel of experts discussed WBE and its advantages, such as development of assays, cost-effectiveness, and an unbiased approach towards public health. By harnessing the power of statistics and modelling, it is now possible to have a real-time approach towards building robust prediction models, which can help health authorities to take informed decisions. WBE approach has been used to tackle diseases such as polio in the past, and with increasing awareness due to the current pandemic, can be employed for other infectious diseases to come up with effective solutions to achieve better public health outcomes.



L - R. Aparna Keshaviah, Principal Researcher, Mathematica; Dr. Madhavi Joshi, Scientist-D & Joint Director, Gujarat Biotechnology Research Centre; Dr. Rakesh Mishra, Director TIGS

6. Striking the right balance for sustainable pest management, 24th June 2022



The history of conflict between humans and insect pests dates back to 2500 BC when Sumerians used sulphur compounds to control mites. The rampant use of synthetic insecticides after World War-II led to the disruption of the ecological balance and had a direct impact on food security for humankind. With time, several strategies have evolved which aim to mitigate such conflicts in the most amicable and sustainable manner. Several physical, chemical, and biological control methods have played their respective roles in shaping the principles of sustainable pest management.

Integrated Pest Management (IPM), an ecosystem-based strategy, came to the fore during the 1970s with the principle aim of combining different pest management methods and resorting to only need-based chemical pesticides, thus ensuring the protection of wildlife, human health, and the environment in a holistic manner. This webinar brought together experts to share recent advances made by carefully examining different facets of pest problems and developing stepwise approaches to manage them. Current strategies were discussed, that combine accurate knowledge of the pests, the level of potential harm caused by them, and their natural mortality factors with multiple tactics to prevent, reduce, or eliminate their effect on the ecosystem.



L - R. Dr (Ms.) Chandish R. Ballal, Former Director, ICAR-NBAIR; Dr. Rakesh Mishra, Director TIGS; Dr. K Murali Mohan, Professor, Department of Entomology, UAS GKVK Bengaluru

7. Rare Diseases in India, 15th July 2022



There is no standard definition for rare diseases. They often manifest at an early age and are genetic in nature, affecting more than 350 million worldwide and ~ 70 million in India. There is a need to prioritize and accelerate diagnosis and treatment options for patients with rare diseases. Especially in India, children suffering from these disorders often do not receive the right diagnosis for many years, affecting their quality of life and possibility of availing therapeutic options, if any. TIGS signed an MoU with the Organization for Rare Diseases and organized a discussion to unravel a few pertinent themes on the rare genetic disorders landscape in India.

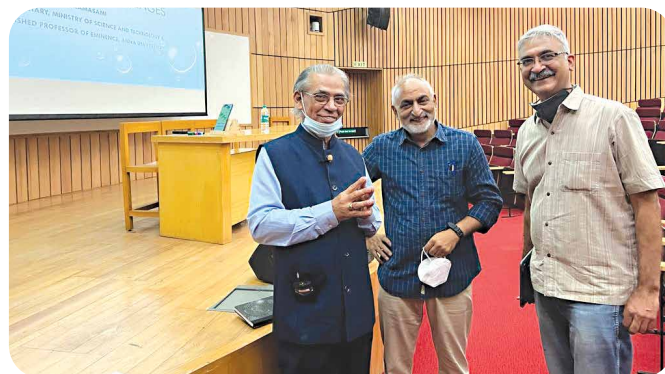


L to R: Dr. Jyoti Bajpai Dixit, Consultant ORDI; Dr. Dipanjana Datta, Consultant ORDI; Mr Prasantha Shirol, Founder & Executive Director, ORDI and Dr. Sudheendra Rao NR, Scientific Advisor, ORDI

8. Science and Technology: For Low Resource Setting and Coping with Diversity Challenges, 22nd August 2022



This lecture was part of the visit by Dr. T Ramasami where he cited several examples of how policy initiatives helped to foster the Science, Technology, and Innovation landscape in India. The formulation of such policies has been made prioritizing socioeconomical welfare and via a bottom-up approach. His talk also explored various schemes which were introduced during his tenure at the Ministry of Science and Technology such as INSPIRE, PURSE etc. which helped to strengthen the S&T ecosystem in India. After the lecture, Dr. Ramasami toured various labs and facilities at TIGS and interacted with the researchers and shared anecdotes from his 4 decade long illustrious career.



L to R: Prof Ramasami, Former Secretary, Ministry of Science and Technology, GoI, Recipient of Padma Sri and Padma Bhushan from the President of India with the staff at TIGS; Prof T Ramasami, Dr. Rakesh Mishra, Director TIGS; Dr. Satyajit Mayor, Director NCBS

9. Making grassroots mind matter: Leveraging community knowledge, 8th November 2022



PROF. ANIL GUPTA

Visiting Faculty
 • IIM Ahmedabad
 • IIT Bombay
 • NIPER Ahmedabad
 • ACSIR Academy Professor

Founder
 • The Honey Bee Network
 • National Innovation Foundation (NIF)
 • Society for Research and Initiatives for Sustainable Technologies and Institutions (SRISTI)
 • Gujarat Grassroots Innovation Augmentation Network (GEAN)

• CSIR Bhatnagar Fellow 2018 - 2021
 • Recipient of Padma Shri from the President of India in 2004



Public Talk

MAKING GRASSROOTS MIND MATTER:

LEVERAGING COMMUNITY KNOWLEDGE

8th November 2022
3 PM

Auditorium (100seater)
inStem Building
NCBS campus

Scan to register

Blending formal and informal science is necessary to leverage people's knowledge for developing viable solutions to many societal problems. Often, a question is asked as to why knowledge-rich communities remain economically poor if their knowledge system is good. The answer lies in the institutional culture which makes traditional knowledge holders share their knowledge openly and freely, without insisting on any reciprocity and even bearing the cost themselves. The Honeybee Network, 35 years ago asked a question; should grassroots innovators and traditional knowledge holders remain poor because they are generous, and we become rich because we are stingy?



Prof Anil Gupta delivering his talk on Making grassroots mind matter: Leveraging community knowledge at TIGS

Unfortunately, scholars continue to publish even unique knowledge without prior informed consent and protecting the IPRs of the communities/TK holders. Prof Anil Gupta, Visiting Faculty IIM A, NIPER A and IIT B and Recipient of the Padma Shri by the President of India, Founder of the Honeybee Network spoke about how we can correct the asymmetry in rights and responsibilities among institutional scientists towards traditional knowledge holders and grassroots innovators



Prof Anil Gupta with the staff of TIGS



ScienTIGS

- recurring monthly meeting at TIGS

ScienTIGS is a recurring monthly at TIGS involving work presentations for regular institutional scientific discussions.

The presentations and discussions include

- » Work updates specifically in the ongoing research projects
- » Brainstorming on certain experimental procedures or protocols
- » Ideation of future/experiments in the context of the ongoing research activities and Suggestions for assembling manuscripts (if any).

This activity aims to keep all the scientific staff at TIGS updated with the research being conducted across all the domains and help one another with feedback, inputs, and suggestions.

Conversations@TIGS

As part of our community engagement program, we started a podcast series Conversations@TIGS, that focusses on communicating our research on topics of value to society and the general public.

Episode 1 - Vision of TIGS



In the first episode, the Director Dr. Rakesh Mishra talked about our vision and the various research programs undertaken at the Tata Institute for Genetics and Society. TIGS is committed to making scientific advances in research on human health and agriculture to benefit India and its population.

Episode 2 - How SARS-Cov-2 Spreads around in the air



The Director Dr. Rakesh Mishra spoke about how the SARS-CoV-2 particles are suspended in the air. He highlighted the work done on studying the virus dynamics at hospitals and residential areas that shows how the virus particles spread out while people interact in the environment. The study is published in the Journal of Aerosol Science.

Episode 3 - Watching Wastewaters to Predict Pandemic Outbreak

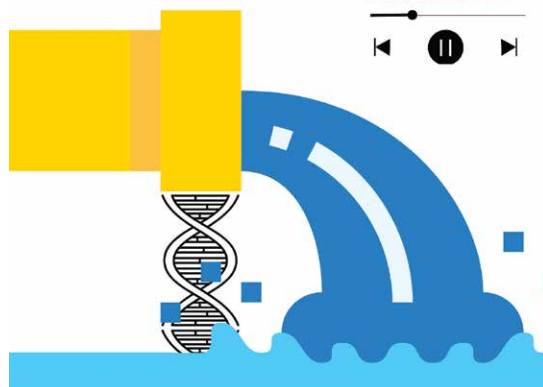


Conversations @ TIGS | Episode 3

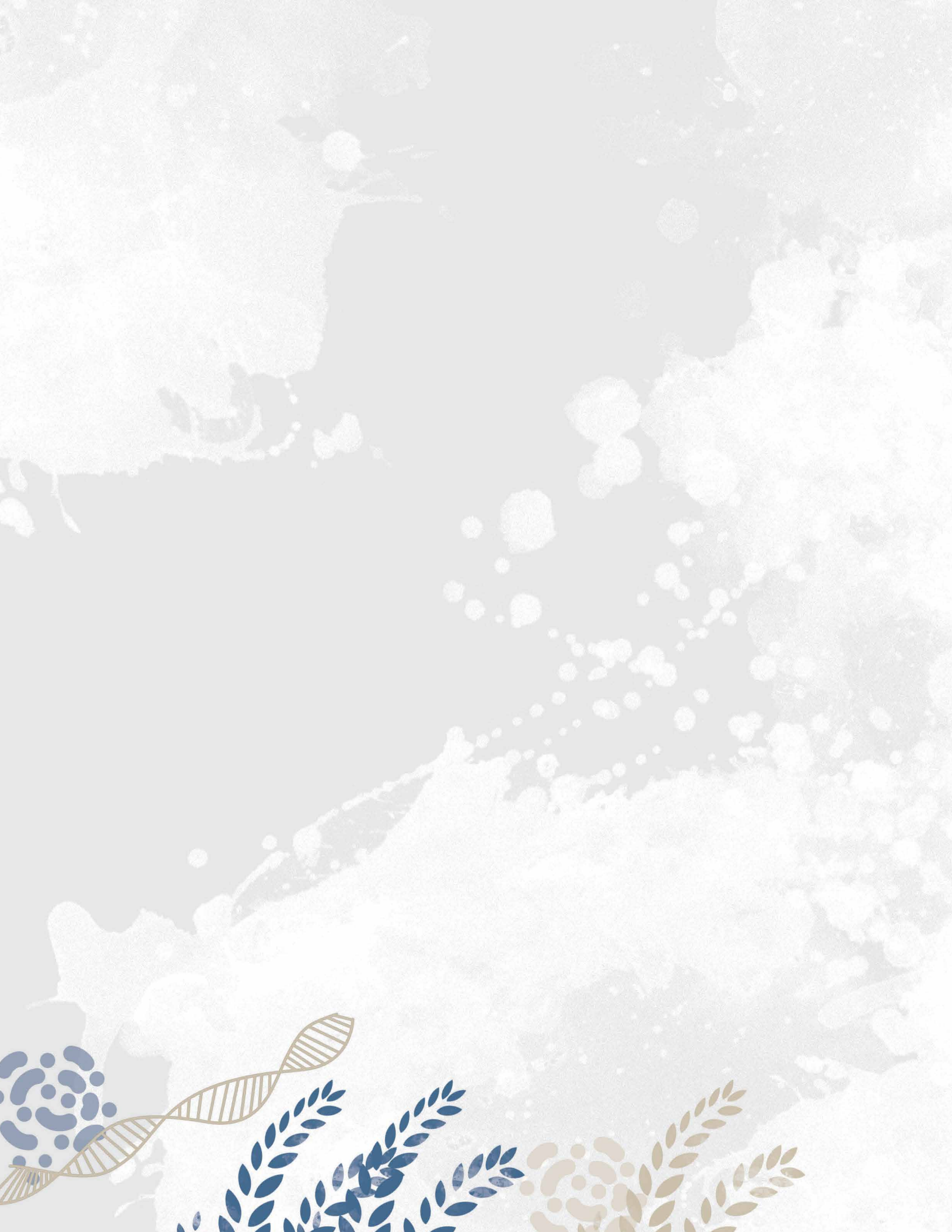
Watching wastewaters to predict pandemic outbreak



Dr. Farah Ishtiaq
Principal Scientist, TIGS



Principal Scientist Dr. Farah Ishtiaq explained how sewage surveillance helps to understand the health of a community and what can be done to improve the public health system. Using genomic sequencing, wastewater samples are tested for pathogens which can inform about the viral load, and even the variants of the virus. Wastewater based epidemiology is an early warning tool for any pandemic or public health emergency. In this episode, Farah talked about her experience in analyzing the wastewater of Bengaluru city from open drains and sewage network.



Collaborative Networks

Multi-stakeholder engagements

At TIGS we believe in developing collaborations with multiple stakeholders so that research is application-oriented and dispersed where it is needed. Sharing of infrastructure and expertise also significantly reduces costs of taking technology to society. Connecting with the end-users allows for a nuanced understanding of societal challenges for which cutting-edge science can be used to bring forth a sustainable solution which is affordable, efficient and relevant to the vulnerable and resource-poor communities in need.

Integration of TIGS into the Bangalore Life Science Cluster (BLiSC)

Bangalore Life Science Cluster (BLiSC) is a unique hub of excellence in biological research in India. BLiSC was created with the aim of developing best practices for inter-institutional collaborations. This year, TIGS became an integral part of BLiSC, comprising the National Centre for Biological Sciences (NCBS), Institute for Stem Cell Biology and Regenerative Medicine (inStem) and Centre for Cellular and Molecular Platforms (C-CAMP). True to our mandate, we collaborate closely with academic as well as non-academic institutions to find solutions to the problems faced by our country. We look forward to developing synergistic associations within the Bengaluru cluster that will have a larger impact on life sciences research than the sum of individual contributions from each institution. As a distinct entity within BLiSC, 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.



TIGS was integrated as the fourth member of the Bangalore Life Sciences Cluster (BLiSC) on 21st March, 2022.

L to R Mr. L C DAS, MD Social Alpha, Prof Uma Ramakrishnan, Head Outreach and Communications, NCBS, Prof. Satyajit Mayor, Director, NCBS, Mr. Manoj Kumar, CEO Social Alpha, Dr. Taslimarif Saiyed, CEO, C-CAMP, Dr. Rakesh Mishra, Director TIGS, Dr. Aravind Ramanathan, Head of Research, inStem, Dr. K Thangaraj, Director CDFD

Over the past year, we have developed several research initiatives within the BLiSC ecosystem, including city-wide wastewater based epidemiology, and dengue detection via RNA-based sensor systems with NCBS, cell-based therapeutics and diagnostic assays for rare genetic disorders with inStem, as well as technology projects with start-ups incubated at C-CAMP.

TIGS is a new entrant in the AcSIR Ph.D program

TIGS is proud to host a PhD program in collaboration with the Academy of Scientific and Innovative Research (AcSIR). We aspire to create the next generation of innovators through research and a pedagogical curriculum designed to harness modern advancements in science and devise novel solutions for the most pressing needs of our society.



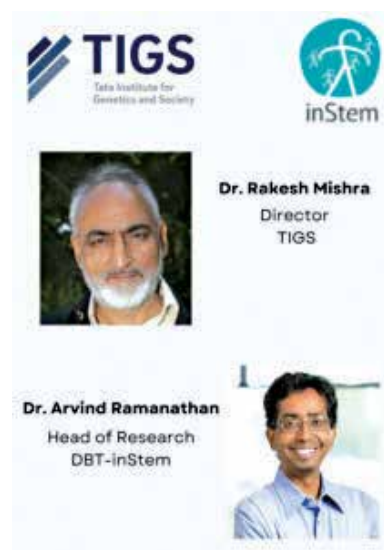
We have opened admissions for candidates for our graduate program, for the January and August 2023 sessions. Students interested in using genetics, technology, engineering principles, or computational skills in addressing issues plaguing human health and agriculture can now join our program to obtain experience in research that can translate into direct societal benefit.

TIGS and inStem join hands to work on rare genetic diseases

Vasanth Thamodaran and Arvind Ramanathan

TIGS has joined hands with the Institute for Stem Cell Science and Regenerative Medicine (inStem) to work together towards addressing some of the unmet needs in treating rare genetic diseases, particularly neuromuscular diseases. Teams from both institutions will focus on developing cost-effective diagnostics and disease modelling platforms that enable drug screening for rare genetic diseases.

Since early and accurate diagnosis of rare diseases have a significant impact on the disease prognosis, rapid point-of-care diagnostics can greatly help clinicians and families strategize the management of the disease. We aim to initially build a platform that enables genetic diagnosis and rapid analysis of biochemical markers associated with disease progression in rare genetic diseases, such as Duchenne Muscular Dystrophy and fatty acid oxidation disorders, which can then be adapted to other rare diseases. We will also develop 'Disease in a Dish' models, which can be used for screening of drugs and nutrient-based treatments.



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

Farah Ishtiaq

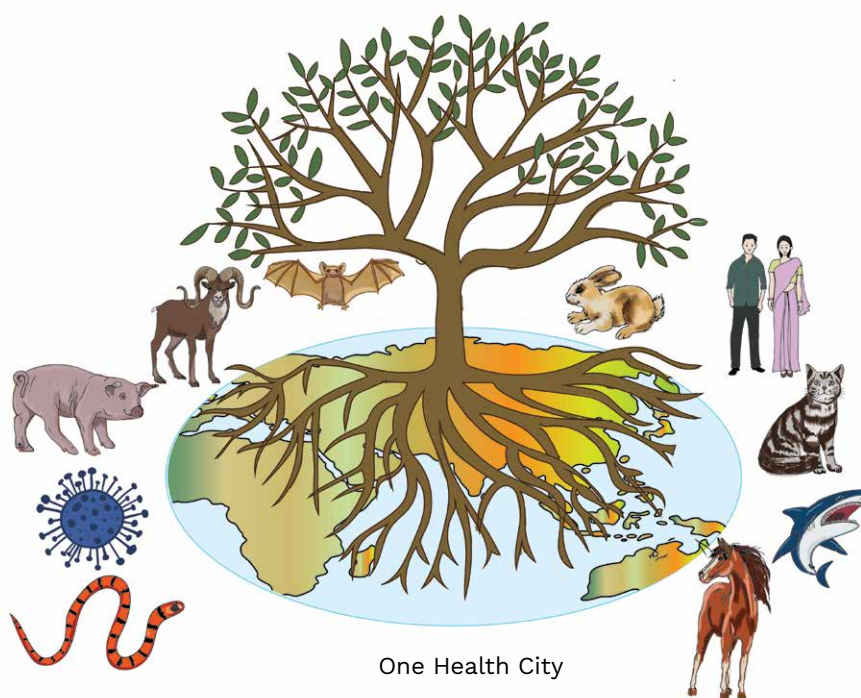
[In collaboration with NCBS, TIGS, BBMP, Biome Trust, ATREE, Azim Premji University, IISc, Ashoka University, IIPH, Molecular Solutions, Climate Action, Echo Network]

One Health recognises the interconnectedness between environment, animal, and human health. To this end, TIGS is a leading partner in a transdisciplinary collaborative effort to propose and implement research, policy, and programmes at a local and regional scale in Karnataka. The goal is to build a Bengaluru One Health Platform - a network of practitioners and scientists who will evaluate the value of shared environment, biodiversity and livestock monitoring for pathogens in the changing milieu of a large and active Indian city. This network will engage

with and inform policy makers, city planners and the health authorities which is critical for the smooth implementation of scientific knowledge. TIGS and NCBS have developed a comprehensive framework for developing the Bengaluru One Health City (<https://bengaluru.citizenmatters.in/one-health-approach-zoonotic-diseases-70742>).

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

The Bengaluru Science and Technology cluster is now also formalized by the PSA office. Bengaluru Science and Technology Cluster (BeST) <https://www.bestkc.in/thematic-areas/>



A pan-India consortium for developing pathogen surveillance programs

Surabhi Srivastava and Rakesh K Mishra

[In collaboration with the Rockefeller Foundation, NCBS, CSIR-CCMB, PKC, CSIR-NCL, IISER-Pune, CSIR-IGIB and Ashoka University]

Tracking and control of infectious diseases, microbiome and anti-microbial resistance (AMR) are central to the concept of One Health. Public health surveillance systems must generate disease information that drives action, and these data must be of sufficient quality and quantity and with a 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 via their Pandemic Prevention Initiative. 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 as well as enhancing bioinformatics and data analytics pipelines. Leveraging the scientific and clinical collaborative networks developed with hospitals, laboratories and academic institutions, we next aim to undertake capacity building for real-time environmental surveillance and disease epidemiology for multiple infectious pathogens 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.



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

Setting up pathogen surveillance systems beyond SARS-CoV-2

Research and operational groups will be at the forefront of future responses to emerging infections and to build systems for reducing disease burden; however, they need to work together in a constructive and transparent collaborative framework to be prepared to respond effectively to existing challenges and future outbreaks. 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.

Partnerships developed

Partnerships are a key component of community engagement at TIGS, where we establish strong collaborations to add rigour and strengthen our work. In the past year we have established over 15 partnerships with various academic, clinical, NGO and industry partners via MoUs that will allow the development of collaborative programs and projects.

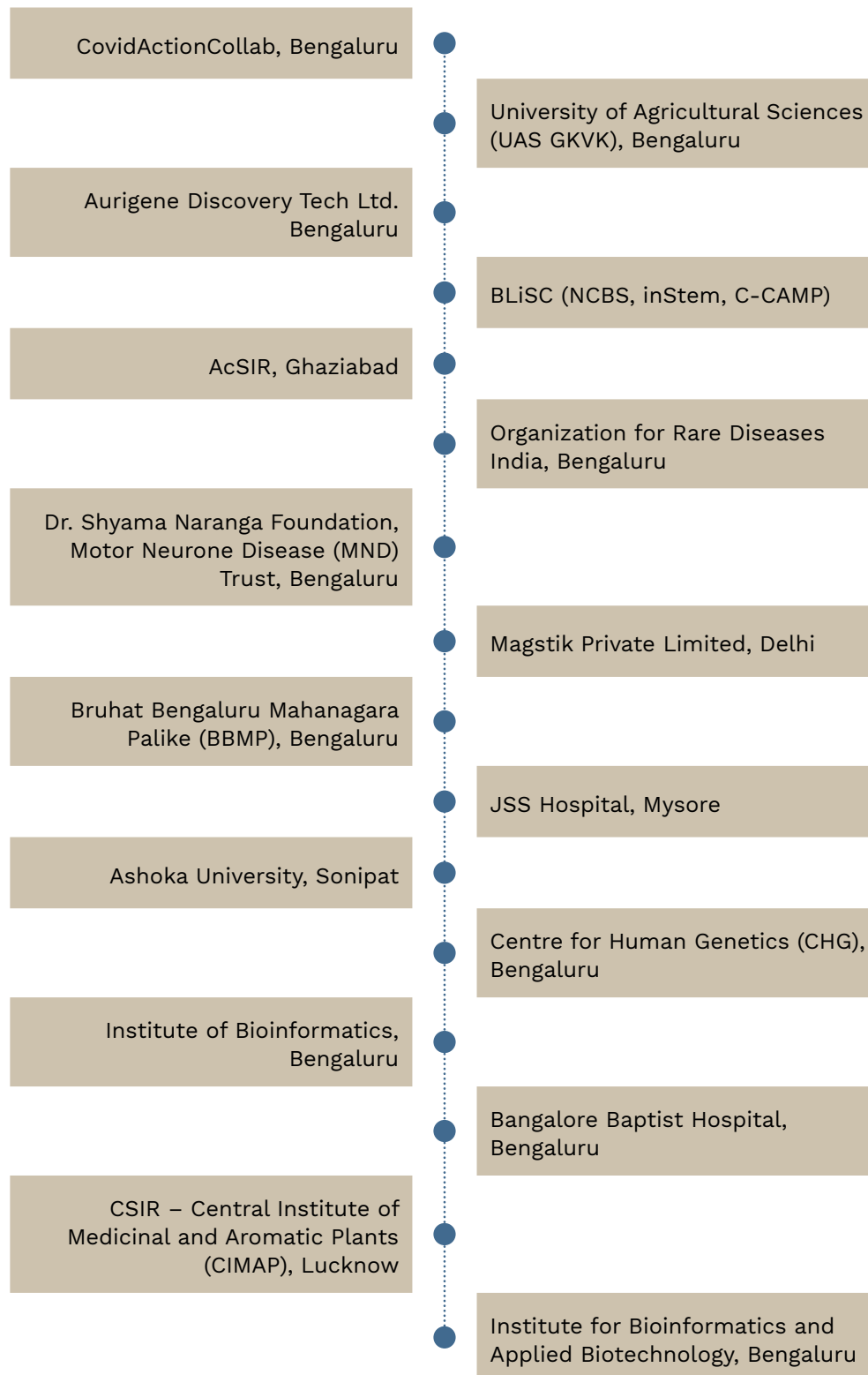


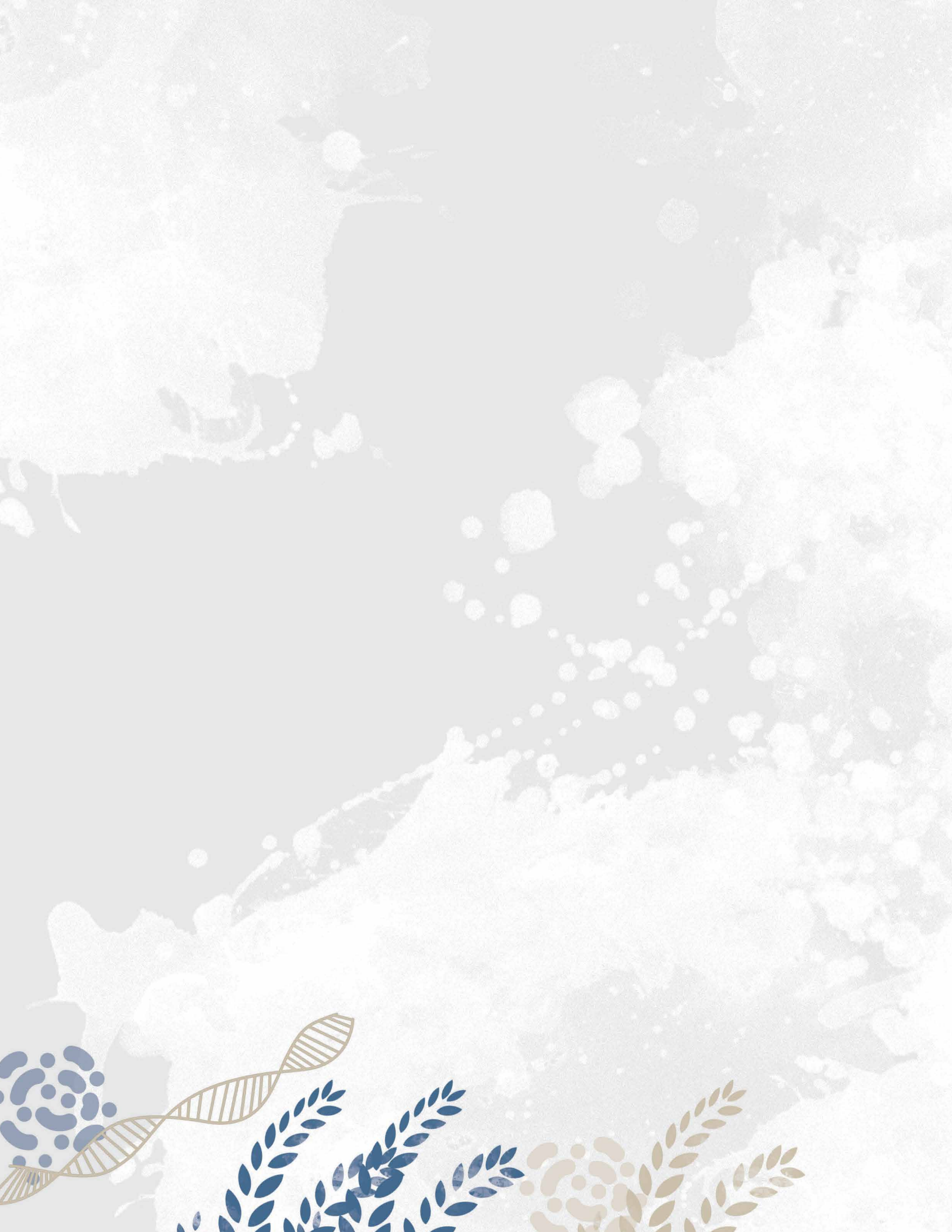
MoUs signed by Dr Rakesh Mishra, Director TIGS with L to R (top): Mr. Prasanna Shirol, Co-Founder and Executive Director, ORDI; UA Vasanth Rao, MND Trust; Director, JSS Medical College, a constituent college of JSS Academy of Higher Education and Research, Mysuru (along with staff from JSS and TIGS);

L to R (middle): Dr. S Rajendra Prasad, Vice Chancellor, GKVK (with Dr. Suresh Subramani, Former director, TIGS and Professor at UCSD along with staff from GKVK and TIGS); Dr. Prabodh Trivedi, Director CSIR-CIMAP and Dr. Dinesh Nagegowda, Scientist and Head CIMAP Bengaluru; and

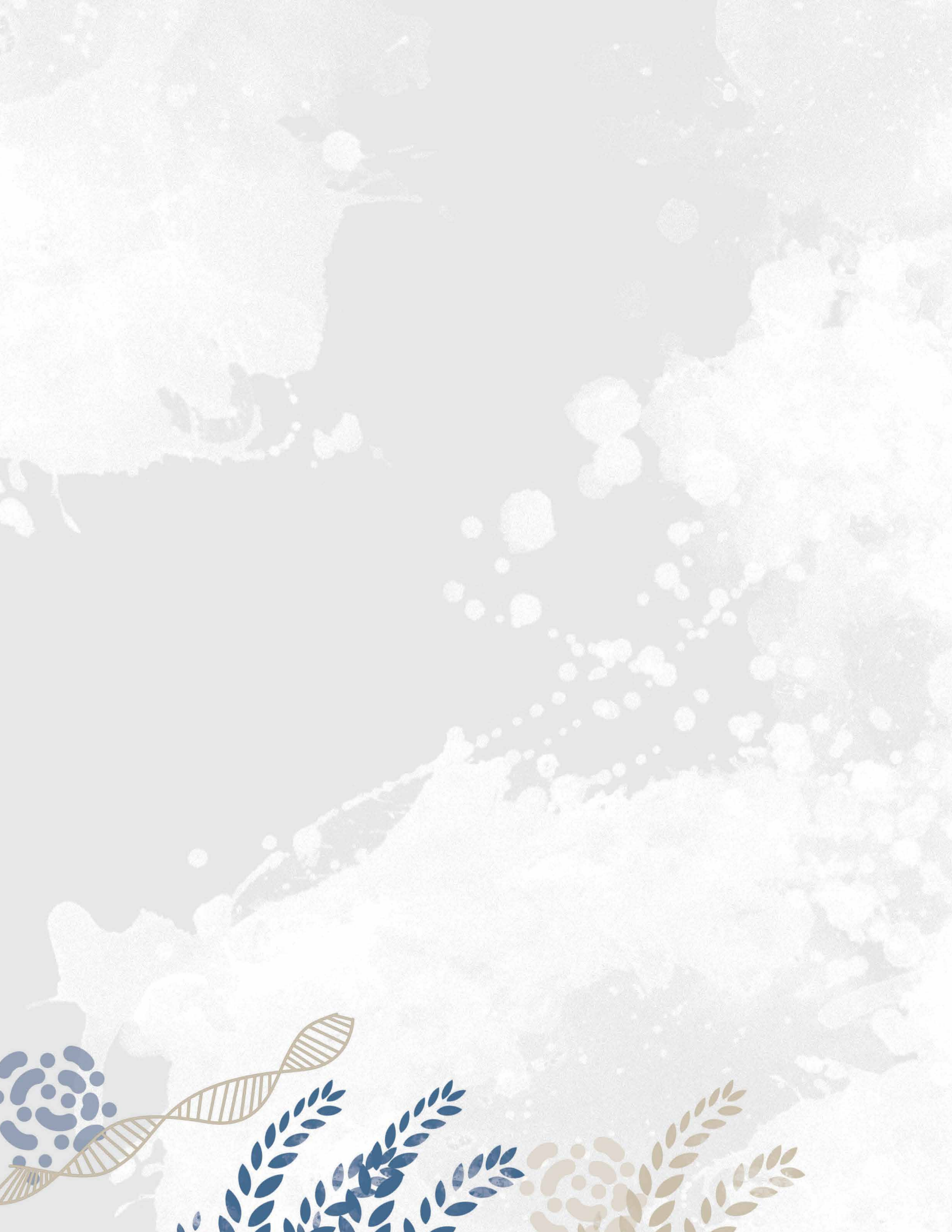
L to R (bottom): Dr. Spurgeon, Director and CEO, Bangalore Baptist Hospital (along with staff from BBH and TIGS); and Dr. Gayatri Saberwal, Dean, Academic Affairs, IBAB, Bengaluru

TIGS collaborations in the past year





Management and Administration



Director's Team



Rakesh K Mishra
Director



Surabhi Srivastava
Chief Scientific Officer



M K Sham Bharadwaj
Communications
Coordinator



Hemanth Rao
Executive Secretary



Gottivedu Jyothirmmai
Office Coordinator



Mahesh
Office Assistant

Program and Lab Management Team



Pankaj Gupta
Senior Program
Manager



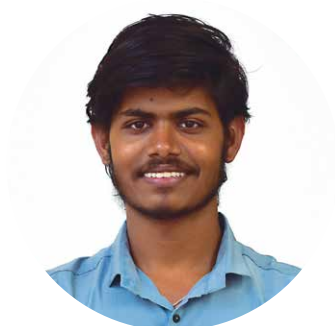
**Kokilavani
Varadharajan**
Assistant Lab
Manager



Namratha A
Senior Executive,
Accounts



Vinutha KS
Assistant Manager,
Procurement



Vidyasagar
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



Pushpalatha V
Senior Executive,
Finance

Scientific Advisory Board

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

Prof. Ramesh Sonti

Professor and Chair, Biology and Dean Faculty
Indian Institute for Science Education and Research, Tirupati, India

Prof. Anil Gupta

Visiting Faculty
Indian Institute of Management, Ahmedabad, India

Dr. K. Thangaraj

Director
Centre for DNA Fingerprinting and Diagnostics, Hyderabad, India

Dr. Sanjay Singh

Chief Executive Officer
Gennova Biopharmaceuticals, Pune, India

Dr. Shahid Jameel

Fellow
Green Templeton College, University of Oxford, UK

Prof. Gagandeep Kang

Professor of Microbiology and Head, The Wellcome Trust Research Laboratory
Christian Medical College, Vellore, India

Dr. Krishna Reddy

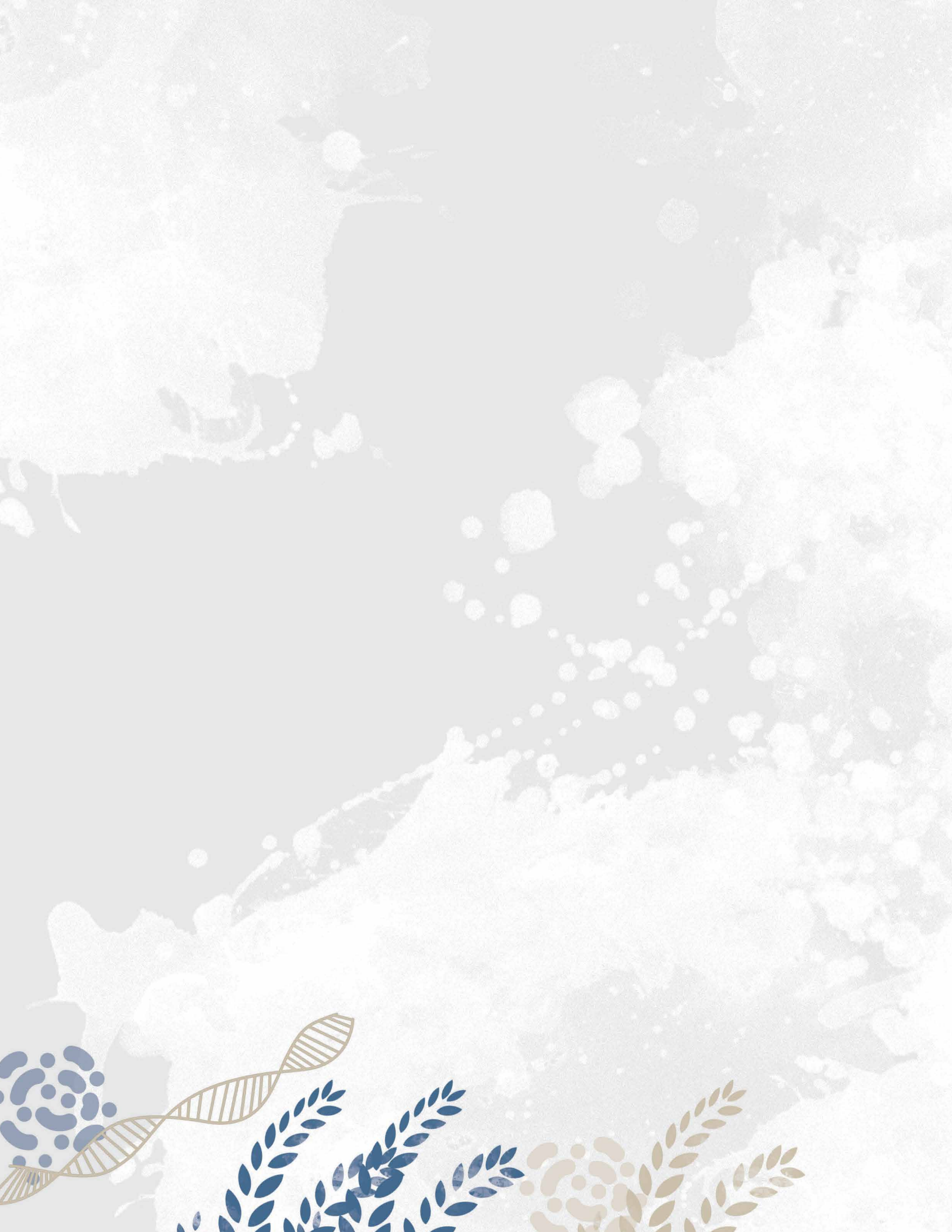
Regional Director, South Asia
ACCESS Health International, Hyderabad, India

Prof. Suresh Subramani

Distinguished Professor
University of California, San Diego, USA

Dr. Rakesh Mishra

Director
Tata Institute for Genetics and Society, Bengaluru, India



Knowledge Sharing

Activities and events

In order to communicate our research to a broader audience, the scientists and staff at TIGS organized as well as participated in multiple events on campus, involving young students as well as the general public from all walks of society. Our aim is to make a significant impact on society through our research endeavors. We believe that popularizing scientific research to inspire young minds is a step towards the right direction.

1. TIGS at the Rare Disease Day run organized by ORDI, 26th February 2022

The Organization for Rare Disease India (ORDI) organizes a run called 'Race for 7' on the last Sunday of February each year across the country, to create awareness about the 7000 or so rare diseases that impact mainly children. Participants include patients and their families along with supporters for the cause. Apart from awareness, the run is intended to highlight the need for attention towards research and policy on rare diseases. Staff from TIGS participated in the run and strengthened our commitment to pursue R&D for cost effective diagnostics and treatment for rare and neglected diseases in the country.



TIGS participants at the Race for 7 to extend support towards the cause of the rare disease patients in India

2. Visit by the students of the Azim Premji University, 24th April 2022

Enthusiastic students from Azim Premji University spent a day at the TIGS campus for a visit to various technology platforms and facilities such as Stem cell lab, Insectary (mosquito facility), Fly (*Drosophila*) facility, Protein lab and Crop improvement labs. They interacted with the scientists who explained about the research at TIGS



Students from Azim Premji University at various labs and facilities at TIGS

3. Integrated Urban Environment Surveillance Program: Microplanning Workshop to Support Public Health Decision Making, 5th May 2022

Dr Farah Ishtiaq conducted a microplanning workshop with the Bruhat Bengaluru Mahanagara Palike (BBMP) and the Bengaluru wastewater and sewage board (BBMP-BWSSB-PPHS Hybrid Platform) to raise awareness on the importance of pathogen surveillance from wastewater and to integrate environmental surveillance with public health initiatives.



Participants at the microplanning workshop on environmental surveillance

4. National Dengue Day 2022 in collaboration with BBMP, 16th May 2022

May 16th is observed as National Dengue Day to create awareness on prevention of Dengue, a vector-borne viral disease caused by the day bite of Aedes mosquitoes. They breed in stagnant water, taking 7-12 days to complete their life cycle. It is a seasonal disease, prevalent in Bengaluru in the rainy season, Dengue can cause severe illness and even death in some people. It is a preventable disease if appropriate measures are taken. Researchers at TIGS are working with BBMP Special Health, to identify mosquito larval breeding sites & come up with solutions to reduce the dengue disease burden of the city.

TIGS partnered with the Bruhat Bengaluru Mahanagara Palike (BBMP), the local municipality to participate in an awareness walkathon from Mahatma Gandhi Road to BBMP office, Bengaluru. ASHA workers, ground level PHC staff, health authorities, government and private hospitals doctors, epidemiologists and several NGOs were in attendance.



Participants from TIGS and the BBMP on National Dengue Day

For our efforts in reducing the burden of infectious diseases, we also won recognition by the National Centre for Vector Borne Diseases, MoHFW, Government of Karnataka.



5. Celebrating one year with the Precision Health Surveillance initiative, Bengaluru, 17th June, 2022

An event marking the first year milestone of being part of the Environmental surveillance initiative by Precision Health was held in Bengaluru in June. TIGS is proud to be a part of the consortium along with other stakeholders in building an early-warning system for COVID19 in Bengaluru, and impact public health policy decisions through our science,



L to R (from top): Dr. Rakesh Mishra, Director TIGS along with other dignitaries inaugurating the session; Dr. Farah Ishtiaq participating in a panel discussion during the event; Dr. Farah and others unveiling the first playbook on Environmental Surveillance for COVID-19 - a comprehensive guide for city wide surveillance; TIGS researchers Namrata Daroach, Dr. Farah Ishtiaq, Dr. Saveetha Meganathan and Dr. Sanjay Lamba

6. Visit by a delegation from the University of Manchester, 28th September 2022

A scientific delegation from the University of Manchester, led by President and Chancellor Prof. Dame Nancy Rothwell, visited the Bangalore Life Sciences Cluster in

September. TIGS Director Dr Rakesh Mishra, Chief Scientific Officer Dr Surabhi Srivastava and scientists from TIGS participated in the discussions to facilitate future collaborations between the two institutions. The delegates visited the insectary facility at TIGS along with other shared facilities at BLISC and discussed the research activities that presented some common synergies.



The delegation from the University of Manchester at the TIGS insectary

7. Visit by a delegation from Swissnex India, 7th October 2022

On October 7th, we were pleased to host a scientific delegation from Swissnex India to the BLiSC campus. An overview of the research programs at TIGS was presented, followed by an exchange of ideas on how to promote collaborations in research and innovation between India and Switzerland.



Swissnex delegation along with researchers at TIGS

8. Application of mRNA platform for rare genetic disorders, 8th October 2022

TIGS organized a one-day brainstorming meeting on the 'Application of mRNA platform for rare genetic disorders' in partnership with Ashoka University and World Without GNE Myopathy. It was attended by scientists from Ashoka University-Delhi, Centre for Stem Cell Research-CMC Vellore, CSIR-Centre for Cellular and Molecular Biology-Hyderabad and other stakeholders such as Gennova Bio and Atal Incubation Centre-CCMB, Hyderabad. Pharmaceutical companies and members of patient advocacy groups involved in various aspects of mRNA therapy as well as representatives from the

Department of Biotechnology, GoI also participated in the event.



Delegates at the mRNA platform brainstorming meeting

The challenges for developing rare disease treatments, designing mRNAs and delivery systems and issues with preclinical and clinical development of mRNA therapies were discussed. The meeting saw active participation from various stakeholders who gave valuable insights on how mRNA platforms can help in addressing the needs of rare disease patients, and we are developing a comprehensive roadmap for development and indigenization of these lifesaving technologies in India.

9. Rare Genetic Diseases Research Summit (REDRESS), 24th- 25th November, 2022

REDRESS 2022, a 2-day working summit was organised by TIGS and the Organization for Rare Diseases India (ORDI) on 24th and 25th November at Bengaluru. REDRESS is envisaged as a platform to bring together a comprehensive group of RGD stakeholders in India, with the aim of indigenization and acceleration of diagnostics, therapeutics, and management of RGDs. Interactive sessions were organized at this first summit with the aim of indigenization and acceleration of rare genetic disease diagnostics, therapeutics, and management, through potential cross-disciplinary collaborations. Multiple panel discussions were also held on nurturing the ecosystem for basic and translational research in RGDs, accelerating diagnostics and drug development, enabling clinical trials in India, providing access to RGD medications and celebrating a few success stories in the Indian context. Finally, the summit covered India's journey in the field so far with speakers presenting their view as well as posters describing their work. Several potential collaborations and partnerships were discussed, involving multiple stakeholders. Such

partnerships are the need of the hour to fast forward solutions and alleviate the suffering of a substantial proportion of the population of our country.

Importantly, patients and patient support groups were also represented and discussed their views and the issues faced by the RGD patient community. With an attendance of over 200 (in-person as well as online participation), REDRESS 2022 helps develop a one-of-its-kind RGD community that will be part of a robust and focussed research ecosystem encompassing science, healthcare, innovation, entrepreneurship, and policy.



Participants during a session at REDRESS 2022



Participants at REDRESS 2022

10. Farmers outreach program: promoting farming practices backed by a scientific basis, 23rd December, 2022

Agriculture is a major occupation in India. For farmers to gain maximum profits, it is extremely important to know and implement the best farming practices that are driven by the latest technologies. As climatic conditions change, SOPs need to be developed to adapt to issues such as delayed monsoon. Recognizing the importance of engaging farming communities, TIGS has joined hands with various partners to communicate scientific breakthroughs in crop improvement and develop meaningful platforms for outreach.

One of our models is to initiate joint programs to

enrol participants from farming communities by supplying seeds free of cost and training them to use the associated best practices. A good example is that of identifying and promoting local food grain varieties that are rich in nutrients but are on the verge of being lost. Nutritional profiling of two such varieties (Tinni red rice and kala namak) has already been performed, and farming of these beneficial strains is being promoted. Participating farmers would be educated on the best farming practices related to these varieties and a business model set up for buying the product from them at competitive prices, so that the farmers gain profit. Consumers would also benefit as the nutrient-rich varieties would reach the market and would be made available to the people.

We conducted the first such farmer outreach event on the occasion of 'Kisan Diwas' at Deoria, a village in Eastern UP.





In collaboration with Magstik Private Limited (MPL), TIGS has adopted a village in Eastern UP and 23 farmers are being encouraged to cultivate improved rice varieties developed in collaboration with CSIR-CCMB. Seeds are procured from CSIR-CCMB, Govt of India and supplied to the farmers at their doorstep free of cost. Dr Rakesh Mishra, Director of TIGS, Dr. Shivrangani Moharir, scientist at TIGS, Dr Saurabh Pandey, scientist and representative of Magstik Pvt Ltd, representatives from DeHaat (a startup in the agri-innovate sector), Vikasshil Kisan Krishi Producer Company (a Farmers Producer Organization), CMP Medical College, Prayagraj, and more than 50 local farmers participated in the event. Going ahead, high-quality government-approved microbial and micronutrient-treated seeds will be supplied to the farmers, with MPL providing organic formulations to be used during the growing season for various stages. Farmers are educated to improve seed quality using specific microorganisms and micronutrient treatments that will further assist in the enrichment of soil fertility.

11. CUSAT students visit, 27th December, 2022

Students pursuing their Master's in Biotechnology and Microbiology from the Cochin University of Science and Technology (CUSAT), Cochin, Kerala spent a day at TIGS as part of their academic tour. They were introduced to the research at TIGS and the various problems which our scientists are trying to crack using cutting edge technologies. They visited the stem cell facility where a brief about CRISPR-Cas9 technology was given along with how it is being used to address challenges in Rare Genetic Disorders research at TIGS. They also got a chance to visit the Insectary, a unique facility where mosquitoes are reared for studying various aspects of vector borne infectious diseases.

The conversation and field station museum on campus is where the students got to see various mammals, reptiles, bugs, moths, butterflies and insects, collected during field visits by researchers. Later, before ending

the visit, the students interacted with scientists at TIGS to get an idea on the various career prospects in the life sciences domain.



Students from CUSAT visiting facilities on campus and interacting with the scientists at TIGS

12. Insectary workshops and awareness programs (all around the year)

The TIGS Insectary is a state-of-the-art facility managed by a team of skilled vector biologists, working especially with various mosquito species. As a part of the BLISC campus, the insectary hosts multiple visits of scientific delegates, various stakeholders as well as students from schools and colleges. Periodic orientation programs, training, and hands-on workshops are conducted in a bid to raise awareness about insect vectors that spread many diseases.



(Top): Students from 10 schools and colleges of Bengaluru at 'The world of Insects' exhibition, 25th August 2022

(Middle): Teacher's from North Bengaluru at a workshop -16th August, 2022; and Students and teachers from the Viveka scholar program, Sarguru - 22nd November 2022

(Bottom): Students at 'Capacity building in Dipteran Bio-Systematics: Taxonomic and ecological diversity, conservation of Diptera' at UAS, Bangalore - 7th December 2022

Invited talks

Scientists from TIGS attended and spoke at various events across the country and highlighted the potential impact emerging from their work

- Poster on “Wastewater-based epidemiology of SARS-CoV-2 in Bangalore city”. Farah Ishtiaq. *NCBS Annual Talks*, 10th January, 2022.
- Talk on “Single shot COVID-19 vaccines”. Rakesh Mishra. *Neo Science Hub*, 4th February, 2022.
- Talk on “Public Health Perspective on COVID-19 Pandemic”. Rakesh Mishra. *National Remote Sensing Center, Hyderabad*, 8th February, 2022.
- Virtual symposium on “Role of Epigenetics in Health : Challenges and Opportunities”. Rakesh Mishra. *Birla Institute of Technology and Science*, 25th-26th February, 2022.
- Talk on “Public Health Perspective on COVID-19 Pandemic”. Rakesh Mishra. *Sri U V Warlu 20th Memorial Lecture, Knowledge Sharing Session (KSS)*, 27th February, 2022.
- Poster on “Wastewater-based epidemiology as an early warning system of SARS-CoV-2 in Bangalore city”. Farah Ishtiaq. *InStem Annual Review of Research*, 28th February, 2022.
- Talk on “Ecology, Infectious Diseases and NGS: Powerful tool in exploring biodiversity and responding to disease outbreak”. Farah Ishtiaq. *Peek into Biodiversity and Beyond A hands-on training on NGS, IISER-Kolkata*, 4th March, 2022.
- Theme talk on “Industrial vs Academic Research (InvAR)”, *Students’ Research Convention (SRC)*, *IIT Kanpur*, 5th March, 2022.
- Talk on “Hitchhiking Parasites: The Role of Bird Migration in Understanding Disease Ecology”. Farah Ishtiaq. *Department of Biology, Macalester College, Minnesota, USA*, 7th March, 2022.
- Talk on “Lessons learnt from the pandemic and the way forward”. Rakesh Mishra. *Defence Research and Development Lab (DRDL)*, *Hyderabad*, 9th March, 2022.
- Talk in Hindi on “Lessons learnt from the pandemic and the way forward”. Rakesh Mishra. *Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad*, 11th March, 2022.
- Talk on “Capacity building for data-driven pandemic surveillance”. Surabhi Srivastava. *The Rockefeller Foundation - Asia Regional Partners Meet*, 23rd March, 2022.
- Guest Lecture on ‘Avian Diseases’. Farah Ishtiaq. *Nature Conservation Foundation (NCF)*, *Bangalore*, 24th March, 2022.
- Talk on “Impact of Covid-19 Pandemic on Public Life and Future Challenges”. Rakesh Mishra. *MAA ENT Hospitals National Conference, Hyderabad*, 26th-27th March, 2022.
- Discussion on “Genome Sequencing strategy of India and importance to fight the COVID-19 pandemic”. Rakesh Mishra. *NDTV/Banega Swasth India*, 22nd April, 2022.
- Sense making workshop on “Environmental Surveillance of COVID-19, Genomics, AMR using Wastewater”. Farah Ishtiaq and Sanjay Lamba. *Bruhat Bengaluru Mahanagara Palike (BBMP)*, 5th May, 2022.
- Talk on “Environmental surveillance in context”. Farah Ishtiaq. *Gates Foundation*, 16th May, 2022.
- National Technology Day Lecture on “Lessons learnt form the pandemic and the way forward”. Rakesh Mishra. *CSIR-Central Institute of Medicinal and Aromatic Plants (CSIR-CIMAP)*, *Lucknow*, 17th May, 2022.
- Talk on “Lessons learnt form the pandemic and the way forward.” Rakesh Mishra. *The Skill Development Center, School of Life Science, University of Hyderabad, Hyderabad*, 23rd May, 2022.
- Talk on “NCURA’s Contract Negotiation and Administration workshop” at IRMI’s Coffee and Conversations session. Pankaj Gupta. *India Research Management Initiative, DBT/Wellcome Trust India Alliance, Hyderabad*, 25th June, 2022.
- Talk on “Explore Bioethics in the Indian Context.” Saveetha Meganathan. *IndiaBioScience*, 28th June, 2022.

22. Talk on “Covid-19 Genomic surveillance program in Bengaluru.” Rakesh Mishra. *Bruhat Bengaluru Mahanagara Palike (BBMP)*, 17th July, 2022.
23. Talk on “Importance and the Future of Genetics to India.” Rakesh Mishra. *GUARDIAN, Institute of Genomics and Integrative Biology (CSIR-IGIB)*, 20th July, 2022.
24. SERB - GE Call for Proposal under FIRE scheme; PMRC Meeting.” Rakesh Mishra. *SERB-DST, Gol*, 26th July, 2022.
25. Talk on “Unravelling the Importance of Research Protocols and Publication Ethics: Need of the Hour.” Saveetha Meganathan. *Kalasalingam Academy of Research and Education (KARE)*, 29th July, 2022.
26. Pandemic preparedness workshop. Farah Ishtiaq and Sanjay Lamba. *Art Park and Indian Institute of Science (IISc), Bengaluru*, 7th August, 2022.
27. Participant at NCURA meeting (recipient of NCURA Catherine Taylor-Core minority travel award). Pankaj Gupta. *64th NCURA Annual Meeting, Washington, D.C, USA*, 8th August, 2022.
28. Talk on “Pandemic Response and Environmental Science.” Rakesh Mishra. *Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR)*, 9th August, 2022.
29. Talk on “Recent Trends in Genomics and Transgenesis.” Rakesh Mishra. *Department of Biotechnology, School of Science, GITAM, Visakhapatnam*, 16th-17th August, 2022.
30. Talk on “Innovations during COVID-19: From diagnostics to monitoring sewage and air.” Rakesh Mishra. *Women Driving S&T in India*, 26th August, 2022.
31. Talk on “Environment surveillance and genomic sequencing of wastewater in Bengaluru city.” Farah Ishtiaq. *NASA x Rockefeller meeting on Environmental surveillance*, 8th September, 2022.
32. External expert for faculty selection meeting. Rakesh Mishra. *Shiv Nadar University*, 9th September, 2022.
33. Talk on “Genome based environmental surveillance of infectious diseases:Emerging and essential tool for public health system.” Rakesh Mishra. *FDP sponsored by AICTE, ATAL sponsored Computational Biology, IIT Allahabad*, 11th October, 2022.
34. Talk on “One Health and Environmental surveillance.” Rakesh Mishra. *16th IKP Knowledge Park annual innovation conference, IKMC 2022*, 29th October, 2022.
35. Participant at IRMI Annual Conference 2022. Pankaj Gupta. *India Research Management Initiative (IRMI), DBT/Wellcome Trust India Alliance, Hyderabad*, 31st October to 4th November, 2022.
36. Talk on “Bioethics.” Saveetha Meganathan. *Symbiosis International University*, 15th November, 2022.
37. Panellist at “One Health and Pandemic.” Farah Ishtiaq. *Bengaluru Tech Summit, Bangalore Palace*, 17th November, 2022.
38. Talk on “Wastewater-based epidemiology for SARS-CoV-2 and beyond.” Farah Ishtiaq. *ALARM 2022, Amrita University*, 17th November, 2022.
39. Participant at the Hands-on training workshop, WHONET. Mansi Malik. *45th annual conference of the Indian Association of Medical Microbiologists, Bhubaneswar*, 24th-25th November, 2022.
40. ‘Prof. G.N. Ramachandran Memorial Lecture’. Rakesh Mishra. *Department of Biosciences and Bioengineering IIT Roorkee, Roorkee*, 12th December, 2022.

Scientific publications

1. Anirudha Lakshminarasimhan. Prophage induction therapy: Activation of the lytic phase in prophages for the elimination of pathogenic bacteria. *Medical Hypotheses*. 2022;169: 110980. December 2022 DOI: <https://doi.org/10.1016/j.mehy.2022.110980>
2. Farah Ishtiaq. India must scale up wastewater analysis for health surveillance. *Nature India* ISSN 1755-3180 (online), December 2022 DOI: <https://doi.org/10.1038/d44151-022-00130-5>
3. Mansi Malik, Parvathy Vijayan, Deepak K. Jagannath, Rakesh K. Mishra, Anirudha Lakshminarasimhan. Sofosbuvir and its tri-phosphate metabolite inhibit the RNA-dependent RNA polymerase activity of non-structural protein 5 from the Kyasanur forest disease virus, *Biochemical and Biophysical Research Communications*, Volume 641, 2023, pp 50-56, December 2022 DOI: <https://doi.org/10.1016/j.bbrc.2022.12.023>
4. Thirunavukarasou A, Kaur S, Khera HK. Metagenomics for Studying Microbes in Wastewater Treatment Plants. Chapter 11; *In Microbial Community Studies in Industrial Wastewater Treatment* (pp. 171-183). CRC Press. (Book Chapter, eBook ISBN 9781003354147) December 2022. DOI: <https://doi.org/10.1201/9781003354147>
5. Shagufta Khan, Rakesh K Mishra, Surabhi Srivastava. Epigenetic regulation of cis-regulatory elements and transcription factors during development. *Perinatal and Developmental Epigenetics; Elsevier Translational Epigenetics Series*, Vol 35. December 2022 (Book Chapter) ISBN: 9780128217856.
6. Kannan, V., Meganathan, S. and Mishra, R. Wastewater surveillance for public health: Beyond the pandemic. *Journal of Science Policy & Governance*, Vol 21, 02. November 2022 DOI: <https://doi.org/10.38126/JSPG210207>
Available at: https://www.sciencepolicyjournal.org/article_1038126_jspg210207.html
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TIGS in the NEWS

Home > India > COVID mutant 'XE': TIGS Director Rakesh Mishra urges citizens not to panic, says 'closely monitor the development of variant'

COVID mutant 'XE': TIGS Director Rakesh Mishra urges citizens not to panic, says 'closely monitor the development of variant'

ANI | Updated: Saturday, April 02, 2022, 09:35 PM IST



'Covid variant XE has been around since Jan, no cause of concern as of now'

Rakesh Mishra, Director of the Tata Institute of Genetics and Society, Bengaluru, said the XE variant is a recombinant of BA.1 and BA.2, the sub-lineages of SARS-CoV-2

Topics
health | Coronavirus

Press Trust of India | Mumbai
Last Updated at April 6, 2022 23:18 IST

Impact of Covid 'is down but not out', do not be careless: Health experts

"It is important for all to take adequate precautions to curb the impact of the virus. It is observed that if the cases rise in an area, there is a chance that another variant exists"

Topics
Coronavirus | public health | Omicron

ANI General News
Last Updated at April 28, 2022 14:40 IST



ताज़ातरीन ख़बरे

जीनोम सीक्वेंसिंग क्या है और यह COVID-19 महामारी से लड़ने में कैसे मदद कर रही है?

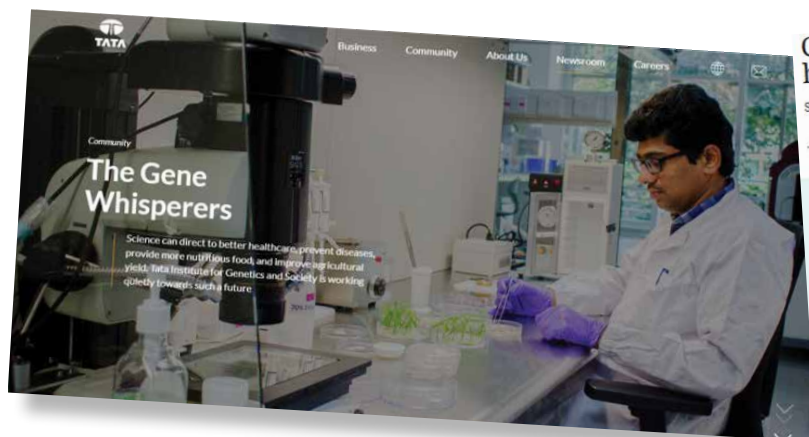
टाटा इंस्टीट्यूट फॉर जेनेटिक्स एंड सोसायटी, बेंगलूर के निदेशक डॉ. राकेश मिश्रा का कहना है कि मल्टीपल होने के चलते कोरोनावायरस में म्यूटेट होने की प्रवृत्ति होती है, ऐसे में ये हानिकारक है, लाभकारी है या प्रभाव डालने में सक्षम है या नहीं, ये जानने के लिए जीनोम सीक्वेंसिंग का ट्रैक रखना महत्वपूर्ण है

कोरोना अपडेट: चीन के शहर में लॉकडाउन के बीच विशेषज्ञों की चेतावनी, कोरोना के नए वैरिएंट पर कही यह बात

न्यूज डेस्क अमर उजाला, नई दिल्ली Published by: शिव शरण शुक्ला Updated Sat, 12 Mar 2022 05:36 PM IST

हिन्दी मिलाप





Coronavirus particles found in air can infect humans, experiments show

Scientists found that the virus could be detected in air around Covid-19 patients

By PTI | Updated: May 04, 2022 10:08 IST



भारत की Genome Sequencing रणनीति और COVID-19 से लड़ने में इसका महत्व

No need to panic due to rise in Covid infections

TELANGANA

Wastewater surveillance advocated for COVID tracking

ad: The surge in Covid infections in Delhi and neighbouring should not become a cause of panic among people in Telangana, experts and biologists said, pointing out that there was no evidence of a new virulent Omicron variant behind the rise in Covid infections in ... in Covid infections in [...]

'Not Done With Covid Pandemic Yet': Experts Say Future Depends On New Variants, Need To Be Watchful

Rakesh Mishra, Director of Tata Institute for Genetics & Society is not right to declare that India is done with the COVID pandemic



'Booster doses, Covid-appropriate behaviour key to check virus spread'

July 24, 2022 - Updated 10:46 am IST | Hyderabad, July 24

The possible problem that may occur, though the chances are less, is the emergence of a new variant, says Director of Tata Institute for Genetics and Society

Don't exhale just yet, COVID isn't over

Waste water sampling showing more cases than what is reported but mask is 'super vaccine', says top scientist

April 13, 2022 08:09 pm | Updated April 14, 2022 10:34 pm IST - HYDERABAD

Covid-19: Top scientist asks to increase the genome sequencing amidst rising cases



NEWS FEATURE | 29 May 2022

Quick sequencing offers a better chance at COVID control

A giant global genome-sequencing database played a crucial role in helping countries respond to emerging variants of the SARS-CoV-2 virus

Indians shouldn't panic by COVID-19 scare in China: Dr Rakesh Mishra

The Omicron sub-variant BF.7, the Covid strain causing China's current spike in cases, has been found in at least four cases in India so far

Monkeypox is not COVID, but need to keep a watch, says top scientist



V. Geetanath

HYDERABAD AUGUST 02, 2022 00:06 IST

UPDATED: AUGUST 02, 2022 13:48 IST



Experts push for mask rule in closed spaces

Bangalore Mirror Bureau / Updated: May 5, 2022, 06:00 IST

National

'Booster doses, Covid-appropriate behaviour key to check virus spread'

PTI | Hyderabad, July 24 | Updated On: Jul 24, 2022

'Booster doses, Covid-appropriate behaviour key to check virus spread'

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Time to eliminate 'silent killer' TB, say top scientists

An Uphill Battle

March 31, 2022 10:21 pm | Updated 10:21 pm IST - HYDERABAD

By Deepika S and Ranjini Raghunath

Researchers, doctors and communities work together to manage a neglected disease

Stem Cell technology offers new hope for treating rare genetic disorders: Rakesh Mishra

"The very nature of disease that the gene is defective makes it very difficult to identify, diagnose and the treatment is a challenge as well as extremely expensive,"

Sewage monitoring may hold key to handling future pandemics

Sewage surveillance would help in public health responses, preventive care, says TIGS director

March 02, 2022 06:37 pm | Updated March 09, 2022 10:41 am IST - HYDERABAD

India must scale up wastewater analysis for health surveillance

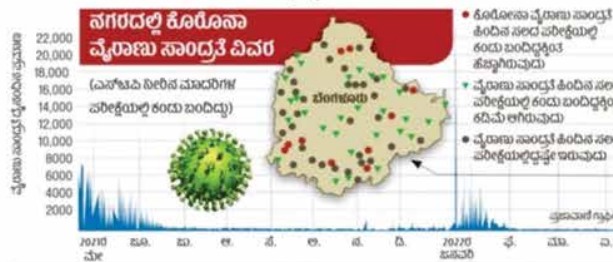
Wastewater testing helped identify COVID-19 hotspots almost a couple of weeks before clinical data could

ఎస్.టి.సి. నీరిన పరీక్షేయ ఫలితాంశం ఆధారంలో నడೆಯుత్తిదే నియంత్రణ కార్య

కొవిడ్ మున్నోచనే నీడవ శౌచనీరు!

• ప్రవీణ్ కుమార్ పి.వి.

పంగాలు: నగర యావ ప్రదేశంలో కొవిడ్ ప్రమాణ తీవ్రమైనది ఎంబి బిగ్ మున్నోచనే పడేయి దిద్దింది వినూకణ కార్యకర్తల మోదయోగి. కొవిడ్ నీరిన కున్నోచనువ ఫలకాలలో (ఎస్.టి.సి.) నీరిన మూదరిగన్న నిరంతరంగా కొవిడ్ పరీక్షింప ఉపయోగపడే మూలక కొవిడ్ ప్రమాణం మామికి పడేయియోగి.



'కొవిడ్ రోజువారీయ సుఖం'

"ఎస్.టి.సి. నీరిన మూదరిగన్న పరీక్షింప ఉపయోగపడే మూలక కొవిడ్ ప్రమాణం మామికి పడేయియోగి. కొవిడ్ నీరిన మూదరిగన్న పరీక్షింప ఉపయోగపడే మూలక కొవిడ్ ప్రమాణం మామికి పడేయియోగి. కొవిడ్ నీరిన మూదరిగన్న పరీక్షింప ఉపయోగపడే మూలక కొవిడ్ ప్రమాణం మామికి పడేయియోగి."



డా. ఫరూఖ్ ఇషియాక్

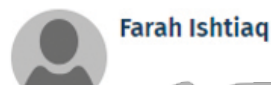
DISPATCHES

Wastewater analysis can help predict virus breakout faster

RAVI SHARMA

Print edition : Aug 25, 2022

Wastewater surveillance reveals infection dynamics



Farah Ishtiaq

JULY 23, 2022 19:40 IST
UPDATED: JULY 28, 2022 11:41 IST

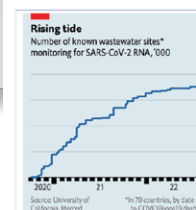
Mongabay Series: Environment And Health

Dumped plastic containers lead to mosquito abundance on the Lakshadweep islands

by Sahana Ghosh on 10 August 2022

The Economist September 10th 2022

63



called scores has been monitoring levels of cocaine and cannabis in cities across the continent since 2010.

Farah Ishtiaq, a researcher at the Tata Institute for Genetics and Society in Bangalore, is interested in using sewage sampling to track antibiotic resistance, in which bacteria evolve defences against drugs that had previously been fatal to them. Antibiotic resistance worries Indian public-health experts in particular. One paper, published in 2010, estimated that around a quarter of new tuberculosis cases in the country were resistant to at least one of the drugs commonly used to treat the disease; 3.5% were resistant to several.

Others want to monitor health in a broader sense. In 2018 researchers at Arizona

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