Co-organised by

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THE 3rd RARE GENETIC DISEASES RESEARCH SUMMIT (REDRESS)

28th - 29th November 2024

Bengaluru

Meeting Proceedings

INDEX

About REDRESS

The Rare Genetic Diseases Research Summit (REDRESS) is a flagship event of the Tata Institute for Genetics and Society (TIGS). It was launched in 2022 and co-organised with the Organization for Rare Diseases India (ORDI). REDRESS is an indigenous and recurrent platform to bring together all rare genetic disease (RGD) researchers and stakeholders working for the Indian rare disease population. The summit provides an opportunity to evaluate the current status of the field in India and focus on new avenues in RGD research, especially in the context of indigenization and acceleration of diagnostics, therapeutics, and management. In 2023, the Indian Council of Medical Research (ICMR) joined hands as a knowledge partner, further strengthening the event's mission in bringing an integrated solution to the RGD ecosystem. This two-day event is a unique platform that facilitates in-depth discussions on the pressing challenges in the RGD field and gaps that need to be bridged in the Indian healthcare landscape. It also promotes cross-disciplinary collaborations between experts from research, healthcare, entrepreneurship, and policy field to collectively address R&D gaps in the RGD space.

The third edition of REDRESS was held on 28th – 29th November 2024 at the Bangalore Life Sciences Cluster (BLiSC) campus. Focused sessions and panel discussions covered a range of key topics including the current status of RGD diagnostics, application of gene editing and mRNA technologies for therapeutic development, and the importance of implementation of newborn, population, and community level screening programs in India. The summit also emphasized on regulatory and policy dimensions of indigenization of orphan drug development and conducting clinical trials and spotlighted the industry perspectives of therapeutic and diagnostics. The event had a participation of 200 people ranging from diverse backgrounds, including over 35 eminent speakers and panellists who provided glimpses into their work and views to tackle specific aspects of rare diseases. More than 60 posters were presented by academicians, students and start-ups working on rare diseases, acting as a catalyst for interactions among the participants from all over the country.

Patient advocacy groups (PAGs) play a crucial role in raising awareness about rare diseases by amplifying the voices of affected individuals and families. Recognising the unique challenges faced by PAGs and spotlighting the efforts made by them remains central to the REDRESS mission. Therefore, REDRESS-2024 introduced the 'PAG corner' - a dedicated space for showcasing the efforts of six selected patient advocacy groups to encourage patient-centric dialogue.

For a comprehensive overview of the discussions and outcomes from REDRESS 2024, refer to the detailed proceedings that follow.

THE 3rd RARE GENETIC DISEASES RESEARCH SUMMIT (REDRESS)

Inaugural Session

Dr. Rakesh Mishra

Director, Tata Institute for Genetics and Society

Mr. Prasanna Shirol

Co-founder and Director, Organization for Rare Diseases India

Dr. LS Shashidhara

Director, National Centre for Biological Sciences, Bengaluru

Dr. Monika Pahuja

Scientist E, Discovery Research, Indian Council of Medical Research, New Delhi

Dr. Amlin Shukla

Scientist E, Delivery Research, Indian Council of Medical Research, New Delhi

Inaugural Session

Dr. Runa Hamid from the organizing committee commenced the summit with a warm welcome to one and all. The inaugural dignitaries included Dr. Rakesh Mishra, Mr. Prasanna Shirol, Dr. LS Shashidhara, ICMR representatives Dr. Monika Pahuja and Dr. Amlin Shukla.

Dr. Rakesh Mishra, director of TIGS introduced the third edition of REDRESS 2024, co-organized with ORDI and ICMR as knowledge partner. He emphasized on the progress, possibilities and the potential of new technologies that can be taken to the patients. Dr. Mishra welcomed all the participants and stakeholders who had gathered to attend REDRESS 2024.

Mr. Prasanna Shirol, founder ORDI delivered his inaugural remarks reminiscing about the formulation of REDRESS from 2022. In 2007, ORDI was formed by parents of children with rare genetic disorders for advocacy. In 2010, LSD support society was started and rare disorder day was observed for the first time in the country. Diagnosis was a huge challenge back then, the PAG efforts were recognized by Dr. VM Katoch, Director General of ICMR (2008-2015) leading to LSD taskforce being formed, and diagnosis of LSD was made available free of charge at six centres. Consistent efforts from parents, stakeholders as well as committed politicians like Former Chief Minister of Delhi, Ms Sheela Dikshit propelled the cause which popularized rare genetic disorders awareness throughout the country. He highlighted the efforts made by the state for RGD patients and the national rare disorder policy that offers financial support under group 1 and group 2 conditions. Cost and access for diagnosis has significantly improved in last 15 years as compared to several countries, however, treatment aspect of rare genetic disorders is still uncertain. Many of these conditions have no available treatment, and for the few that do, the cost is unaffordable for most parents. Mr. Shirol emphasized the present collective efforts towards awareness, diagnosis and advocacy, may still be deficient in addressing the concerns of patients, he highlighted the need to progress on the treatment front as it is essential to alleviate the quality of life of the patients and the parents. ORDI thus partnered with TIGS to bring all stakeholders together to improve the therapeutic and treatment options for rare genetic disorders. The momentum has started for drug development and research. India can develop low cost and effective therapy. The agenda for the summit is to present a platform that delivers faster and affordable drugs for the patients not only in India but globally. Mr. Shirol concluded his remarks by extending an invitation to the “Race for 7” event, a national multicity marathon organized by ORDI in February each year.

Dr. LS Shashidhara addressed the summit by introducing the Bangalore Life Science Cluster (BLiSC) campus, the ecosystem of basic, applied and translational science in different frontiers housed in one avenue. He stated that we are in an era of advanced deep technology in life sciences across all scales especially in genetics and genomics. He reiterated the concerted efforts of scientific community and civil society demonstrated during the Covid-19 outbreak for diagnostics, surveillance, vaccine development. Similar efforts can be replicated in indigenization of diagnostics and therapeutics for addressing the challenges of rare genetic disorders. The Genome India Project's dataset of 10,000 Indian genomes will serve as a vital baseline reference to accelerate research on rare genetic disorders. He applauded the efforts of senior scientists like Prof Thelma, Prof Bamezai, Prof YK Gupta, and Prof Alok Bhattacharya for setting the stage for translational work by using molecular diagnostics at the clinical level. With the current public-private partnership and affordable genome sequencing, he foresees the impact being delivered to more individuals affected with rare genetic disorders.

Dr. Monika Pahuja, Scientist-E at the Discovery Research Division of ICMR was the next dignitary on the dais for the inaugural. Under her guidance, the National List of Essential Medicines was released in 2022. She began her talk by discussing the comparative health economics of rare diseases in India and the United States, highlighting the disparities between the pharmaceutical budgets of both countries. Dr. Pahuja identified several challenges associated with rare diseases, including the lack of early diagnostics, limited treatment options, and a scarcity of data. These factors make it difficult for research institutions and pharmaceutical companies to successfully operate in this field. Despite these limitations, she proposed several potential solutions to address these issues. These included the need for well-informed and strong patient support groups, more affordable diagnostic methods, centralized databases for data access, and government policies that facilitate support. She also highlighted various government initiatives, such as the National Registry for Rare Diseases for collecting useful data on demography, phenotype, natural history, evolution and outcomes of specific diseases with and without treatment. She also highlighted the role of the Central Technical Committee for Rare Diseases in providing technical guidance on rare diseases, particularly in relation to the National Policy for Rare Diseases (NPRD) 2021 and its implementation. Additionally, she discussed ICMR's special initiatives, which encourage funding for research in areas like newborn screening, gene therapy, and regulatory pathways, while also promoting collaboration among stakeholders. She emphasized the efforts to be concerted towards developing cost effective diagnostics, well defined biomarkers, natural history studies, animal models, validation of findings through organoid development, interlaboratory and intralaboratory analysis for developing newer therapies, extended trials for interventions that has completed phase I and phase II studies in other nations and repurposing, palliative care devices. Moreover, Dr. Pahuja talked about the high-priority research questions that are being encouraged for funding and mentioned upcoming grants such as the Small Grant, Intermediate Grant, and Centre for Advanced Research.

She emphasized how funding agencies and the government are collaborating to support research in the field of rare diseases. Dr. Pahuja expressed confidence that organizations like ICMR are dedicated for providing funding for important research opportunities to improve treatment and diagnostics for patients with rare diseases. She concluded her talk with a quote that stated, "Political will and incentives can turn science into treatment."

The concluding talk for the inaugural was delivered by Dr. Amlin Shukla, a senior paediatrician and scientist (Scientist E) in the Division of Delivery/Implementation Research at ICMR. She oversees the coordination of the National Registry of Rare and Other Inherited Disorders. Dr. Shukla began by introducing the registry, explaining the genesis of its establishment. She provided a brief timeline of the work that initiated the registry and discussed the progress made since its inception. When the National Policy for Rare Diseases was developed, it was noted that the policy lacked necessary data support, highlighting the need for a registry. Dr. Shukla outlined the key milestones that led to the establishment of the registry, including the receipt of letters of intent from various organizations in 2017, the finalization of protocols and consent forms in 2018, and the development of a web portal to collect and report all generated data. The registry that is hospital based and prospective in nature was officially launched in 2019. She reported that the registry currently has 14,720 rare disease patients enrolled with about 213 rare genetic disorders with 24 centres contributing to this effort. Dr. Shukla discussed the aims and objectives of the registry, as well as the criteria for patient inclusion like definitive genetic diagnosis. She identified the twelve centres of excellence contributing to the registry, including AIIMS-Delhi, MAMC-Delhi, ICH-Chennai, and CHG-Bangalore. Dr. Shukla presented snippets of the data collected, which include family history, diagnostic details, treatment information, consanguinity, and socio-demographic details. She emphasized the quality assurance checks and regulations in place to ensure the reliability and accuracy of the reported data. Additionally, she elaborated on the electronic checks and ICMR interventions implemented to ensure data completeness and timeliness. Every patient enrolled in the registry in tagged to a centre of excellence for seamless integration. She also shared statistics regarding various disease categories and their representation in the latest registry update like group 1 disorders with storage conditions having 1609 patients, group 2 availing small molecule-based therapy with 930 individuals. Notably, the analysis revealed gender and age disparities in reported cases, with a predominance of males (76%) and about 83% of patients under the age of 19. These findings have prompted adjustments to approaches and policies aimed at addressing data disparities at state and city level. She elaborated that about 23% already had a family history and about as high as 30% having consanguinity in certain rare genetic disorders categories reiterating the need for genetic counselling. Dr. Shukla mentioned the diagnostic delay within 3 years for about 44% emphasizing the need for awareness. She concluded her talk remarking the registry would be launched for public access shortly with real-time dashboards for aggregated data.

From Left: Dr. Monika Pahuja, Dr. YK Gupta, Dr. Alok Bhattacharya, Mr. Prasanna Shirol, Prof. RNK Bamezai, Dr. LS Shashidhara, Dr. Amlin Shukla

From Left: Dr. LS Shashidhara, Mr. Prasanna Shirol, Prof. RNK Bamezai

Session 1: Advances in Diagnostics & Management of Rare Genetic Diseases in India

SESSION CHAIR
Dr. Anil Vasudevan
Professor, St. Johns Medical College, Bengaluru

Dr. Harsh Sheth
Assistant Professor, FRIGE'S Institute of Human Genetics, Ahmedabad

Dr. Rajdeep Das
Assistant Professor, GITAM deemed to be University, Visakhapatnam

Dr. Arshad Pandith
Associate Professor, Sher-e-Kashmir Institute of Medical Sciences, Srinagar (SKIMS), Srinagar

Dr. Sunita Bijarnia Mahay
Clinician and Metabolic Geneticist, Sir GangaRam Hospital, New Delhi

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PATIENT ADVOCACY GROUP

Ms. Shalini Kedia
Fragile-X Society India, Mumbai

Session 1: Advances in Diagnostics & Management of Rare Genetic Diseases in India

Development of Indigenous Technologies in the Field of Rare Disease: Dr. Harsh Sheth

Dr. Harsh Sheth's talk focused on the development of indigenous technologies in the field of rare genetic disorders. He began with elucidating smMIP(single molecule molecular inversion probes) for capturing the region of target interest as a powerful tool for targeted variant analysis using lysosomal storage disorders (LSDs) as an example explaining its cause, inheritance pattern and prevalence. Dr. Sheth highlighted the development of an India-specific LSD panel using next generation sequencing approach along with a particular focus on copy number variants in LSDs. He further elaborated on the expected diagnostic yield in suspected cases and patent acquisition for this innovative diagnostic approach. Additionally, he talked about the “Disha” program that is an initiative in association with Sanofi to provide free biochemical and genetic diagnosis for five LSDs: Gaucher disease, some MPS1 cases, Fabry disease, and ASMD. Lynch Syndrome was another key topic, with discussion on - discovery of gene, pathway, prevalence and associated risks. He highlighted the role of microsatellites in Lynch Syndrome cancer identification. He also presented favorable findings on a study on aspirin administration for cancer prevention. Dr. Sheth presented insights on the development of India’s first prospective Lynch Syndrome database and its global acceptance. Towards the end, he touched upon male infertility, its genetics and its anticipated impact on public health and outcomes.

Landscaping of Rare Genetic Disorders in a Unique Population: The Valley of Kashmir – Dr. Arshad Pandith

Dr. Arshad Pandith began his talk by highlighting the global burden of rare genetic disorders, affecting 350 million people worldwide, with approximately 7 million in India. Rare diseases are the second leading cause of infant mortality, with 30% of affected children dying before the age of 5 years. Dr. Pandith emphasized that 70% of these diseases manifest in childhood and 95% lack approved treatments. He discussed the importance of various genetic tests like carrier testing, prenatal, predictive, and newborn screening, which play a vital role in disease risk profiling and therapy selection. He also outlined the economic and clinical challenges faced in diagnosing and managing rare genetic disorders. Dr. Pandith pointed out the bottlenecks in the field, including limited clinical data, lack of population-specific databases, and challenges in genomic data analysis and sharing. Currently, only 3,200 genes for 4,500 diseases are known, but it is predicted that 6,000 genes may cause up to 10,000 rare diseases.

Advancements in NGS are discovering 150 gene functions and 100 new disease-gene relationships each year. Dr. Pandith also discussed the unique genetic landscape of Kashmir, where endogamy and high consanguinity rates (35-50% of the population, often first cousins), contribute to a higher prevalence of rare genetic conditions, especially recessive conditions. He shared several case reports, including a high incidence of hearing loss in Dadhkai village (the "village of silence"), progressive pseudorheumatoid dysplasia in Arai village, a village of deaf and mute in Paralkot with approximately 80% of the population being deaf and mute with high endogamous background and Huntington's disease in Charari Sharif village, highlighting the implications of consanguinity in the region. He also touched upon the regional challenges, such as limited access to target populations, lack of patient registries, and a scarcity of therapeutic options, all contributing to a psycho-social and economic burden. Dr. Pandith concluded by outlining plans for establishing a bio-repository, creating an interactive database, conducting awareness programs, and utilizing NGS for genetic profiling to better understand and manage rare genetic disorders in the region.

Application of Mass Spectrometry in Molecular Medicine: Dr. Rajdeep Das

Dr. Rajdeep Das began his talk by highlighting the application of mass spectrometry (MS) in molecular medicine, with a particular focus on hemoglobinopathies. He discussed clinical symptoms, prevalence and the importance of diagnosing hemoglobinopathies. Conventional methods such as alkaline gel electrophoresis and automated HPLC for identifying hemoglobin defects were explained followed by an introduction to the approach of Nano LC/ESI-MS (Nano liquid chromatography coupled with electrospray ionization mass spectrometry), for hemoglobin variant characterization. Dr. Das elaborated on the experimental setup he developed, using patient and control samples to validate this approach, and emphasized the significance and potential of mass spectrometry in accurately diagnosing hemoglobin variants. A significant portion of the discussion was dedicated to sickle cell anemia, its genetic etiology, and the challenge of lacking a known structure for oxygenated sickle cell hemoglobin. He also highlighted how this gap is crucial for the drug development area and presented his research on developing the structure using his approach. He also mentioned his lab’s research interest in analyzing the sickle cell variant from different regions of India, particularly the eastern and central parts by using MALDI-IMS as the method. Additionally, Dr. Das introduced the approach of using DESI-MS for the detection of inborn metabolic errors and small molecular disorders in newborn, hence promising advancements in neonatal diagnostics.

Advances in Diagnostics and Management of Rare Genetic Diseases in India: Dr. Sunita Bijarnia Mahay

Dr. Sunita Bijarnia Mahay began the talk by discussing India Story- the evolution of genomic technologies in India, transitioning from Sanger Sequencing to MLPA and then to Next Generation Sequencing now advancing to newer technologies. She emphasized that genomics is no longer the sole focus, as researchers in this field are now exploring transcriptomics, proteomics and metabolomics i.e. multiomics approach. She highlighted the importance of multiomics in clinical research, diagnostics, biomarker identification, phenotypic spectrum and its implications in the field of therapeutics. She also briefly discussed Optical Genome Mapping (OGM) which is the new frontier for the identification of structural variants surpassing the capabilities of conventional techniques. Using an example related to Facioscapulohumeral Muscular Dystrophy (FSHD) and its causative gene DUX4, she explained how the unique genetic makeup of large repeat contractions of this gene makes it difficult to diagnose using NGS, whereas OGM allows for faster and more accurate diagnosis. She presented a patient case study in which OGM successfully diagnosed FSHD, reinforcing its clinical utility. Dr. Sunita also discussed the trajectory of rare discovery following the development of diagnostics and various methods of therapeutic strategies.

Another key focus of her talk was RNA therapeutics, mainly RNA interference (RNAi) as a promising treatment for genetic disorders. She illustrated this with a case of a patient who had Primary Hyperoxaluria, who was treated with RNAi- based therapy Lumasiran drug. The treatment resulted in a significant improvement in the patient's overall well-being, demonstrating the potential of RNA therapeutics in clinical applications.

Challenges in Raising Awareness and Diagnosing Fragile X Syndrome: Ms. Shalini Kedia

Ms. Shalini Kedia delivered the talk on the challenges in raising awareness and diagnosing Fragile X syndrome in India which is a leading cause of inherited intellectual disability and a single gene cause of Autism. She is the Chairperson of Fragile X Society India, Board member of Fragile X International, and a parent of a child with Fragile X syndrome. She reiterated the lack of awareness among the public and medical professionals often results in missed genetic testing opportunities. The Fragile X Society is a nonprofit organization started in 2003, has supported over 12500 families in India, using the LEAP approach- Listen, Empower, Awareness and Personalize to help families lead independent lives. Ms. Kedia emphasized that societal ignorance and the taboo surrounding genetic disorders contribute to delayed diagnosis.

During the Covid-19 pandemic, the Society expanded awareness efforts to general public, resulting in increased diagnosis. She also highlighted the impact of FMR gene repeats on women’s fertility and the need for more awareness in IVF and genetic counseling. The organization also connects patient groups through social media to share experiences and makes sure right information is passed on avoiding any misleads. She also shared a testimony highlighting the importance of early genetic testing, which could prevent inheritance of this syndrome. The availability of guidelines by Indian Academy of Pediatrics on Fragile X syndrome and an educational course on Udemy on basic understanding of this condition in layman language also with quick guidelines was shared in her talk. In the last section of the talk, Ms. Shalini shared her family’s journey from her son being diagnosed with this condition to how her family is trying out different techniques and management plans for her son to lead a normal life.

From Left: Dr. Arshad Pandith, Prof. RNK Bamezai, Dr. Anil Vasudevan

From Left: Dr. Anil Vasudevan, Prof. RNK Bamezai, Ms. Shalini Kedia

Panel Discussion 1: Status of Orphan Drug Development, Implementing Treatment Protocols & Clinical Trials for Rare Diseases in India

MODERATOR

Dr. Alok Bhattacharya
Professor, Ashoka University, Sonipat

Mr. Prashanth Reddy
Lawyer and Author

Prof. R.N.K. Bamezai
Former Vice Chancellor, Shri Mata Vaishno Devi University (SMVDU), Katra

Dr. Y K Gupta
Former Professor, AIIMS New Delhi and Chairman, Governing Council, AIIMS Jammu

Dr. Arkasubhra Ghosh
Director, GROW Research Laboratory, Narayana Nethralaya Foundation, Bengaluru

Dr. Satyajit Mohapatra
Director, SRM Centre for Clinical Trials & Research, Kattankulathur (TN)

Dr. Monika Pahuja
Scientist E, Discovery Research, Indian Council of Medical Research, New Delhi

Panel Discussion 1: Status of Orphan Drug Development, Implementing Treatment Protocols & Clinical Trials for Rare Diseases in India

After a brief introduction of all the distinguished panelists, Prof. Alok set the tone for the discussion beginning with insightful exploration of the book “The truth pill” written by Dinesh S Thakur and Prashanth Reddy which provides a drug regulatory insight in India. The panel stressed on the coordinated collaboration of all the stakeholders to work towards a unified objective by highlighting the difficulties posed by rare genetic disease community like heterogeneity in phenotype, a smaller number of patients and lack of established guidelines.

The challenges of drug development are not subtle indeed. The uncertainty of the estimated number of patients is one of the significant obstacles when it comes to the profit margins of pharma sectors investing in orphan drug production. Another highlight of the discussion remained to redress innovative solutions for reducing the time-consuming process of drug development and prolonged clinical trials. The testing situations with clinical trials arise with absence of clarity on patient selection criteria and ambiguity over the natural history of the disease which ultimately causes lack of assurance with respect to selecting appropriate endpoints for a rare disease clinical trial. Moreover, well designed clinical trials can only be achieved when there is an appropriate diagnosis, making the enhancement of rare genetic disease diagnosis a pressing necessity.

The recruitment of patients for clinical trials encounters an additional challenge due to the dispersed and limited population of the patients. While discussing the challenges of clinical trials, the panelists suggested the implementation of Emergency Use Authorization (EUA) approach which India has already uncovered during COVID-19 pandemic, and it can be reattempted for rare disease trials. However, the EUA approach expects thorough consent and legal representation. The panel emphasized patient compensation clauses and a fast-track approval process for specific needs of regulations for rare genetic diseases.

The opinions from the experts in the panel underscored the importance of strong regulatory guidelines for pharma industries to address the challenges such as regulatory transparency and pointed out the understanding of increased demands of exemptions from pharmaceutical advisory committee (PAC)

The panelists further talked about the grants offered by Indian Council for Medical research (ICMR) and its tech transfer policy with a case-by-case approach for rare disease research. ICMR has 75 centers across India involved in clinical trials, with 4 centers dedicated to phase 1 trials. Moreover, ICMR is in the process of adding more than 60 RGDs to the standard care workflow. The advisory panel suggested that ICMR should also highlight the need for systemic approach to diagnosis, treatment and prevention as well as grouping the rare genetic disorders according to the common symptoms. Besides that, the latest updates on the disease registry from ICMR were addressed with an emphasis on expediting its completion.

The panel mentioned the use of Artificial Intelligence (AI) and challenges pertaining to it in redressing the rare genetic disease challenges. The experts emphasized that AI could enhance patient selection and recruitment or can be used to predict risks and benefits, however challenges with data bias and legal liabilities will remain.

The key takeaway from the discussion was promoting the provision of incentives to pharma companies and promoting awareness and government responsiveness. Clinical trials including only one patient (n=1) in terms of its feasibility can be encouraged. The collaboration of the stakeholders was stressed by all the panelists. Consistent efforts from all the areas can pace up the advancement of orphan drug development in India.

From Left: Dr. Alok Bhattacharya, Mr. Prashanth Reddy, Dr. Monika Pahuja, Dr. Satyajit Mohapatra, Dr. Arkasubhra Ghosh, Dr. YK Gupta, Prof. RNK Bamezai

From Left: Dr. Monika Pahuja, Dr. Satyajit Mohapatra, Dr. Arkasubhra Ghosh, Dr. YK Gupta

Session 2: Gene Therapy: A Leap for Rare Genetic Diseases in India

SESSION CHAIR

Dr. Ramachandran Shaji
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Dr. Indumathi Mariappan
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PATIENT ADVOCACY GROUPS

Ms. Bhavana Mehra
Vice Chair, Huntington's Disease Society of India (HDSI)

Ms. Sanjana Goyal
President, Indian Association of Muscular Dystrophies, Solan

Session 2: Gene Therapy: A Leap for Rare Genetic Diseases in India

Transformative Potential of Gene Therapy in Hematological Disorders- Alok Srivastava

Dr. Srivastava's talk provided an insightful overview of the transformative potential of gene therapy for treating genetic disorders, with a specific emphasis on hematological conditions like beta-thalassemia, sickle cell disease, and haemophilia. He explained complex concepts like how gene therapy is reshaping the future of medicine. The session highlighted two main approaches to gene therapy: *in vivo*, where genetic material is delivered directly into the patient's body, and *ex vivo*, where cells are genetically modified outside the body and then transplanted back into the patient. Both approaches carry their own set of challenges and opportunities. For hemoglobin-related disorders, Dr. Srivastava discussed the use of gene edition and advanced gene-editing technologies such as CRISPR-Cas9, which have shown promising results in treating conditions like beta-thalassemia and sickle cell disease. These therapies have provided renewed hope to many patients, but their high costs remain a significant barrier, limiting accessibility, especially in resource-limited settings like India. In addressing hemophilia, a disorder marked by clotting factor deficiencies, he highlighted the groundbreaking advancements in AAV-based gene therapies, which have demonstrated the ability to restore near-normal clotting activity in patients. However, the challenge of pre-existing immunity to viral vectors remains a key technical hurdle that must be overcome for widespread adoption. Dr. Srivastava also emphasized the urgent need for a clinical trial infrastructure in India. Strengthening this system would facilitate local innovation and expedite access to life-saving treatments. Cost reduction strategies were identified as crucial for making gene therapies accessible beyond elite healthcare settings, ensuring that they reach the broader population. The session concluded with an optimistic outlook, acknowledging that while gene therapy is still in its developmental stages, it holds tremendous potential to revolutionize the treatment of genetic disorders. Dr. Srivastava stressed that continued research, international collaboration, and policy reforms are essential to ensure that these therapies can reach the patients who need them the most, transforming lives across India and beyond.

Regulatory Challenges and Advances in Gene Therapy for Retinal and Neuromuscular Disorders: Dr. Arkasubhra Ghosh

Dr. Arkasubhra Ghosh began his talk by elucidating the importance of regulatory processes in gene therapy, highlighting that producing clinical-grade vectors and adhering to necessary regulations are crucial for advancing gene therapy treatments. He illustrated this by sharing successful examples from his lab, starting with Stargardt disease, a form of inherited retinal dystrophy caused by mutations in the ABCA4 gene. Patients with Stargardt disease progressively lose their central vision due to retinal degeneration. Dr. Ghosh explained how treatments using AAV vectors targeting the ABCA4 gene successfully reduced lipofuscin accumulation, a hallmark of the disease, and stabilized opsin proteins, ultimately restoring vision in animal models, as evidenced by improved electroretinogram readings.

He then moved on to discuss Duchenne Muscular Dystrophy (DMD), a severe fatal genetic disorder caused by mutations in the dystrophin gene, which plays a critical role in maintaining the structural integrity of muscle fibers. Dr. Ghosh demonstrated how introducing micro dystrophin constructs in animal models can restore muscle function. He mentioned that high doses of the therapy led to severe adverse events, prompting efforts to optimize the vector efficiency. Through the optimization of AAV vectors and enhancing the stability of dystrophin constructs, his team was able to achieve therapeutic levels of dystrophin expression at lower doses, thereby reducing the risk of adverse effects while maintaining functional force generation in animals. He also discussed their work on gene editing for FENIP, a brain disorder, where AAV-delivered Cas9 constructs and base editors were tested across various delivery routes and serotypes. This work showed promising results, with effective expression in the brain, demonstrating potential for clinical applications.

In the final part of the talk, Dr. Ghosh focused on the practical aspects of gene therapy development, including the establishment of a clean room for GMP-grade vector production and the necessary infrastructure to scale up production for clinical trials. He also discussed the importance of screening patients for neutralizing antibodies to ensure the success of gene therapy treatments. He concluded by acknowledging the challenges ahead, such as expanding the production facility for large-scale clinical trials and reducing costs to ensure broader accessibility. Despite these challenges, Dr. Ghosh expressed confidence that significant progress has been made in gene therapy, which could revolutionize the treatment of a wide range of genetic disorders.

Stem Cell and Gene Editing Approaches for Inherited Retinal Diseases: Dr. Indumathi Mariappan

Dr. Indumathi Mariappan began her presentation by emphasizing the growing prevalence of inherited retinal diseases, particularly retinitis pigmentosa (RP), which causes progressive vision loss and blindness. She introduced her lab's work in addressing these diseases, underscoring the complexity and challenges in treating them. Retinitis pigmentosa is caused by mutations in over 300 different genes, making it a highly heterogeneous disease, with each mutation affecting the retina differently. One of the key challenges Dr. Mariappan discussed was the cost of available treatments. She mentioned the gene therapy for RP caused by mutations in the RPE65 gene (such as LUXTURNA), which has shown promising results but remains prohibitively expensive. While this therapy offers hope, it's largely inaccessible to patients in developing countries like India due to the high cost. She pointed out the need for more affordable, accessible treatments that can benefit the broader population, especially those in underserved regions.

To address these challenges, Dr. Mariappan and her team have been working on developing stem cell-based therapies for retinal diseases. One innovative approach they are exploring is the use of induced pluripotent stem cells (iPSCs). iPSCs are generated from healthy donor cells (such as skin or blood cells) and can be reprogrammed into retinal cells. Their lab has made significant strides in differentiating these iPSCs into retinal pigment epithelial (RPE) cells, which play a crucial role in the health and function of the retina by nourishing and protecting the photoreceptors. The potential of these iPSCs in retinal cell replacement therapy is substantial, as they could be used to replace or repair damaged retinal cells in patients suffering from conditions like RP (Retinitis Pigmentosa).

Dr. Mariappan also touched on the exciting prospects of CRISPR gene editing technology in retinal disease treatment. She explained that while gene therapy has been explored for treating retinal conditions, the precision of gene editing techniques like CRISPR could provide a more targeted and efficient method of correcting mutations at the genetic level. Her lab has been working with adenine base editors—a CRISPR-based tool that can correct single nucleotide mutations without introducing DNA breaks. This offers a potentially safer and more effective approach to editing genes responsible for retinal degenerative diseases. By precisely correcting genetic defects, this technology could open the door to personalized therapies tailored to individual patients based on their specific genetic mutations.

She also highlighted iStem, a company based in India that is developing stem cell-based therapies for retinal diseases. iStem has recently launched clinical trials for these therapies, which marks a significant milestone for stem cell research and regenerative medicine in India. The trials are a promising step toward providing accessible and cost-effective therapies for retinal diseases, especially in India, where genetic retinal diseases are prevalent but often underdiagnosed and underfunded.

She expressed optimism about the potential of stem cell therapies and gene editing techniques to transform the treatment of inherited retinal diseases. While challenges remain, particularly in terms of cost, scalability, and regulatory hurdles. The advancements her lab is making in regenerative medicine, CRISPR technology, and stem cell research could ultimately offer new hope for patients suffering from these debilitating conditions. She emphasized the importance of continued research, collaboration, and innovation in bringing these promising therapies to the clinic and improving accessibility for patients worldwide. Through her work, she highlighted the potential to change the future of vision restoration and treatment for inherited retinal diseases, with the ultimate goal of improving the quality of life for patients affected by these conditions.

mRNA Therapeutics for Hemophilia B: A Non-Viral Gene Therapy Approach- Dr. Srujan Marepally

Dr. Marepally's talk focused on a long-lasting mRNA-enabled protein replacement therapy using a liver-specific lipid nanoparticle system, using Hemophilia B as a model disease. He began by introducing gene therapy and the role of AAV vectors in this field and also highlighted certain limitations of using AAV vectors for liver disorders, particularly the prevalence of AAV antibodies in the serum of most individuals and the extremely high costs associated with gene therapy, which make it inaccessible to the general public. Keeping these limitations in mind, he emphasized the potential of alternative non-viral vectors, such as lipid nanoparticles or polymers, while noting the challenges associated with these alternatives. He emphasized that overcoming these challenges could lead to the development of efficient and feasible substitutes for AAV vectors.

Dr. Marepally provided examples of FDA-approved lipid-siRNA drugs currently in use, such as ONPATTRO (Patisiran) for hereditary ATTR amyloidosis and GIVLAARI (givosiran) for acute hepatic porphyrias. Dr. Marepally explained the process of using lipid nanoparticles for mRNA therapeutics and discussed why they cannot be used for DNA therapeutics. A lipid nanoparticle (LNP) consists of a positively charged lipid membrane and negatively charged plasmid DNA, which combine to form a lipoplex that is then introduced to the target site. The lipoplex is endocytosed into the target cells. He referred to this method as a common platform for addressing rare diseases, as it becomes easier to develop treatments for various disorders once a standard approach is established.

For his research, he chose hemophilia as the model disease, aiming to achieve a 10% protein replacement. The team focused on extending the half-life for long-term protein expression, with the approach of developing liver-specific LNPs and optimizing the structure of mRNA to meet their objectives. They utilized a combination of polymer micelles and LNPs for the mRNA delivery system to prolong mRNA half-life and its expression. He noted that the GaliNA5 galactosylated lipid formulation exhibited superior physicochemical properties and higher cellular uptake, while still falling within the acceptable size range.

Considering the promising results, they proceeded to engineer the mRNA to develop a vaccine and conducted clinical trials in mice, which showed positive outcomes. Dr. Marepally concluded his talk by stating that the research will continue, and clinical trials will be conducted to assess the safety and efficacy of the therapy.

The Patient Perspective: Navigating Life with a Rare Genetic Disorder- Ms. Bhavana Mehra

Ms. Bhavana Mehra, delivered a compelling talk on Huntington's Disease (HD), a rare neurodegenerative disorder. She shared her personal experience, revealing how at the age of 17, she learned of her mother's HD diagnosis, which highlighted the genetic nature of the disease and the 50% chance of inheriting it. Ms. Mehra stressed the lack of awareness about HD in India, particularly the absence of government recognition as a rare disease, which hinders patients from accessing critical financial and policy support. She highlighted ongoing research, including gene therapy, and the role of Bangalore's research institutes like NIMHANS in both advancing scientific knowledge and spreading awareness. Despite these efforts, Ms. Mehra pointed out significant challenges such as high cost of medicines, inadequate palliative care, and the lack of information reaching patients about the policies like National Policy for Rare Diseases (NPRD).

Ms. Mehra discussed the pivotal role of patient advocacy groups like HDSI, which was co-founded primarily by NIMHANS doctors in 2019 and now includes families, healthcare professionals, and caregivers. The society works to support the HD community, raise awareness, and improve care. She spoke about HDSI's initiatives, including a free clinic in Koramangala, the HD Care social media group, and virtual support groups during the pandemic. The society also empowers patients to share their stories, participate in public campaigns, and raise awareness.

Ms. Mehra concluded by discussing the challenges of collaborating with the government to include HD under the NPRD, secure benefits like disability claims, and establish specialized centres for HD care. She shared optimistic updates from recent meetings, with Arogya Soudha which included ministers from Bangalore and a member from National Rare Disease Cell, a commitment from the Karnataka government to establish a multi-speciality centre for HD. She emphasized the need for continued collaboration and efforts to support HD patients in India.

Empowering Patients Through Advocacy and Awareness- Ms. Sanjana Goyal

Ms. Sanjana Goyal shared the remarkable work the organization has been doing since its inception in 1992. Diagnosed with Muscular Dystrophy (MD) along with two family members, Ms. Sanjana founded IAMD with a mission to improve the quality of life for those living with MD. IAMD has organized numerous initiatives across India, including medical and awareness camps, physiotherapy support, and counseling centres in Chandigarh and Delhi. The association also provides diagnostic services and aids in wheelchair distribution. Notably, the first summer camp was held in Sadhupul in 1995, attended by 29 MD warriors. Subsequent camps have reached several states, like Rajasthan, Andhra Pradesh, Himachal Pradesh, Gujarat, and Maharashtra spreading awareness and offering support to the community. IAMD celebrates ‘International Duchenne Muscular Dystrophy Day’ on September 7th, every year to raise awareness among students, medical professionals, and the general public. One of the organization's major milestones is the establishment of the Manav Mandir Integrated Muscular Dystrophy Rehabilitation Centre (IMDRC) in Solan, Himachal Pradesh, in 2018. This wheelchair-friendly, 7-storied facility provides a comprehensive range of services including physiotherapy, hydrotherapy, DNA testing, psychological counseling, and more. The centre has become a beacon of hope for MD patients, offering pain management, mobility enhancement, and overall well-being. Ms. Sanjana highlighted the significant achievements of IAMD- 1727 patient visits, 1266 patients in 7 days camp, 461 patients in more than 7 days camp, catered to around 99 patients with conditions other than MD, more than 649 DNA samples being sent for testing along with training over 300 volunteers, 741 physio and occupational therapists to provide physiotherapy to improve mobility in numerous patients. She encouraged more volunteers to join the cause, spread awareness, and contribute to the growing impact of IAMD.

From Left: Ms. Sanjana Goyal, Ms. Bhavana Mehra, Dr. Srujan Marepally, Dr. Arkasubhra Ghosh, Dr. Indumathi Mariappan, Dr. Alok Srivastava

From Left: Ms. Sanjana Goyal, Ms. Bhavana Mehra, Dr. Srujan Marepally, Dr. Arkasubhra Ghosh

Session 3: Population and Newborn Screening in Indian Contexts

SESSION CHAIR

Dr. B K Thelma
Professor, Department of Genetics, University of Delhi

Dr. Lakshmi B R
Director and Managing Trustee, Molecular Diagnostics, Counselling, Care and Research Center (MDCRC), Coimbatore

Dr. Vykunta Raju K.N
Professor, Pediatric Neurologist, Indira Gandhi Institute of Child Health (IGICH), Bengaluru

Dr. Gurjit Kaur
Professor, Department of Physiology, Govt. Medical College and Hospital, Chandigarh

Dr. K Thangaraj
TIGS - CCMB Outstanding Scientist

PATIENT ADVOCACY GROUPS

Ms. Vaishnavi Prasad J R
Primary Immunodeficiency Patients Welfare Society (PIDPWS), Bengaluru

Session 3: Population and Newborn Screening in Indian Contexts

Screening for Duchenne Muscular Dystrophy – a decade of experience at MDCRC: Dr. Lakshmi B R

Dr Lakshmi spoke about the work for muscular dystrophies patients done by MDCRC, a not-for-profit institution set up in 2011. She described the Genetics & Public Health framework created at MDCRC with Duchenne's Muscular Dystrophy (DMD) as one of the main focus areas, combining sensitivity to societal needs, leadership and management to implement scientific and technological innovations for disease alleviation and elimination.
Beyond the debilitating effects of the disease itself, DMD with its X-linked recessive inheritance pattern affecting male children of mothers who are carriers, has huge social problems. Being a lethal genetic disorder with no cure, prevention is the only way to tackle disorders such as DMD. MDCRC, since its inception as a foundation, has therefore focused on disease identification towards prevention, and has very well-established pipelines for genetic screening and prenatal and psychosocial counselling.

Additionally, their field teams cover all the 45 health unit districts of Tamil Nadu to understand the disease prevalence and spread awareness about muscular dystrophies. The NRHM-DPH trains the Primary Health Centre (PHC) doctors and Village Health Nurses (VHNs), as well as students and volunteers for door-to-door surveys to track the number of children in the districts. These field staff spot any kids with muscle issues or walking and balance problems in an effort towards early identification of DMD and Spinal Muscular Atrophy (SMA). The centre networks with District Collectors and Deputy Director of Health Services (DDHS) to ensure data is collected in collaboration with the government agencies.

MDCRC provides free health care services for affected children. The centre runs a multi-disciplinary program for clinical care, rehabilitation, and family support for a holistic approach to tackling DMD. They also conduct regular camps for awareness and sampling, including the latest technologies such as PCR, MLPA, NGS from blood samples without having to resort to muscle biopsies. The DNA samples are tagged along with appropriate consent forms and stored at the centre to enable ease of follow-up and further testing as needed.

The integrated Community Genetics model developed at the MDCRC holistically addresses the issues faced by the muscular dystrophy community – from finding the patients on ground and helping them with sampling and molecular testing, to reaching the appropriate treatment at PHCs and developing a reliable tertiary clinical network. Clinicians from all the specialities are brought together making it easier for families to tackle the multiple health problems faced by these children.

“MDCRC’s pilot project is funded by the National Rural Health Mission, Government of India and the Department of Public Health and Preventive Medicine, Government of Tamil Nadu developed a healthcare model over a decade ago for disease identification and prevention”.

The centre’s Vision for 2022 was to have no DMD and they have covered all of rural districts in Tamil Nadu to achieve their goal. Dr. Lakshmi concluded by sharing their plans going forward for tackling dystrophies among the state’s urban population.

NBS screening program at GMCH, UT Chandigarh: Dr. Gurjit Kaur

Dr. Gurjit Kaur shared her decade-long experience in establishing NBS and prenatal screening for metabolic disorders at the Government Medical College Hospital Chandigarh, starting with a grant in 2002. She described the challenges and successes in setting up newborn screening for G6PD deficiency in the hospital and then expanding it to include other hospitals in the city. Within a few years, congenital hypothyroidism and congenital adrenal hyperplasia were also added to the G6PD screening program.
Over 8 years, 1 lakh babies were screened in this program, along with meticulous systems for follow-up to ensure parents understood the need for such screening and consented to the babies’ sampling. The talk highlighted pertinent issues in the Indian context where tracking can be difficult once the baby is discharged from the hospital after the delivery. The team overcame some of these issues by registering the family and collecting grandparental address details and reaching the family home in case of a positive sample. Several optimizations were done to ensure sampling within the relevant time window, standardized at 24 hrs post birth, in view of the changing metabolite profiles in newborns.

Dr. Kaur described how the team incorporated learnings from a visit and QC training program at the Centers for Disease Control and Prevention (CDC), Atlanta, developing their own protocols considering humidity, sunlight, and storage and transport requirements. The program continued till 2022 despite multiple setbacks due to the COVID-19 pandemic but then was halted following changes in the administration. A similar model was also developed with the Government of Haryana but stalled after screening of just over 2000 babies.

Dr. Kaur concluded her talk by highlighting her learnings and recommendations for NBS programs, outlined below.

Challenges

- Lack of awareness among professionals and general population
- Educating parents about newborn screening is a challenge
- The baby looks normal at birth so it is difficult for parents to understand that the child may carry certain metabolic disorder, not expressed during birth or few days after birth, but which may later on lead to serious mental and physical abnormalities
- Lengthy purchase procedures
- No local dealer
- Screening has to be done each day including holidays, therefore sufficient manpower is required otherwise exact prevalence can't be calculated
- Timely confirmatory diagnosis is a big challenge
- No complete developed software for NBS program - neither for recruitment during prenatal period nor for minimum of 3 years of follow up

Recommendations

- Awareness must be created
- Comprehensive Hypothyroidism screening must be mandatory, so that state-wise problems of NBS screening program can be identified
- SOPs may be developed for India
- Sick babies must be screened for complete panel of metabolic disorders
- "Special clinics" and panel of doctors should be constituted in each state with the help of experts
- Each component like genetic counseling, sampling, punching, testing for screening disorders, confirmatory diagnosis and management to be an independent component along with integrated program through software for follow-up testing and management.

Newborn screening (NBS) in Indian contexts: Dr Vykunta Raju

Dr. Vykunta Raju began his talk with the reminder that even 50 years after the era of screening for Inborn Errors of Metabolism (IEM) began in countries like the USA, India remains in the primitive stages of NBS. Paediatric clinicians highly recommend adding NBS to the RBSK (Rashtriya Bal Swasthya Karyakram) screening program in the country which currently focuses on vision, auditory and birth defects in infants. NBS for IEMs and congenital hypothyroidism are invaluable in reducing the country’s disease burden because there are simple interventions that can be made following the early identification of these disorders. These interventions are time-dependent and need to be provided at the earliest stages, before the harmful effects set in leading to irreversible mental and physical damage.

Several categories of metabolic disorders associated with protein (amino acid, organic acid, or urea cycle), carbohydrate (galactosemia, gluconeogenesis, GSD) and lipid (fatty acid oxidation and cholesterol synthesis) dysfunction can in fact be easily screened. Dr. Raju outlined several factors that can influence the outcomes of NBS, which need to be resolved while setting up such screening programs to avoid false results. Dr. Raju provided examples of metabolic disorders such as maple syrup urine disease (MSUD) and phenylketonuria (PKU) where children who were diagnosed after a few years had severe disabilities whereas their siblings who were fortunate to get early diagnosis grew up almost normally. Tandem mass spectrometry (TMS) techniques can help test for over 45 disorders of amino acid metabolism, organic acid metabolism and fatty acid disorders via dried blood sampling within 2-5 days of birth. Due to the small sample size needed (75 ul), fast turnaround time and high sensitivity and specificity, it is an ideal technique for NBS programs. He cautioned that it should not be used as a diagnostic test rather as a means to screen babies who can then be shortlisted for further diagnostic testing as needed.

A fixed workflow is required for NBS as well as protocols for follow-up actions in case of a positive disease indication. SOPs for each disorder should guide the timing of sampling, with enough data on incidence. Sampling also requires counselling and informed consent along with proper collection and storage guidelines. Finally, clear path ahead and genetic counselling for next pregnancies need to be mandated as part of the NBS program.

Dr. Raju called for a change in the current dogmas around RGDs in India. Early diagnosis via NBS and population screening needs to be the priority because it can significantly alter the impact of many diseases and reduce the diagnostic odyssey of the patients and their families.

Population Genomics for Public Health: Rare Disease Perspectives: Dr. K. Thangaraj

Dr. Thangaraj provided a fresh perspective to the problem of high RGD burden in India. His talk focused on the recent evolution of population and human diversity in India which has led to an estimated 70 million RGD patients in India currently. Studies over the last few decades have helped understand Indian population history in terms of the two major founding populations in prehistoric India, the ancestral North and South Indian (ANI and ASI).
Following a high degree of ANI and ASI populations admixture that occurred over the last 4000 to 2000 years, endogamy took over in the last 2000 years in the country. There are therefore 25 distinct groups in India currently, and many of these population units continue to marry within themselves. In his lab, the team focused at 275 populations from South Asian regions, including Indian, and one third of the populations had very high IBD (identity by descent) that led to population-specific mutations. Compared to Ashkenazi and Finnish populations, which are well studied for a large number of inherited disorders, the Indian populations have much higher IBD. Thus, many of them share a common haplotype and this explains the passage of deleterious mutations across generations.

Based on the high IBD groups, a population from Tamil Nadu was identified that suffer from Junctional Herlitz Epidermolysis Bullosa (JHEB). The disease is associated with a deletion in the Lamb3 gene, as identified by exome sequencing, and leads to affected newborns dying within a couple of months of birth. Haplotype analysis revealed the same mutation in over 10 such families, as seen in the Genome India project. Genomic data from 8 lakh individuals in global databases, however, confirmed a lack of this specific mutation seen in this population, as well as 8000 Indians genomes (from Indian database) also did not have the JHEB-associated mutation. However, many families within this community suffered from such infant deaths and the parents were found to be heterozygous carriers in each of these families. Though these families did not have a culture of consanguineous marriage in their community, they follow a strong endogamous marriage system, suggesting that the spread of this genetic deletion might be because of founder events.

Humanized CRISPR-Cas9 mouse model: Homozygous mice were generated with the Lamb3 mutation and recapitulated the patient's phenotype - thin and folded skin structures, blisters and severe skin erosions along with neonatal mortality 2 days after delivery - confirming that the identified deletion mutation is the actual cause of the disease. Mice with a slightly larger deletion show symptoms after 4 months and serve as model for understanding JHEB and its effect on the various organs including the skin.

Disease-in-a-dish model for JHEB

Cells isolated from the amniotic fluid used for maternal testing were used to successfully develop an induced pluripotent stem cell (iPSC) model for the disease at TIGS. This line was used to also create a homozygous cell line carrying the patient-specific mutation which will serve as a disease model.

"Translating scientific endeavour for societal benefit: As an inspiring example of how understanding the causative mutation can lead to disease prevention, Dr. Thangaraj described the identification of a lady who had lost two earlier infants to the disease. In her 3rd pregnancy, the team analysed the amniotic fluid, and found the fetus to be a heterozygote like both the parents. Hence, the family was counselled to proceed with the pregnancy, resulting in their third child being born normal."

Screening and prevention: A model for eliminating rare diseases: Dr. Thangaraj's team at CCMB, in collaboration with TIGS, has developed a proposal to screen all the individuals of reproductive age in this region (~4000 individuals), for approval by the Government of Tamil Nadu's Directorate for Public Health and Preventive Medicine. Once all the carriers are identified by the mutation screening, premarital and prenatal counselling will be provided and public health officials will be trained for the same. This will go a long way in eliminating the birth of affected babies and significantly reducing the financial, emotional and social stress accompanying their birth and early death.

Primary Immunodeficiency Patients Welfare Society (PIDPWS): Ms. Vaishnavi Prasad

The session concluded with a talk by a patient advocacy group dedicated to patients affected by Primary Immunodeficiencies. The PIDPWS was founded by patients' families, with the current Secretary of the society, Ms. Rukhsana Haneef in 2013. The PIDPWS works towards bringing the unseen trials of these vulnerable patients into focus, arranging support from the medical community and the government and guiding the patients in multiple other ways to lead a healthy life with easy and free access to diagnostics and treatment. Over 450 PIDs exist in India, however they are not screened at birth so the diagnosis is delayed and the patients are severely impacted. They spend many years in hospitals and meeting multiple doctors for their repeated infections. PIDPWS advocates for mandatory NBS for SCID and to include PIDs under the Disabilities Act. PID is now registered in NPRD 2021, and patients can avail financial support upto 50 lakhs INR.

Children affected by PIDs are susceptible to continuous infections and awareness is needed to ensure timely treatment following an early diagnosis. Ms. Prasad highlighted the challenges faced by children with primary immunodeficiencies (PIDs) as they transition into adulthood. At the Centre of Excellence (CoE) in Karnataka, the Indira Gandhi Institute of Child Health (IGICH) provides intravenous immunoglobulin (IVIG) treatment to affected children. However, since IGICH is a pediatric facility, treatment is discontinued once patients turn 18. A recent petition to the Karnataka High Court provided some relief, allowing adult patients to receive IVIG infusions at Victoria Hospital. However, as Victoria is not a designated CoE, adult patients continue to face significant challenges in accessing appropriate care and recognition. The high cost of IVIG—approximately ₹15,000 for a 5g dose required every 21 days—places a substantial financial burden on families, compounded by the travel required to reach CoEs in cities like Bengaluru. Ms. Prasad advocated for the establishment of Centres of Excellence and Diagnostics specifically for PID patients, along with dedicated research centres across the country rather than in just a few metropolitan areas. Although the estimated prevalence of PIDs is around 1 in 2,000, the actual numbers are likely much higher, underscoring the urgent need for comprehensive epidemiological data collection nationwide. Similarly, research efforts need to be scaled up, as despite the existence of approximately 250 subtypes of PIDs, much remains unknown about their characteristics and disease progression.

Recommendations

1. Increase NBS, rather than waiting for the current 6-12 year age for diagnosis.
2. Develop indigenous solutions (current IvIg therapy is expensive and needs cold storage and clinical settings).
3. Advocate for support from government agencies for patient care.

From Left: Dr. K Thangaraj, Dr. Vykunta Raju KN, Dr. Gurjit Kaur, Dr. Lakshmi BR, Ms. Vaishnavi Prasad JR

From Left: Dr. K Thangaraj, Dr. Vykunta Raju KN, Dr. Gurjit Kaur, Dr. Lakshmi BR

Session 4: Clinical Research on Rare Genetic Diseases: Challenges & Opportunities in India

SESSION CHAIR

Dr. Anju Shukla
Professor, Kasturba Medical College, Manipal

Dr. Sridhar Sivasubbu
Senior Consultant, Vishwanath Cancer Care Foundation, Bengaluru

Dr. Atchayaram Nalini
Professor, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru

Dr. Sanjay Singh
CEO, Gennova Biopharmaceuticals Limited, Pune

Dr. Raghu Padinjat
Senior Professor, National Centre for Biological Sciences, Bengaluru

Dr. Charu Gautam
Senior Medical Director, IQVIA, Ahmedabad

PATIENT ADVOCACY GROUP

Mr. Vaibhav Bhandari
Founder, Swavlamban Foundation, Rajasthan

Session 4: Clinical Research on Rare Genetic Diseases: Challenges & Opportunities in India

Prioritizing Rare Genetic Diseases in Public Health and Genomic Research: Dr. Sridhar Sivabasu

Dr. Sridhar Sivabasu began his talk by emphasizing the need to make rare genetic diseases (RGDs) a public health priority, especially in a country like India, where such conditions affect approximately 1 in 1,000 individuals. He highlighted the importance of advocacy, policymaking, science, implementation, and screening in addressing this hidden burden. He highlighted the IndiaGen Initiative, a genomic program focused on sequencing diverse ethnic populations in India. He emphasized that 30% of genetic variations in India are unique, providing crucial insights into treatable genetic diseases. He raised thought-provoking questions, such as why existing molecules are not effectively utilized in treating rare genetic diseases, and emphasized the importance of exploring genetic variability, including differences in cancer susceptibility. Additionally, he advocated for screening approaches to enable early diagnosis and treatment, including newborn screening, parental screening for genetic counseling and prenatal testing, and pre-emptive screening for adult-onset diseases in at-risk individuals. He also discussed GUaRDIAN, a genomic research consortium in India, and presented case studies such as Familial Adult-Onset Myoclonic Epilepsy (FAME), which led to a Tamil Nadu government policy for diagnosis and intervention. Other examples included primary immunodeficiency disorders and cardiac channelopathies, which require scaling solutions through clinical phenotyping, sequencing, evidence building, awareness, advocacy, and action. He concluded by emphasizing the need for scalable solutions in RGDs that are not only relevant to India but also impactful globally.

Addressing Regulatory Hurdles and Pioneering Innovation: Dr. Sanjay Singh

Dr. Sanjay Singh outlined the intricate challenges involved in the regulatory approval process for new drug development in India. While acknowledging the reduction in required licenses from 28 to 21 as a step forward, he highlighted that the pathway remains arduous. The multi-layered process demands approvals from the Review Committee on Genetic Manipulation (RCGM), test licenses from the Central Drugs Standard Control Organization (CDSCO) and state FDA, and additional clearances from both RCGM and CDSCO. Dr. Singh advocated for streamlining these regulatory procedures, suggesting that the CDSCO could ease certain requirements to foster innovation. He emphasized that collaboration among regulatory authorities, industry leaders, academic institutions, and research organizations is essential to overcome these barriers. A robust and transparent regulatory framework, he argued, is critical to accelerating drug and therapy development for rare genetic diseases. Looking ahead, Dr. Singh underscored the transformative potential of technologies like CRISPR-Cas9 in advancing cell and gene therapy (CGT) in India.

He urged stakeholders to leverage such cutting-edge tools to enhance research and treatment outcomes. Concluding his address, Dr. Singh called for a shift in focus from capacity building to delivering tangible results, inspiring the audience to take meaningful actions for impactful change.

Navigating Clinical Trial Challenges with Patient-Centric Solutions: Dr. Charu Gautam

Dr. Charu Gautam provided an in-depth analysis of the unique obstacles faced in designing and conducting clinical trials for rare genetic diseases. These challenges stem from the small patient population, delayed diagnoses, limited data, and an incomplete understanding of disease mechanisms and natural histories. Additionally, she highlighted the evolving regulatory landscape and the high costs associated with drug development as major hurdles. Dr. Gautam emphasized the need for innovative and patient-focused approaches to clinical trials. She advocated for designing trial protocols that minimize burdens on patients and sites, while addressing practical challenges faced by patients and caregivers. Building strong, well-trained study teams and establishing rapport with participants, she noted, are crucial for smooth trial execution. On patient recruitment, she proposed leveraging laboratory data and data mining techniques to identify eligible participants. She also highlighted the pivotal role of patient advocacy groups (PAGs) in raising awareness and instilling confidence among patients to participate in trials. To reduce patient burdens, Dr. Gautam suggested providing logistical and emotional support, maintaining consistent communication, and offering site training to improve accessibility. She introduced the concept of decentralized clinical trials, where care is delivered at the patient's home, minimizing the need for travel to trial sites. Dr. Gautam concluded with actionable strategies to accelerate progress in India, including participation in global clinical trials, increasing awareness through PAGs, establishing clear patient pathways, and incentivizing patient engagement. Her insights provided a holistic view of the challenges in rare disease research and offered pragmatic solutions to address them effectively.

Modeling Developmental Origins in Lowe's Syndrome: Dr. Raghu Padinjat

Dr. Raghu Padinjat focused on Lowe's syndrome, a rare X-linked recessive disorder with a prevalence of 1 in 100,000. This condition primarily affects the eyes, kidneys, and brain. He highlighted challenges in treating RGDs and potential therapeutic strategies, including drugs, dietary modulation, mRNA therapies, and gene therapies. Dr. Padinjat emphasized the importance of understanding when these treatments would be most effective—during adult life or the developmental phase. He presented insights into the time course of disease progression, particularly the role of the OCRL gene mutation in Lowe's syndrome. Additionally, he discussed the mechanisms of brain development and disease, drawing from studies on febrile seizures in neurons.

He highlighted the need for understanding early neuronal development to determine the optimal timing for therapeutic interventions, especially for diseases where the affected tissues undergo minimal post-developmental changes. Dr. Padinjat concluded with a quote from Max Planck: "Insight must precede application", emphasizing the necessity of foundational knowledge in advancing treatments.

Patient Advocacy and Support: Mr. Vaibhav Bhandari

Mr. Vaibhav Bhandari shed light on the real-life challenges faced by patients with rare diseases. He underscored the value of hope, which advocacy efforts can bring, and shared key insights: Many patients struggle with basic tasks like dressing, eating, and drinking due to the progressive nature of their conditions. While provisions such as ramps and financial assistance exist under the Rights of Persons with Disabilities (RPwD) Act, gaps in implementation leave many patients without adequate support. He emphasized that employment, dignity, and accessibility should be central to rare disease policies. Mr. Bhandari advocated the three P's: a patient-centric approach, policy improvements, and progress through research.

This session offered valuable perspectives on integrating research, policy, and advocacy to improve the lives of individuals with rare genetic diseases, while emphasizing scalable and sustainable solutions.

Phenotype-Genotype Correlation in Rare Neuromuscular Disorders: Dr. Atchayaram Nalini

Dr. Nalini has been leading a multidisciplinary neuromuscular disorder clinic since 1991, where over 20,000 inherited neuromuscular disorder (NMD) cases have been registered. Inherited NMDs are fascinating areas of study due to ongoing research, advancements in gene therapy, and the development of drugs in the pipeline targeting these conditions. Dr. A. Nalini provided an in-depth discussion on specific congenital muscular dystrophy (CMD) disorders, such as Collagen Type VI-Related Disorders and Dystroglycanopathies, which challenge the traditional "one gene, one disorder" paradigm. She noted that approximately 40–60% of dystroglycanopathy cases lack mutations in known genes, suggesting the involvement of multiple genetic factors. These disorders may also be associated with brain anomalies, as seen in Fukuyama Congenital Muscular Dystrophy.

She also addressed congenital myopathies, characterized by static or slow progression. Common phenotypic features include slender builds, rigid spines, and ptosis. These conditions are often inherited in an X-linked recessive pattern.

Dr. Nalini further elaborated on Limb-Girdle Muscular Dystrophy (LGMD), which typically has a later onset. Its inheritance patterns are diverse, including autosomal recessive, autosomal dominant, and X-linked recessive. The prevalence of LGMD varies widely, ranging from 1 in 15,000 to 1 in 45,000, depending on the population and geographic region. She highlighted the role of various mutations in causing this disorder, emphasizing the genetic complexity and variability of CMDs and LGMD. The discussions highlighted several recurring themes, such as the complexities of regulatory approvals, the need for innovative and patient-centric approaches to clinical trials, and the importance of collaboration among stakeholders, including regulatory authorities, industry leaders, academia, and patient advocacy groups. The speakers acknowledged the unique challenges posed by rare genetic diseases, such as small patient populations, high costs, and limited understanding of disease mechanisms. Despite these challenges, the session also emphasized the significant opportunities to transform the landscape of rare disease research in India. The potential of cutting-edge technologies like CRISPR-Cas9 and decentralized clinical trials was underscored as game-changers for research and treatment. Additionally, fostering global partnerships, leveraging data-driven strategies, and strengthening advocacy efforts were presented as pathways to accelerate progress.

In conclusion, the session underscored a collective call to action—to simplify regulatory processes, innovate clinical trial methodologies, and prioritize patient-centric solutions. The experts collectively inspired the audience to move beyond identifying challenges and take decisive steps to deliver impactful results, ultimately improving the lives of patients with rare genetic diseases.

From Left: Mr. Vaibhav Bhandari, Dr. Charu Gautam, Dr. Sanjay Singh, Dr. Sridhar Sivasubbu, Dr. Raghu Padinjat

From Left: Mr. Vaibhav Bhandari, Dr. Charu Gautam, Dr. Sanjay Singh, Dr. Sridhar Sivasubbu, Dr. Raghu Padinjat

Panel Discussion 2: Advancing Diagnostics and Therapeutics for Rare Diseases in India

MODERATOR

Mr. Samir Sethi
Chairman, Advocacy Committee, ORDI

Dr. Sakthivel Murugan
Medgenome, Bengaluru

Dr. Nishant Kumar Singh
Medical Lead - Rare Diseases, Southeast Asia & India Sanofi, New Delhi

Dr. Venkatasubramanian Narayanan
Co-Founder, Peptris Technologies, Bengaluru

Dr. Hardik Vasnawala
Astrazeneca, India Medical Affairs, Ahmedabad

Dr. Arun Shastry
Dystrophy Annihilation Research Trust (DART), Bengaluru

Panel Discussion 2: Advancing Diagnostics and Therapeutics for Rare Diseases in India

Setting the Context: The Urgency for Improved Diagnostics

Mr. Sethi initiated the discussion by emphasizing the pressing need for indigenous solutions to address the challenges of accessibility and affordability in rare disease treatments. The panel began by highlighting the diagnostic landscape, identifying the significant gaps in patient identification, and the role that genetic testing can play in bridging these gaps.

Dr. Sakthivel Murugan elaborated on the advancements in genomic testing and its growing affordability, with costs for whole-exome sequencing having dropped significantly. He stressed the necessity of standardized protocols to ensure test accuracy and the importance of increasing accessibility across urban and rural areas. Additionally, the panel noted that early and accurate diagnosis remains critical not just for individual patients but for entire families where genetic disorders often reoccur.

Role of AI in Rare Disease Diagnosis and Drug Discovery

Dr. Venkatasubramanian Narayanan highlighted the increasing role of artificial intelligence (AI) in accelerating rare disease diagnosis and drug discovery. AI and deep learning models are being utilized to analyze extensive datasets, identify genetic mutations, and streamline drug repurposing. However, he cautioned that AI is not a "silver bullet"—while it can expedite processes, human oversight and clinical validation remain essential.

The discussion also touched upon the challenges of data standardization and the limitations of AI in environments with sparse, unstructured medical records. The need for comprehensive electronic health records and structured disease registries was underscored as essential for maximizing AI’s potential in rare disease research.

Regulatory Hurdles and the Need for Policy Reform

Dr. Arun Shastry (Dystrophy Annihilation Research Trust, DART) addressed regulatory bottlenecks in drug development for rare diseases in India. He emphasized the absence of an “Orphan Drug Act” in India, which could provide crucial incentives for pharmaceutical companies to invest in rare disease therapeutics. While regulatory agencies have become more receptive to rare disease clinical trials, existing guidelines still lack provisions for emerging therapies like antisense oligonucleotide (ASO) treatments.

Addressing the High Cost of Treatment

One of the major challenges discussed was the high cost of rare disease therapies, making them inaccessible to most patients. Dr. Nishant Kumar Singh provided insights into the economic considerations behind drug pricing. He explained that the limited patient pool and lengthy drug development cycles significantly impact costs. However, he acknowledged that local manufacturing and strategic collaborations with Indian pharmaceutical firms could help bring costs down.

The panel explored possible solutions, including:

- Public-Private Partnerships: Encouraging collaborations between global pharmaceutical companies and Indian manufacturers to produce affordable therapies.
- Flexible Licensing Agreements: Developing region-specific licensing agreements to allow the production of rare disease drugs at lower costs for Indian patients.
- Government Support and Incentives: Implementing tax benefits, subsidies, and regulatory exemptions for companies investing in rare disease drug development.

Strengthening Disease Registries and Data Collection

A recurring theme throughout the discussion was the need for robust patient registries. The panel pointed out that without accurate patient data, the true burden of rare diseases in India remains speculative.

Dr. Hardik Vasanawala and other panelists called for a nationwide effort to build structured, standardized, and real-time registries. The success of such registries in countries like the Netherlands was cited as an example, where patient numbers and disease trends are monitored effectively to guide drug development and policy-making.

Conclusion and Call to Action

The discussion concluded with a consensus on the following key actions:

- Advocacy for an Orphan Drug Act: Strengthening regulatory policies to provide incentives for rare disease drug development.
- Investment in Local Manufacturing: Encouraging Indian pharmaceutical companies to take a leading role in developing cost-effective treatments.
- Expanding AI and Genomic Testing: Leveraging technology to improve early diagnosis and streamline treatment pathways.
- Developing Nationwide Registries: Ensuring structured data collection to support research and policy decisions.

The panelists reaffirmed their commitment to continued collaboration among researchers, policymakers, and industry stakeholders. With a unified approach, India can accelerate its progress in addressing rare disease challenges and ensure better healthcare access for affected patients.

The discussion served as a reminder that while challenges persist, the momentum toward improved rare disease diagnostics and therapeutics in India is stronger than ever. The collective will of all stakeholders will be pivotal in shaping the future of rare disease management in the country.

From Left: Mr. Samir Sethi, Dr. Nishant Kumar Singh, Dr. Arun Shastry, Dr. Venkatasubramanian Narayanan, Dr. Sakthivel Murugan

From Left: Dr. Nishant Kumar Singh, Dr. Arun Shastry, Dr. Venkatasubramanian Narayanan, Dr. Sakthivel Murugan

Session 5: Progress and Way forward

SESSION CHAIR

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Session 5: Progress and Way forward

Strategies across industries and start-ups to ensure a pipeline that would lead to a new therapeutic

Tackling rare genetic diseases requires prioritization of the focus areas for the country that can make a large and timely impact in terms of diagnostics and therapeutics. Dr. Sanjay Singh recommended the development of a white paper emerging from the deliberations at REDRESS, that creates a matrix to shortlist key target disorders with clear deliverables. Dr. Anju Shukla stressed that without an understanding of the cause and mechanism of disease occurrence and progression, therapeutics cannot be developed. Government health services, regulatory agencies and think tanks such as The Indian Council of Medical Research (ICMR), The Central Drugs Standard Control Organisation (CDSCO) as well as the National Institution for Transforming India (NITI Aayog) can be invited to be part of the deliberations seeded by this analysis. This would ensure strategizing in the right direction for areas where indigenous therapy can be developed and brought into market.

Developing a supportive ecosystem for clinical research for RGDs

The panel also discussed some of the challenges in conducting clinical research such as patient recruitment, trial design, and regulatory frameworks. Dr. Ramachandran Shaji explained that while we have efficient teams to make lentiviral vectors for gene therapy, there are many other hurdles that need to be overcome. These include identification of targets, fast track approvals, and capacity for large scale production to go to the next phase of clinical trials and finally quality controls for actually administering into patients. While many laboratories in the country have the capacity to produce gene therapy vectors, scaling up will remain a bottleneck unless we collaborate with the right experts and industry partners.

Improving early diagnosis - steps needed for bridging the gap between clinicians and researchers to support RGD patients.

Dr. Anju Shukla recommended the formation of a consortium such as REDRESS because it is a platform that brings diverse expertise together and ensuring timely diagnosis of RGDs requires multiple stakeholders to come together. Since RGD patients tend to be fewer in number for a given disorder, and scattered across the country (and globally), such a consolidated platform working across borders and regions is the need of the hour.

More clinicians need to join hands with basic researchers and bioinformaticians to prove new gene associations and identify population specific pathological variants so that targeted diagnostics can be developed. Clinicians play a crucial role in facilitating timely connections with genetic counsellors, enabling families to make informed decisions. One key recommendation, therefore, is to incorporate genetics and genomics courses at the undergraduate level, particularly within medical education.

“Prevention is a key goal, especially in populations or families that are known to have a high frequency of occurrence. Genomic screening in such cases needs to be prioritized. In many cases next generation sequencing (NGS)-based diagnosis is compromised due to the detection of variants of unknown significance (VUS). Further research is essential to resolve such issues. Scaling up genomic testing therefore requires not just advances in technology but also expertise in interpretation and counselling.”

Newborn screening as an early diagnostic tool

Dr BK Thelma spoke at length about newborn screening (NBS) as the pillar for early diagnosis. The central government can recommend NBS for testable (and treatable) disorders, especially those where early interventions can make a huge difference in health outcomes. There is an urgent need to scale up such programs, requiring systematic state-wise implementation since Health is a prerogative of state governments policy. NBS fits well with the United Nation’s Sustainable Development Goals on Health and can be packaged as a proactive means to expedite India’s progress towards SDG3. Disorders associated with inborn errors of metabolism (IEMs) were particularly recommended as priority areas for screening. Training in the dry blood swab (DBS) method, containing newborn blood sample from a heel pinprick, enables testing across all levels of healthcare as the DBS can be transported and analysed at suitable labs and tertiary centres. This can be merged with the existing Rashtriya Bal Swasthya Karyakram (RBSK) program where newborns are checked for 32 common health conditions including birth defects at government health facilities and by ASHA workers.

As the program already spans early detection as well as free treatment and management, including surgeries at tertiary level, evidence-based inclusion of RGDs that can be prevented or better managed via early intervention will go a long way in reducing the disease burden in the country. It was however stressed that an ambitious NBS program would require public-private partnership to ensure impactful reach and to provide end to end support for DBS samples storage, transport and analysis, along with appropriate follow-up for counselling and interventions.

Defining the key unmet needs felt by patients and their families

A patient-centric approach is the key to success in alleviating the burden and impact of RGDs. The concluding panel discussion aimed to map the issues from the perspective of patient advocacy groups (PAGs) to outline what a collaboration of clinicians with researchers and policymakers could address. Mr. Samir Sethi reiterated that the main goal that affected families strive for is early and accurate diagnosis. This is followed by affordable and accessible treatment of the affected children and prevention of disease recurrence in their siblings. While some of these issues have been coming together in the Centres of Excellence (CoEs) established by the Government, it is only a start and many problems remain in this path.

- CoEs should create and follow a pipeline that counsels and supports families on the steps ahead once a diagnosis is obtained, in conjunction with PAGs as partners who are already trying to guide families. Amplifying the advocacy and awareness created by patient families and support groups via collaborations with CoEs can enhance and scale the outcomes.
- Following this model, PAGs could guide patients into clinical trials as well by being an intermediary bridge in the CoE network.
- Since the RGD community is a vulnerable population of patients, it is critical that they have a trusted source of advice and guidance which can help them avoid falling prey to false diagnosis and treatments that lead to heavy emotional and financial losses.

The panel stressed on the importance of building India’s population-specific registries for all rare disorders in the country. Due to the complexities involved, this can be a slow and inadequate way of collecting data, which PAGs could help expedite by sharing the data from all the patients and their families registered with the various support groups. Dr. Thelma pointed out that having select government hospital-based registries will lead to inaccurate representation of only children who reach those hospitals and get a positive diagnosis.

"A centralized registry is critical for understanding prevalence and initiating efforts for various RGD patients. A large collaborative network including government as well as private hospitals and on-ground teams such as NGOs, PAGs and PHC and ASHA staff would help ensure greater speed and accuracy in gathering patient numbers and distribution information."

From Left: Dr. Rakesh Mishra, Dr. Ramachandran Shaji, Dr. Sanjay Singh, Dr. Anju Shukla, Dr. BK Thelma, Mr. Samir Sethi

Dr. Rakesh Mishra

Strengthening collaboration among all stakeholders: Learnings from REDRESS

At the conclusion of the 2-day summit, several important learnings emerged from the discussions. There was a general consensus on the benefits of having a single institute or Centre of Excellence (CoE) specific for RGDs in India, that can build on the collaborative platform provided by REDRESS with support from ICMR as knowledge partner. This would ensure that all stakeholders can come together to work beyond the annual summit. Government funding as well as support from philanthropies/NGOs/industry/ PAGs would be crucial for achieving this vision.

Some of the key action points are highlighted below:

- The CoE would primarily bridge the gap between the research findings from academia and facilitate their translation to practical applications to address societal needs in the context of RGDs.
- The CoE would facilitate bringing like-minded collaborators together who share a passion and interest in enabling solutions for the RGD community. The Centre would keep them connected with policymakers, administrators and regulators whenever needed.
- Through such CoEs, incentives need to be established for long-term collaboration between stakeholders. Targeted lists of specific genes, diseases, and focus areas should be collated in the platform to bring interested researchers, industry partners and PAGs together. It was highlighted that announcing calls for funding academia-industry proposals have not yielded suitable results in the past. There is thus a need for a more strategic and sustained approach.
- The focus of the pilot projects should be on clearly defined parameters of achievable deliverables. With demonstratable outcomes, the CoE can validate the model of tackling a disease from identification all the way towards its elimination via a collaborative pipeline. Scientists would help create the techniques that can be easily translatable into practical application, while the CoE can build upon the existing work of institutes/NGOs that are already working towards such models.
- Hospitals with translation centres connected to the CoE can collect data, and help create genetic databases, working better as small units dispersed across the country.
- Genetic literacy and awareness need to reach the common man, as well as clinicians, administrators and across all stakeholders. PAGs can be crucial in scaling up information dissemination via the network.
- The CoE can be the central resource to help map the researchers, companies, institutes and NGOs along with lists of diseases and techniques. Such a platform or dashboard will help in baseline setting. TIGS is ideally placed to take such a database forward and act as the core for the envisioned CoE.

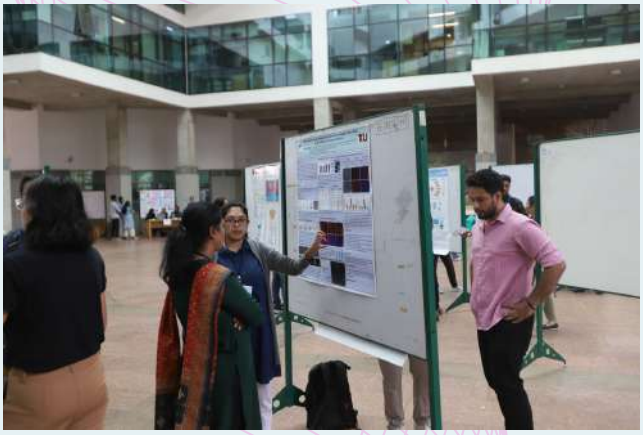
ANNEXURES

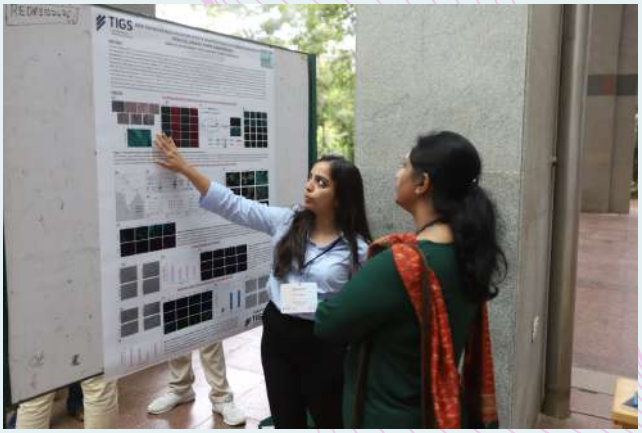
Name	Poster Title
Swadhin Chandra Jana	Understanding the interplay of ciliary transport complex: A way towards establishing diagnostic platforms for related-RD (ciliopathies)
Mandar Naik	CRISPRBITS: Precision CRISPR-Cas cloning constructs for studying Rare Genetic Disorders such as Triplet Repeat Disorders
Srilekha P	Understanding the epistatic interaction of LSD1 and LHX2 in developing mouse cortex
Hrithik Dakssesh Putta Nagarajan	Prevalence and pattern of Congenital Heart Diseases in neonates and children attending a district early intervention centre at a tertiary care hospital
N. Amrisshprakash	Molecular genetic analyses of beta-thalassemia in South India reveals rare mutations in the beta-globin gene
Anjali Krishna. A	Inferring Variants of Uncertain Significance (VoUS) in rare disease genetics: challenges and myths from our case studies
Annes Siji	A CRISPR-cas12-based point-of-care assay for Sickle Cell Anemia: enhancing accessibility and accuracy
Lloyd Tauro	Development of LC-MS/MS Based Diagnostic Method for Monoamine Neurometabolic Disorders
Prof Pranab Roy	Mutational Analysis of Cystic Fibrosis gene
Dr. Archana Varghese	Ambulatory Congenital Muscular Dystrophy: Clinical Insights from a Sibling Pair
Dr. Radha Onkar Joshi	Leukocyte Telomere Shortening in patients with Congenital Heart Defects
Rukhsana Hassan	Telomere Shortening and Its Implications in Spinal Muscular Atrophy: Insights from North India
Keerthanakumari. S	First report of GCH1-related tetrahydrobiopterin (BH4)-deficient hyperphenylalaninemia from Palestine
Rachanashree HN	Molecular Aetiologies of Inborn Errors of Metabolism- Case series
Sivaraj Mohana Sundaram	Bridging the Gap: Advancing Therapeutic Strategies for MCT8 Deficiency in Indian Populations
Shreevidya Parthaje	CAG repeat instability and region-specific gene expression changes in the SCA12 brain
Ishan Maheshbhai Shukla	A Comparative Analysis of Rare Disease Management amongst developed nations & India

Jaya Swathi K	Prader –Willi Syndrome – Extended Deletion of 15q11.2-q13.3 – A Case Report
Manasvi Sharma	*In silico* approaches to AAV engineering in Gene Therapies: Design for Tropism, Safety, Quality analyses
Dr Mahrukh Hameed Zargar	Delineation of rare cytogenetic variants in children with varied phenotypes from Kashmir- North India
Lavanya S	Comparison and Analysis of Anticancer Properties of Cu Metal-organic Framework (NPs) Synthesized by Solvothermal Method in Renal Cell Carcinoma (HEK293)
Lakshmi C	Modulating NADPH Oxidase Function: Docking Studies for Chronic Granulomatous Disease
Divya Swaroopini Shridhar	Exploring Oxidative Toxicity in Beta Thalassemia : A Machine Learning and Toxicogenomic Risk Assessment Approach
Romanshia Celes G A	The nanoparticle coating of tablets to treat rare disease
Aafreen Kerosenewala	Navigating Life with a Rare Disease : Assessing Quality of Life, Mental Well-Being, and Healthcare Challenges faced by patients in the Indian Population
Rajiv Sangle	AI Classification of Variants of Neuromuscular Disorders
Ron George Philip	How do genomic variants determine the outcome of rare genetic diseases ?
Amit Kumar Tiwari	Variants in DOK7 gene results in fetal akinesia deformation sequence
Sacheta Kulkarni	Developing Cost-effective Diagnostics and Pharmacogenomics driven management protocol for Imprinting Disorders
Praveen P	mRNA Biotherapeutics platform for Rare Genetic Diseases.
Venkatesh Rajendran	Cataloguing actionable pharmacogenomic variants to predict impact and demonstrate utility in Indian clinical practice
Vibhaa K	Gene editing reveals mutation specific disease manifestations in a human pluripotent stem cell derived Pompe disease model
Deepalakshmi PD	Decoding Sickle Cell Disorders using Mass Spectrometry
Saniya Mehraj	Leveraging digital polymerase chain reaction for the diagnosis of Spinal Muscular Atrophy: Identification of causative mutations in SMN1 gene and assessment of copy number of SMN2 gene
Arvinden VR	Genomic Approaches to Understand the Genetic Burden of Monogenic Autoinflammatory Disorders

Talika Sibal	Establishing a Huntington’s Disease Patient Registry in India
Pannaga Prasad VG	Assessing CTG Repeat Expansions in the JPH3 Gene in Indian Population
Iliyas Rashid	GenTIGS: Bridging gaps in rare genetic disorder knowledge and patient care – A strategic vision ahead
Manas Kumar Madhukar	Identification of factors binding to GAA repeats in FXN gene using in-silico approaches
Ishan Maheshbhai Shukla	Evaluation of Rare Disease Awareness and Knowledge Gaps Among Medical Professionals in Gujarat: A Survey-Based Study
Amaresh Roy	Myopathy, Neuropathy, Cerebellar ataxia, Dyskinesia and Cardiomyopathy Secondary to Mitochondrial Complex 2 Deficiency in the Second Decade
Harshini Surendra Bava	Patient-specific human induced pluripotent stem cell-based in vitro model to study Alpha-1 anti-trypsin deficiency
Sanyukta Bholay	Advancing Affordable RNAi Therapies for Rare Genetic Disorders through Tissue-Specific Delivery

SNAPSHOTS: POSTER PRESENTATIONS





Group photo of participants at REDRESS 2024

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