MEDGENOME

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Internal Quarterly Newsletter Vol 28 | Jan 2024

COVER STORY

THE GENETIC DRIVERS OF JUVENILE, YOUNG, & EARLY-ONSET PARKINSON'S DISEASE IN INDIA

Scientific Article

Consanguineous **Marriage, Genetics**, & Diagnostic Yield: A Preliminary Analysis

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Book Review

Reverse Innovation in Health Care

WORDS FROM THE **FRONTLINE**

Dr. Anjani Singh
Senior Director - Lab Operations

Dear Colleagues,

As I take a moment to reflect on my journey into MedGenome, I am filled with a sense of gratitude and purpose. This tale is one woven with curiosity, dedication, and a profound passion for making impactful contributions to the world of diagnostics. My path to this esteemed organization has been marked by a harmonious blend of academic rigor and hands-on experience, cultivating a deep-seated fascination with genomics and its transformative potential combined with routine pathology and automation.

Joining MedGenome has transcended being a mere career move; it has become a calling to be part of a pioneering team dedicated to advancing healthcare through the strength of cutting-edge genomic solutions and establishing quality routine diagnostics. My dual goals within the company are clear: to leverage my expertise as a Senior Lab Director in Routine Diagnostics to elevate operational excellence and to champion innovation that drives superior patient outcomes.

At the core of my journey is an incredible team – a cohort of dedicated professionals fuelled by a shared vision of leveraging diagnostics for the betterment of humanity. Together, we form a dynamic ensemble, each member contributing unique skills and perspectives, fostering an environment of collaboration and collective growth.

Presently, my focus revolves around spearheading initiatives aimed at optimizing routine diagnostics processes through cutting-edge technology and automation. Additionally, we are committed to establishing patient-oriented services, including wellness programs, ensuring precision and efficiency in every facet of lab operations. Through meticulous attention to detail and strategic planning, my aim is to streamline workflows, enhance diagnostic accuracy, and ultimately elevate the standard of care for our patients and clients.

Looking ahead, I envision my role as not only contributing to the present success of MedGenome but also shaping its future trajectory. By taking forward the legacy of MedGenome and continuously innovating, we aspire to redefine the landscape of diagnostics. Our goal is to offer novel solutions that empower healthcare providers and significantly improve patient outcomes.

To my esteemed colleagues at MedGenome, I extend my heartfelt gratitude for the warm welcome and unwavering support. Let us continue to embark on this journey fuelled by innovation, compassion, and a shared commitment to transforming lives through quality healthcare. Together, we can build a legacy that positively impacts the future of diagnostics and healthcare."

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Most Talked About

MEDGENOME IN NEWS

October to December 2023

ACTIA • CLARIA • PRIMA • MICRA • Business • Research • Awards • Genetic Counselling • Health Care

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Is Heart Attack a genetic problem? Doctors suggest genetic screening test if there is a family history - Dr Ramesh Menon, Associate Director - Personal Genomics & Genomic Medicine, MedGenome
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Clinical

জনিগত রোগও চোখ রাঙাবে না আর! সুস্থ শিশুর জন্ম দতিে নতুন রাস্তা দখোচ্ছনে বজ্ঞিানীরা - Dr Priya Kadam, Director - Reproductive Genomics, MedGenome
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Diagnoses methods of prostate cancer - Dr Thangarajan Rajkumar, Director of Research (Oncology), MedGenome
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MedGenome Connect

Claria
Reproductive Genetics

The past quarter has been very active for Claria with a focus to engage more clinicians with CME, conference participation, and test specific brochures and mailers like KaryoSeq and NIPT along with social media posts. We have also posted videos of Dr. Priya Kadam speaking on KaryoSeq and NIPT.

Social Media Post- Dr. Priya Kadam Video on NIPT

Webinar on KaryoSeq by Dr. Priya Kadam

Social Media Post- Dr. Priya Kadam Video on KaryoSeq

Mailer on KaryoSeq shared with the clinicians

CME- Society of Fetal Medicine- Jharkhand Chapter at Ranchi

CME on Fetal Medicine at Pune

ACTIA
Inherited Genetics

We had conducted MedGenome 'Geneus Genetic' Quiz at multiple conferences as a part of clinician engagement activities. A lot of CME were conducted on specialties such as Ophthalmologist and Nephrologists. We also launched subsidized price tests to increase the affordability and access to quality diagnostics for underprivileged patients who are living below the poverty line. We also promoted BabySecure – Advanced NewBorn Screening Test across all platforms.

MedGenome thanks all the Geneus Genetic Quiz competition participants organised during IAMG 2023 Conference. We got an overwhelming response.

Congratulations to the lucky winners Dr Niladri Das, and Dr Aradhana dwivedi. Special thanks to Dr Seema Thakur for gracing the event and distributing the prizes.

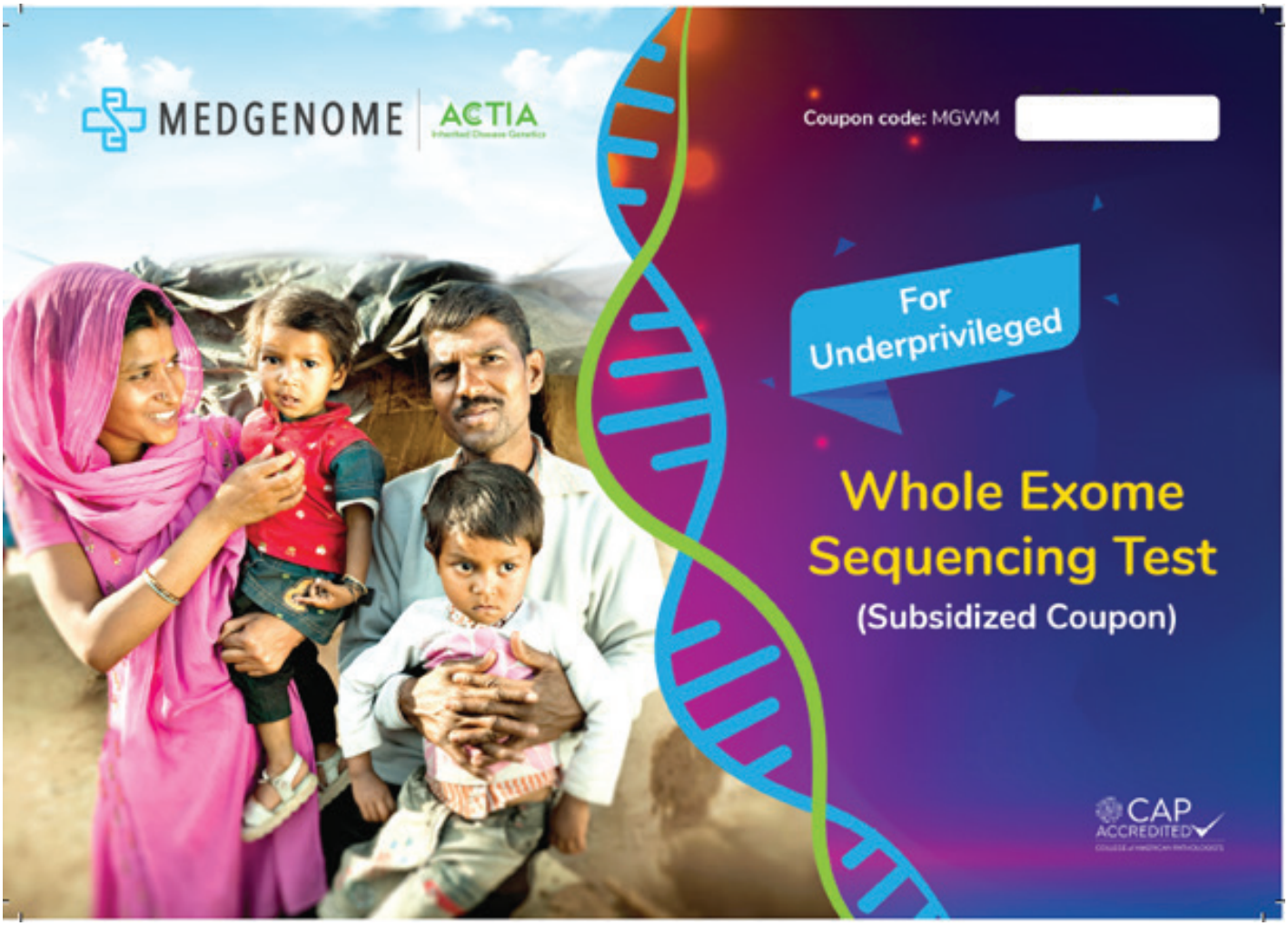
#MedGenomeGeneus #IAMG2023 #GeneticQuiz #WinnersAnnouncement #GenomicExcellence

BabySecure (Advanced NewBorn Screening Test) can help detect over 60 Inherited Metabolic Disorders early on, including disorders like Fatty Acid Oxidation defects, Organic Acidemia, Amino Acidopathies, Urea Cycle defects, and conditions such as Phenylketonuria, Congenital Hypothyroidism, Variant Hemoglobinopathies, G6PD, CAH, Biotinidase Deficiency, Cystic Fibrosis and Galactosemia.

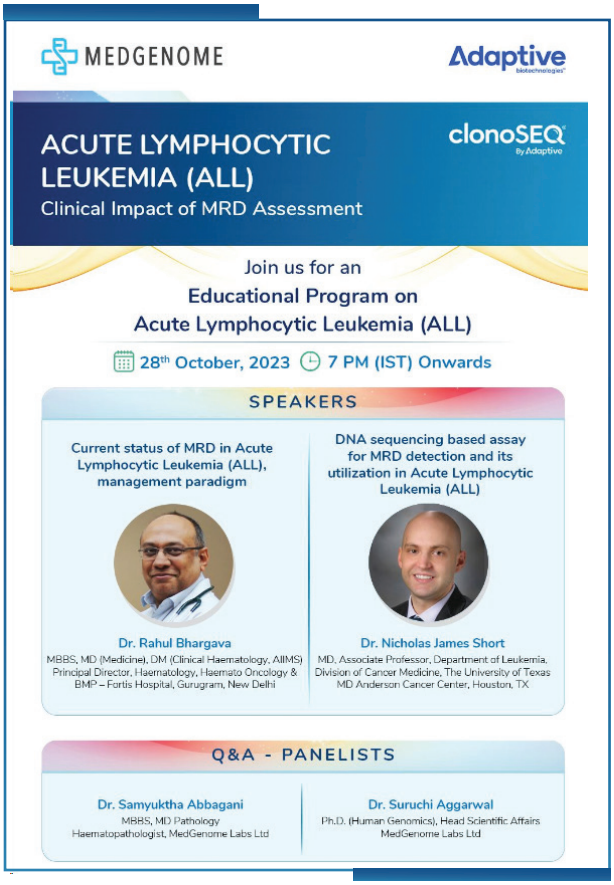
Dr Mukesh Gupta, Consultant Obstetrician and Gynaecology, La Nest Hospital, Mumbai strongly recommends that every child has the opportunity to benefit from this life-saving screening. It's a small step that can make a world of difference.

Let's spread the word and ensure every newborn gets the best start in life.

#NewbornScreening #BabySecure #MedGenome #Actia #MetabolicDisorders #InheritedDiseases #HealthyStart #PreventionMatters #Precision #GeneticTesting



In the past quarter, the campaigns were focused on germline cancer tests along with Liquid Biopsy tests. We had a few insightful case studies, webinar, round table discussion and KOL videos which were promoted across all platforms.

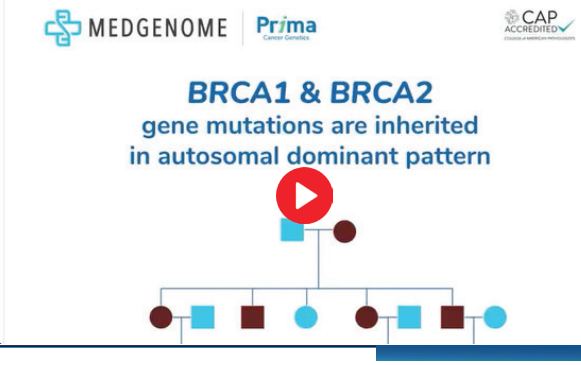


Did you know that your genetic makeup holds vital clues about your risk of hereditary breast and ovarian cancer? The BRCA1 and BRCA2 gene mutations can increase your susceptibility to not only breast and ovarian cancer but also prostate cancer, pancreatic cancer, and melanoma.

A BRCA1/2 gene test can be your guiding light, offering:

- Personal & Familial Risk Assessment
- Tailored Risk Management Strategies
- Disease Prevention through Active Surveillance
- Prophylactic Surgeries
- Determining PARPi Eligibility

#BRCA1 #BRCA2 #MedGenome #BreastCancerAwarenessMonth #HereditaryCancerRisk #GeneticTesting #KnowledgeIsPower #BreastCancer #ProstateCancer #PancreaticCancer

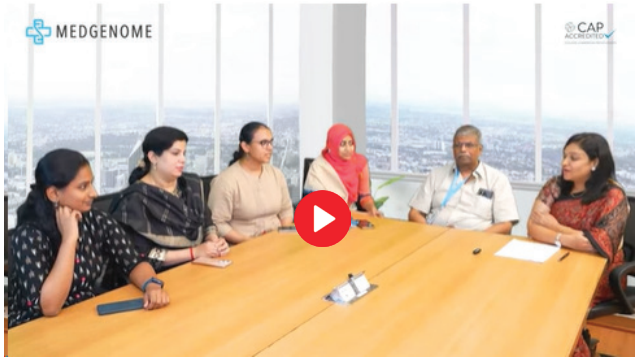


MedGenome Labs organized a compelling conversation featuring a distinguished group of experts in the field, shedding light on the latest advancements and crucial insights.

Dr. Suruchi Aggarwal, PhD, Head Scientific Affairs, Oncology at MedGenome Labs, led the conversation alongside esteemed panelists:

- Dr. Thangarajan Rajkumar, Director Research for Oncology at MedGenome Labs
- Dr. Ambreen Aman, Oncopathologist at MedGenome Labs
- Dr. swaratika majumdar, Consultant Medical Oncology at Narayana Hospital Bangalore
- Dr. Nidhi Tandon, Consultant Medical Oncology at Narayana Hospital Bangalore
- Ms. Supraja Sivakumar, Sr. Genetic Counselor at MedGenome Labs

#MedGenome #BreastCancerAwareness #GeneticTesting #MedGenome Discussion #LeaderinGenetics #Precision #Pioneers

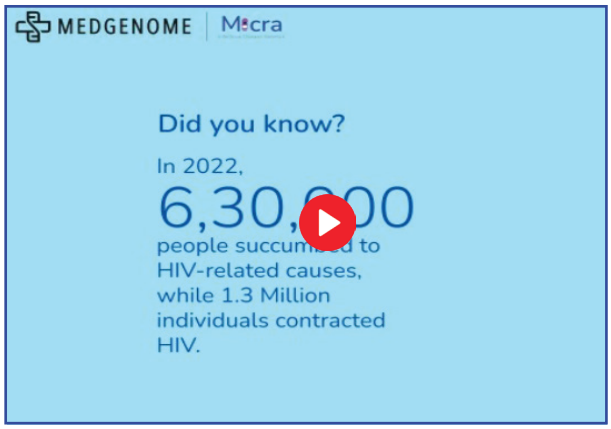


The past quarter was very encouraging and an active month for Micra with a focus to engage more clinicians with CME, conference participation, and test specific mailers along with social media posts. We have also posted videos for World AIDS Day, World Meningitis Day, and World Pneumonia Day on all social media Platforms. We have also posted a video on Sepsis by Dr. Gunisha. The team also completed 11 one pagers on different Micra Panels which contain in-depth information about all the tests along new tests launched in Micra.

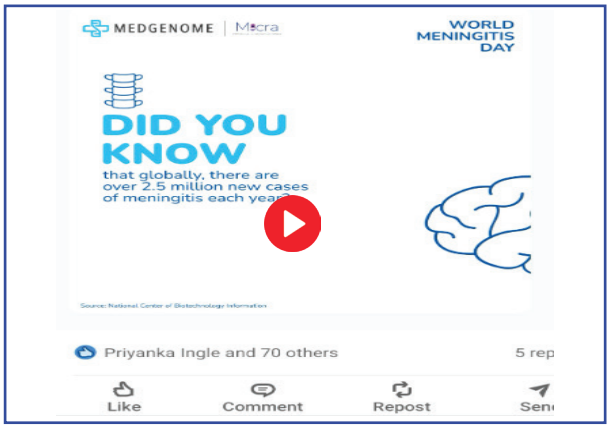
Participation at CME-RESPICON at Kolkata

Social Media Post on World Pneumonia Day

Social Media Post on World AIDS Day



Social Media Post on World Meningitis Day



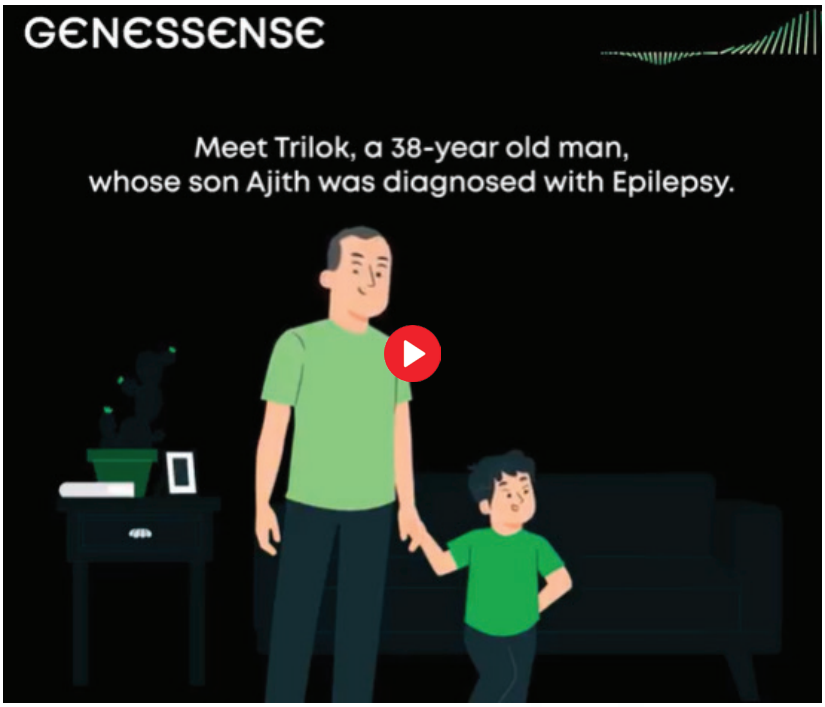
Social Media Post on SEPSIS by Dr. Gunisha Pasricha

GENESSENSE

Powered by MEDGENOME

We continued to evolve the various tests being offered under the Genessense portfolio in this quarter. We focused on forging partnerships with a few aggregators & conversations were initiated with some of the major players in this space. We are also revamping our Genessense Website with fresh perspective and scientific insights. We have also posted Curegen video on all social media platforms.

Social Media Post on Curegen



What's new

Research Publications

The Genetic Drivers of Juvenile, Young, and Early-Onset Parkinson's Disease in India Read more

Journal : *Movement Disorder*

Clinical Utility of Proband Only Clinical Exome Sequencing in Neurodevelopmental Disorders Read more

Journal : *Indian Journal of Pediatrics*

Kindler syndrome with a novel mutation and a rare gynaecological complication Read more

Journal : *Clinical and Experimental Dermatology*

Tests launched

- ComprehensiveGenomic profiling - 526 Genes (Liquid Biopsy)
- Colorectal Cancer Panel (Liquid Biopsy)
- FLEX scRNASeq: for Single cell transcriptomics
- Whole Genome Methylation Sequencing: Enzyme based whole genome methylation
- Sepsis and AMR panel
- Febrile Neutropenia Panel
- Comprehensive Transplant panel

Proud Moment

MedGenome has been honored with the **Best Late-Stage Startup award** at the VCCircle Disruptor Awards 2023 held in New Delhi. Dr. Vedam Ramprasad, the esteemed CEO of MedGenome, graciously accepted the award, symbolizing the collaborative dedication of the entire MedGenome team.

The award, in its inaugural year, is part of the multi-city program 'The Pitch' envisioned as a platform that helps startup founders pitch their business idea to the best suited investors across the country.

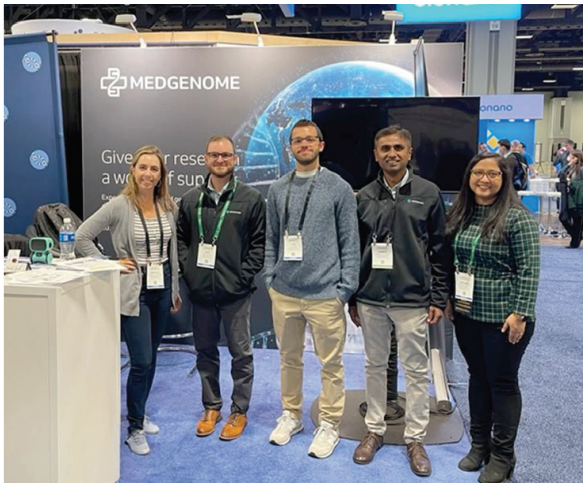
'The Pitch' was run across three cities- Bengaluru, Delhi and Mumbai between September and November, bringing together over 50 investors and hundreds of startups in curated pitching sessions linking entrepreneurs with investors according to the stage of the venture.

The winners were picked via an external jury panel comprising Keki Mistry, adviser at Poonawalla Fincorp and former CEO & vice chairman of HDFC Ltd; Padmanabh Sinha, executive director at NIIF; Kaushik Shaparia, CEO of emerging Asia at Deutsche Bank; Lakshmi Narayanan, chairman of Sovereign Wealth Fund Institute and managing partner at Patel Family Office; besides Rajat Bhargava, CEO of Speciality Sector at RPG.

Our sincere gratitude to VCCircle and the jury for recognizing our unwavering commitment to innovation.

From Our US Office

As we have stepped into the New Year 2024, we wish each one of you a happy and prosperous New Year 2024. In the past quarter, we attended the prestigious ASHG'23 conference, where we had setup our booth in the event. The event was very fruitful in terms of showcasing our services and offerings –Xpress RNA-seq, Single Cell Genomics, *Denovo* Genome Assembly and Annotation, Whole Genome Sequencing and Bioinformatics. ASHG was attended by more than 8,000 scientists from around the globe. This 5-day program showcased the year's most significant new advances in the field of genetics and genomics.



We are equally excited to share that now MedGenome Inc is a 10x Genomics Certified Service provider for single cell sequencing.

Our team took a well-deserved time off towards the end of December 2023. The collective success of the past year is a sheer effort of the hardworking team and the many who have been supporting from India to achieve this goal.

We also celebrated Diwali in a big way where in scrumptious lunch was organised in the office and all dressed up in our traditional Indian attire:

We concluded the year with a Year-end holiday bowling game- a fun evening bowling and competing as random teams followed by dinner in a restaurant

We look forward to the new year with the launch of many new services including Spatial Transcriptomics, Exome Max (proprietary exome capture kit more comprehensive than commercial kits for coverage of most disease relevant mutations in the US) and our streamlined *denovo* genome assembly and annotation services. We also launched a *denovo* genome assembly and annotation grant program in collaboration with PacBio.

To know more:

1. **MedGenome Inc. 10x Certification:** https://www.prnewswire.com/news-releases/medgenome-achieves-10x-genomics-certified-service-provider-qualification-for-single-cell-sequencing-301980090.html
2. **MedGenome PacBio Grant:** https://www.prnewswire.com/news-releases/medgenome-in-collaboration-with-pacbio-announces-a-de-novo-genome-assembly-and-annotation-grant-to-empower-non-model-organism-research-301994863.html

Genetic Drivers of Young-onset Parkinson's Disease Identified in India

Ramesh Menon, Ph.D
Genomic Medicine & Personal Genomics Divisions, Bioinformatics Department

About Parkinson's disease

Parkinson's disease (PD) is the second most common neurodegenerative disorder in adults in the age bracket of 60 years and above. The burden of Parkinson's disease has doubled across the globe over the past two decades. India accounts for approximately 10% of the global burden, which translates to nearly 0.58 million patients living with the disease.

Background of the present study

The genetics of Parkinson's disease is not as studied as common diseases such as type 2 diabetes or coronary artery disease globally. However, there have been few large studies published by consortia like International Parkinson Disease Genomics Consortium (IPDGC). A landmark genome-wide association study (GWAS) was published in 2019 which consolidates the major genetic studies conducted till that period and the meta-analysis provided the comprehensive landscape of PD genetics. Almost at the same time, MedGenome stepped into Parkinson's disease genetics study with a multi-centric clinical collaboration, named as PRAI network, Parkinson's disease Research Alliance in India, recruited initially 100 young-onset Parkinson's disease (YOPD) samples and whole genome data were generated at MedGenome. Deep clinical meta-data was also made available for these samples. Data analysis was done on routine diagnostics pipeline as well as polygenic risk score (PRS) validations. A pilot research paper was published in Advanced Biology journal. After the pilot study, Denali Therapeutics, one of the major pharmaceutical companies in the US working on drugs related to neurological diseases such as PD, got interested to collaborate with MedGenome to conduct a larger genetic study in YOPD. MedGenome's roles were sample recruitment, clinical meta-data collection, data generation, data analysis and manuscript related tasks. There were total 675 samples recruited for this study and a set of 1376 control samples selected from the GenomeAsia project. Deep clinical meta-data was made available by the clinicians for this study. The collaborative project was initiated in 2020 and there were regular monthly meetings to discuss the progress on data generation and analysis with Denali Therapeutics. Highly productive sessions on data analysis strategies and brainstorming sessions played a big role in shaping the quality of the present study. This research study is not only the largest in South Asia's Parkinson's disease genetics so far, but also unique with the comprehensiveness in genetic data analysis. The study got published in the Movement Disorders journal.

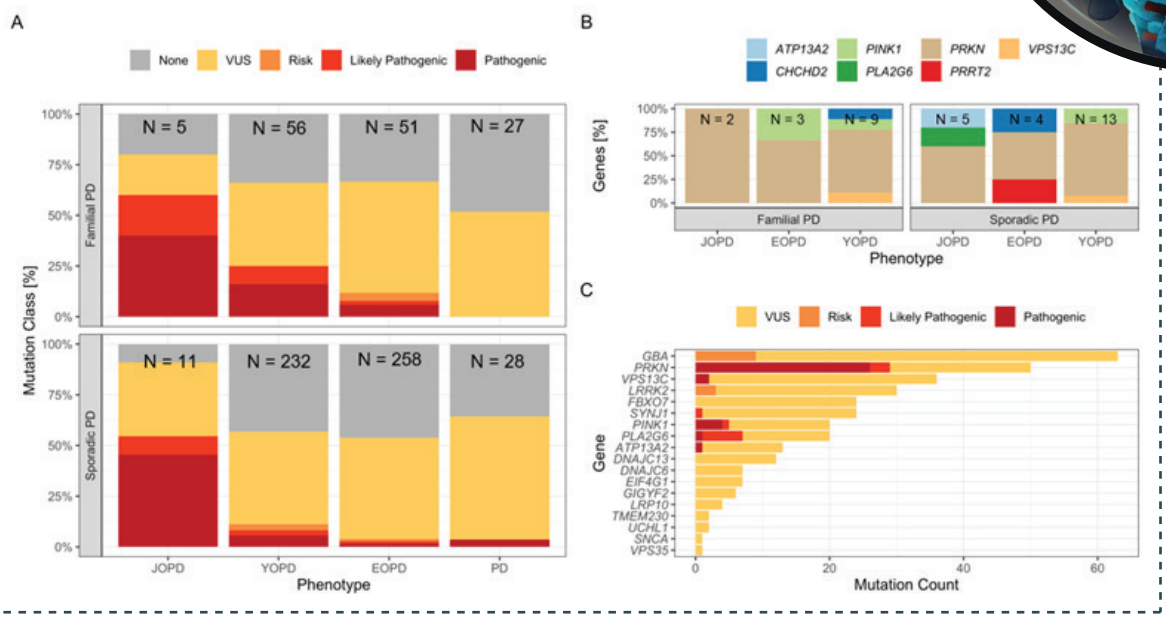
Available data		Common variation (MAF>5%) studies		Rare variation (MAF<1%) studies		
#Subjects	Collected data	PD Diagnosis GWAS	Age of onset GWAS	PRS analyses	Diagnostic Pipeline	Gene burden analyses
PRAI: Parkinson's Disease N= 675	Genotyping Array (SARGAM) N=659	✓	✓	✓ ✓	✓	✓
	WGS N=99 / WES N=576					
GAsph2: Controls N=1376	WGS N=1376	✓		✓		✓

Study design

Data were generated from 675 cases and 1376 controls and the data analysis on rare and common variants were based on whole genomes/exomes and genotyping array. The patients were classified based on age of disease onset such as, Juvenile, Young and Early-onset. The control samples were selected from the GenomeAsia project dataset.

Key diagnostic findings

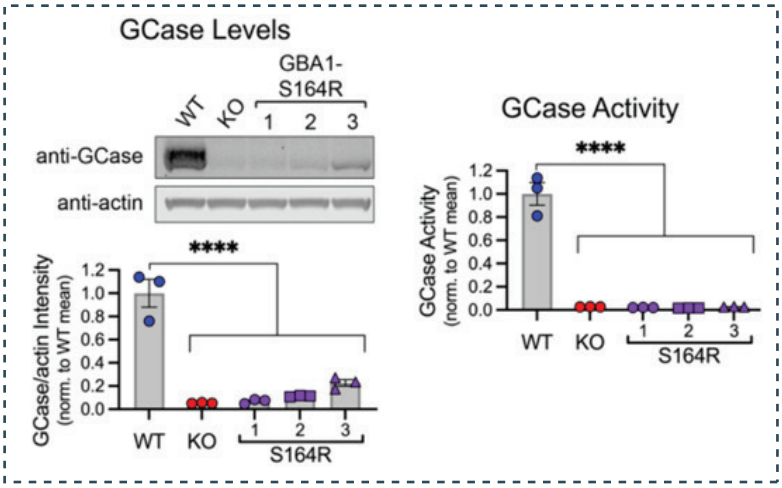
Thanks to the excellent work done by the GA team in finding the pathogenic/likely pathogenic mutations, majority of them in were reported in PRKN gene. Also a significant amount of VUS was also seen. Diagnostic yield was about 8% with pathogenic/likely pathogenic variants among which majority of them were in PRKN mutations, followed by GBA, PINK1 etc.



Genetic diagnostics findings summary: (A) Distribution of mutation type in known PD–related genes, by diagnostic group and familial/sporadic PD status. (B) Distribution of genes affected by pathogenic variants, by diagnostic group and familial/sporadic PD status. (C) Mutation counts and type breakdown for all identified mutations in Mendelian PD genes, VUS = variant of uncertain significance.

GBA loss-of function mutation behaves similar to knock-out mutations *in-vitro*

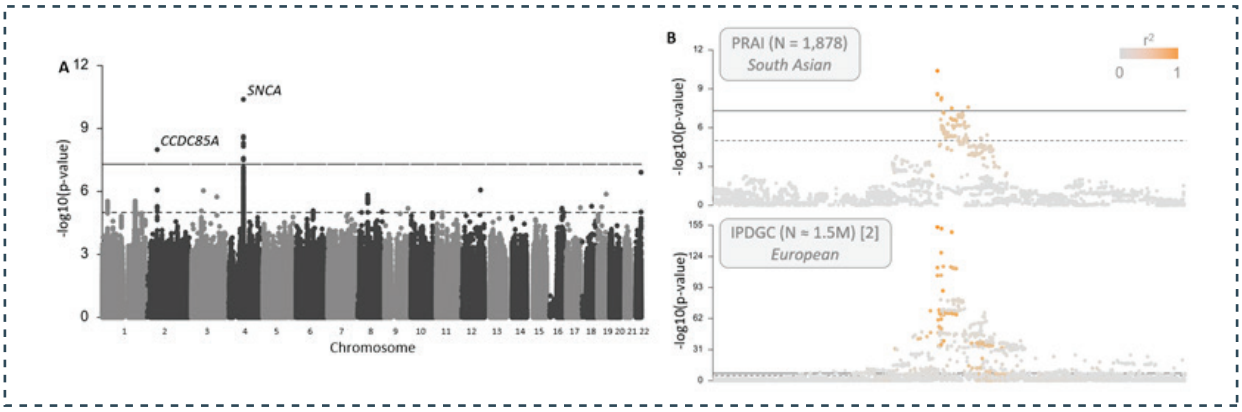
Interestingly, the GBA mutation p.S164R loss-of-function for type the first time is reported in South Asian PD patients found by diagnostic analysis. GBA gene mutations are the well-known for Parkinson's disease, the gene that encodes glucocerebrosidase (GCase) enzyme that works inside lysosomes, the part of cells that breaks down lipids. Lysosomal dysfunctions can lead to PD. The *in-vitro* experiments were conducted at the laboratory of Denali Therapeutics.



(Left) Western blot and quantification of total cellular GCase (β-glucocerebrosidase) levels from GBA1-wild type, GBA1-KO (knock out), and three clonal GBA1-S164R variant cell lines. Bars represent mean GCase levels (normalized to β-actin loading control within each sample) normalized to the mean WT (wild-type) value across all replicates, and points represent values from individual replicates. (Right) Flow cytometry measurement of GCase activity in A549 GBA1-wild-type, GBA1-KO, and three clonal GBA1-S164R variant cell lines.

SARGAM array, Imputation and GWAS results

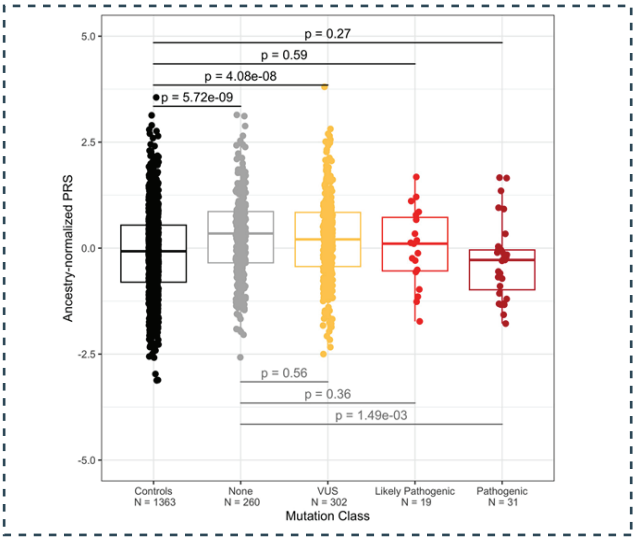
In the common genetic variants analysis, we used the SARGAM genotyping array, a 100% custom genotyping developed by MedGenome. This is the first study using the SARGAM array. The data generated from genotyping served three purposes: a) GWAS analysis b) Age of onset analysis c) Polygenic risk scores. SARGAM array data analysis optimization needed several iterations and re-analysis (4 times!) arising the QC sanity checks. Thanks to the bioinformatics pipelines in-house which enabled the swift analysis. Genotype imputation utilized the GenomeAsia reference dataset, the largest South Asia imputation panel available. SARGAM array design was optimized to perform well with GenomeAsia reference panel. The GWAS analysis was conducted with a higher stringency to avoid any potential false signals, which resulted in the discovery of two genome-wide signals: SNCA and CCDC85A gene loci. The most significant hit from SNCA gene is well-known to be associated with PD in European ancestry, evidenced by very large meta-analysis by IPDGC. SNCA gene encodes the protein alpha-synuclein. In brain cells of individuals with Parkinson's disease, this protein gathers in clumps called Lewy bodies. Mutations in SNCA gene can cause early-onset Parkinson's disease. Of note, the CCDC85A gene is expressed in various tissues and interestingly, highly expressed in cerebral cortex. This GWAS signal is not previously reported in the European cohort to be associated with PD and needs replication studies and additional validations. The CCDC85A gene has a role in cell-cell adhesion and epithelium development through its interaction with proteins of the beta-catenin family. β-Catenin is a crucial transcriptional factor in Wingless–Int (Wnt) signaling, and plays important role in regeneration.



GWAS results: (A) Manhattan plot for PD diagnosis using imputed SARGAM data, (B) SNCA region association plots for PRAI cohort and latest European GWAS, comparison of PRAI and European GWAS SNCA region signal in terms of

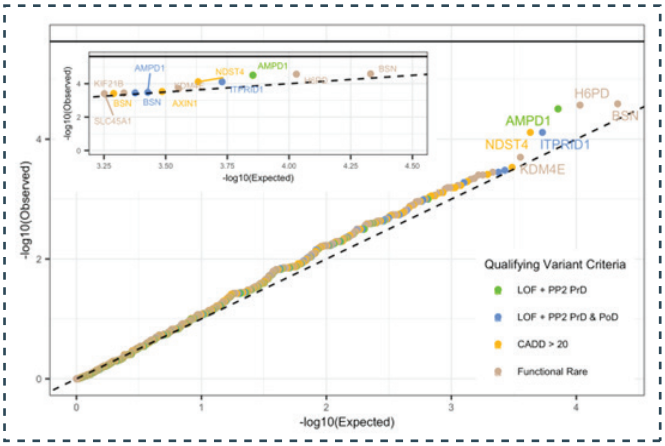
PRS as a genetic risk screening tool

Apart from validations of PD-PRS in South Asian population, the comparison of the PRS between controls and several groups of PD patients defined by the presence of a PD-related mutation ("VUS," "likely pathogenic," or "pathogenic") or lack thereof ("none"), and within those same PD case groups. The "none" and "VUS" groups exhibited significantly higher PRS than the control group, adjusted for age and sex. Interestingly, the "pathogenic" group exhibited significantly lower PRS compared to the "none" group, adjusted for age and sex. This means, like monogenic mutations, high polygenic risk can explain the genetic basis of the disease, where no pathogenic mutations are found.



Next, we compared the PRS between controls and several groups of PD patients defined by the presence of a PD-related mutation ("VUS," "likely pathogenic," or "pathogenic") or lack thereof ("none"), and within those same PD case groups. The "none" and "VUS" groups exhibited significantly higher PRS than the control group, adjusted for age and sex. Interestingly, the "pathogenic" group exhibited significantly lower PRS compared to the "none" group, adjusted for age and sex. No other comparisons achieved nominal ($P < 0.05$) statistical significance.

Gene burden analysis clues potential targets and the unmet need for expansion study in India

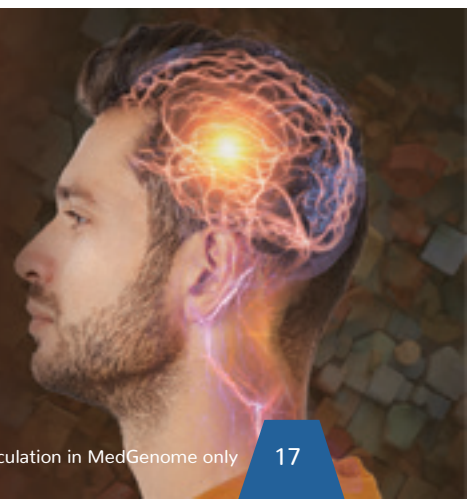


QQ-plot displaying results of gene burden studies across various qualifying criteria. Though the sample size is not enough to derive conclusive results from the gene burden analysis, but suggested genes such as BSN (bassoon) as the most significant, which interestingly is highly expressed in brain.

Conclusion

The study identified the well-known disease-causing genetic mutations in the Indian YOPD patients. The common genetic variations that confers a risk of developing PD were analyzed through GWAS. Polygenic risk score validations were conducted and compared with the diagnostic pipeline results. The study was extended to gene burden analysis as well. Overall, the results not only validated the existing knowledge in the Indian PD patients, but also advances the PD genetic research globally.

Further, the PD-PRS screening test was developed to determine the risk of developing Parkinson's Disease. This opens door for a first ever genetic screening test in India for Parkinson's Disease that can be taken voluntarily by any individual.



Kudos to our colleagues from various team

A big applause to all the contributing members from MedGenome for this important research study; including Sequencing team, Genotyping team, Genome Analysts and (my fellow) Bioinformatics team members.

A big thanks to our visionary leadership for strategically planning the study keeping in mind the bigger picture of the future and inspiring others to set the goals and pursue the long-term vision. This was also evident in the Coronary Artery Disease genetic study conducted 5 years back. I am fortunate and proud to be part of these landmark studies from India.

Footnote: A crisp review of the study was independently and voluntarily conducted by Dr.Veera, a scientist working at Regeneraon Pharmaceuticals.
https://twitter.com/doctorveera/status/1731202662820110744

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Sneak Peek into the World of Science

Consanguineous Marriage, Genetics, & Diagnostic Yield: A Preliminary Analysis

Satish Kumar Kariyaiah, Ph.D
Senior Scientist

The term "consanguineous" is derived from two root words: "con," meaning together, and "sang," meaning blood in Latin. Consanguineous marriage is defined as a legal union of two individuals who are related by blood, such as first cousins. According to a recent study, approximately 10.4% of the world's population is reported to be married to biological relatives. The prevalence of consanguineous marriages varies widely across the globe, with the highest rates found in North Africa, West Asia, and South India, where marriages to biological relatives are culturally favoured and constitute 20-50% of all marriages (Fig.1).

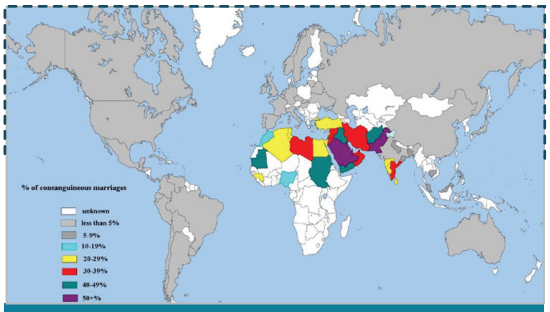

Fig.1: Global prevalence of consanguinity Image from: Acharya, S., & Sahoo, H. (2021).

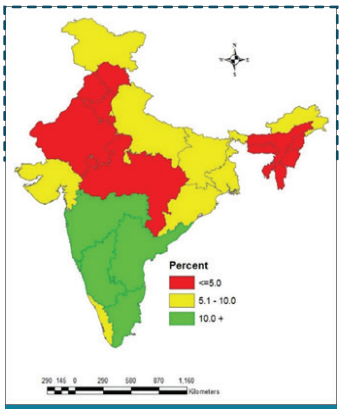

Fig.2: Prevalence of consanguinity in India Image from: Acharya, S., & Sahoo, H. (2021).

In India, consanguineous marriage is prevalent in certain regions, particularly in southern states such as Andhra Pradesh, Telangana, Tamil Nadu, and Karnataka. Based on the extensive data available from the National Family Health Survey-4 (NFHS-4) conducted in 2015-16, the overall prevalence of consanguineous marriage in India was 9.9%. The prevalence of consanguineous marriage was highest in the South region (23%) and lowest in the North-East region (3.1%)(-Fig.2). A more recent survey, the National Family Health Survey-5 (NFHS-5), conducted in 2019-21, found that the prevalence of consanguineous marriage in India had increased to 10.8%.

In clinical genetics, a consanguineous marriage is defined with the inbreeding coefficient (F) value equal to or higher than 0.0156. The inbreeding coefficient (F) is a measure of inbreeding, defined as both the probability that two alleles at any given locus are identical by descent and the probable proportion of an individual's loci containing genes that are identical by descent. This includes unions termed first cousins, first cousins once removed, and second cousins (Fig.3). In South India, the (F) value reaches 0.125, where uncle-niece marriages are commonly practiced.

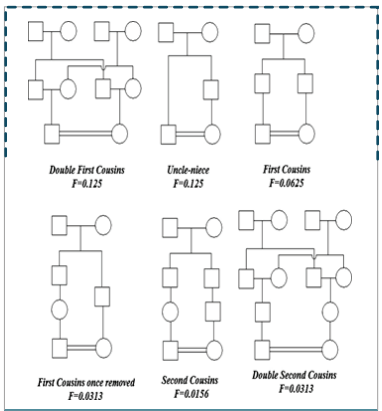

Fig.3: Different from of consanguinity

Studies have shown that consanguineous marriages can lead to an increased risk of congenital malformation, mental disorders, mental retardation, and cognitive disabilities, monogenic disorders, autosomal recessive diseases, stillbirth, and infant death.

This article delves into the implications of consanguinity on diagnostic yield, with a specific focus on the differences observed between samples from consanguineous and non-consanguineous samples from subject who have sought both Chromosomal Microarray Analysis (CMA) and Next-Generation Sequencing (NGS) tests.

In this study, we conducted a preliminary analysis of samples within a diverse population, including both prenatal and postnatal samples. We examined a total of 9,746 individuals who registered for chromosomal microarray analysis (CMA), and a subset of 1,022 (10.48%) individuals who registered for both CMA and next-generation sequencing (NGS).

Chromosomal microarray analysis (CMA) tests was basically performed on an SNP-based array to identify deleterious Copy number variants (CNVs) causative of the phenotype and regions of homozygosity. The Percentage Absence of Heterozygosity (AOH) was calculated using a total autosomal long continuous stretch of homozygosity (LCSH) greater than 3Mb or 5 Mb in size. LCSH can originate from the inheritance of a genomic region of identity by descent (IBD) indicating consanguinity or uniparental disomy (UPD).

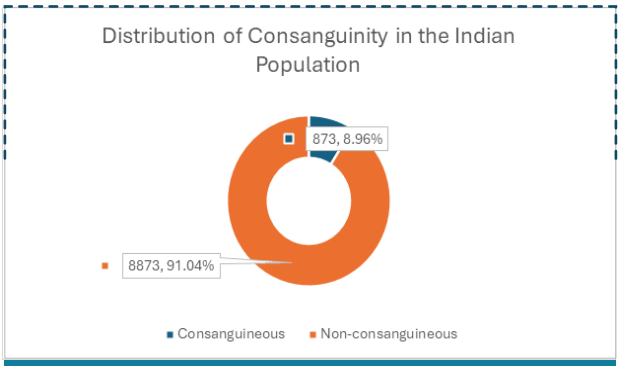

Fig.4: Prevalence of consanguinity in samples registered for CMA testing

Consanguinity status was determined based on the percentage of Absence of Heterozygosity (AOH) observed. Remarkably, 873 individuals were identified as consanguineous, constituting 9.84% of the total cohort (Fig. 4).

The subsequent regional breakdown allowed for a more nuanced understanding of consanguinity patterns. The consanguineous percentages across different zones revealed variations: North (2.48%), East (3.36%), West (7.99%), and South (12.28%) (Fig. 5).

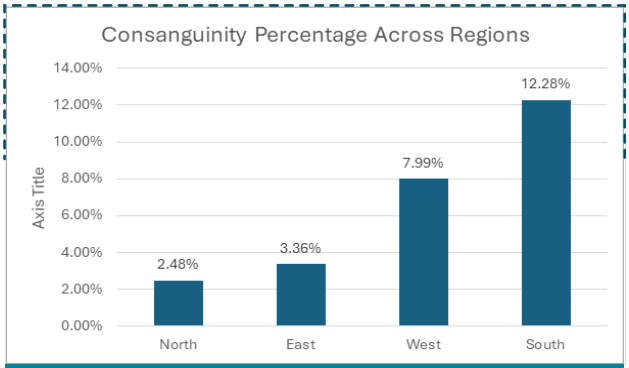

Fig.5: Consanguinity Percentage Across Regions

CMA was recommended for clinical indications common to both groups which included high risk on maternal serum screening in prenatal samples and global developmental delay, microcephaly, speech delay, autism spectrum disorder, hypotonia, seizures, and dysmorphism in postnatal samples.

The overall diagnostic yield of microarray analysis, specifically concerning Copy Number Variations (CNVs), falls within the range of 15-22%. In the context of the current study, consanguineous individuals exhibited a diagnostic yield of 18.61% for CNVs, while non-consanguineous individuals demonstrated a relatively higher diagnostic yield at 30.79% (Fig. 6, 7).

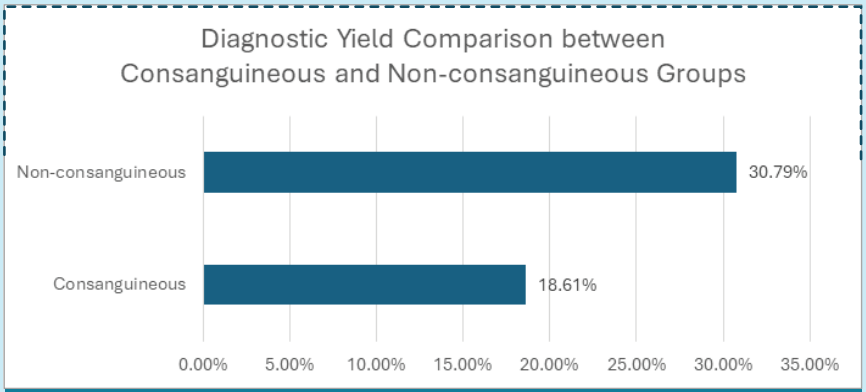

Fig.6: Comparison of diagnostic yield between Consanguineous and Non-consanguineous Groups

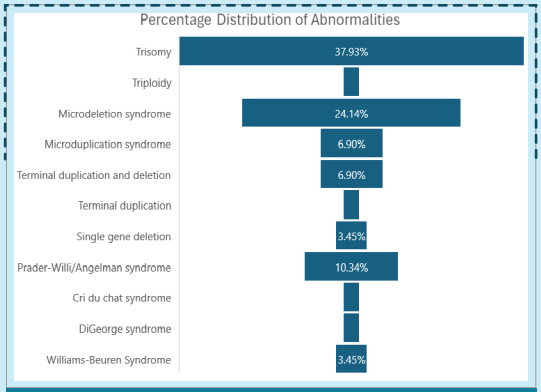

Fig.7 : Percentage Distribution of Abnormalities

To comprehend the disparities in diagnostic yields, a meticulous analysis was conducted within a cohort where Chromosomal Microarray Analysis (CMA) results presented as normal, and individuals were registered for both CMA and Next-Generation Sequencing (NGS) tests. The objective was to identify aberrations (SNVs) in the NGS test results between the consanguineous group (127 samples) and the non-consanguineous group (555 samples), even when CMA appeared normal.

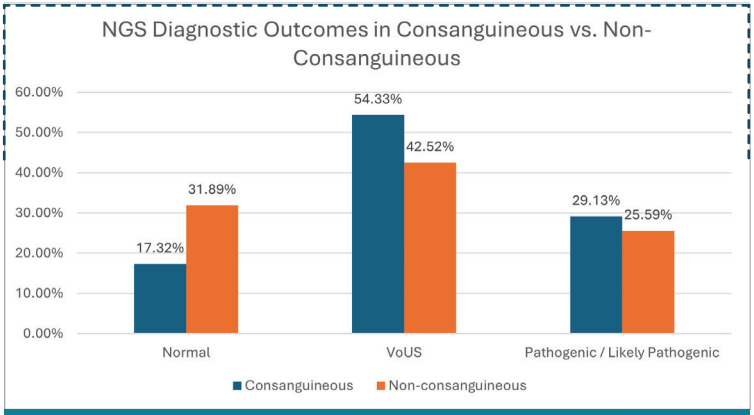

Fig.8: Percentage Distribution of NGS test result in samples which were normal on CMA

Within the consanguineous group of 127 samples, 22 (17.32%) yielded normal results, 69 samples (54.33%) were categorized as Variants of Uncertain Significance (VoUS), and 37 samples (29.13%) were identified as pathogenic, indicating the presence of clinically significant genetic abnormalities (Fig. 8).

In the non-consanguineous group of 555 samples, 177 (31.89%) exhibited normal results, 236 samples (42.52%) were classified as Variants of Uncertain Significance (VoUS), and 142 samples (25.59%) were identified as pathogenic (Fig. 8).

In the comparison between the consanguineous marriage group and the non-consanguineous marriage group, the consanguineous group exhibited an increase in both pathogenic findings by 3.54% and Variants of Uncertain Significance (VoUS) by 11.81%.

In conclusion, our study reveals these key findings. First, the prevalence of consanguineous marriages in our cohort aligns with published literature. Second, the overall diagnostic yield for Copy Number Variations (CNVs) appears slightly lower in consanguineous marriages compared to non-consanguineous marriages. Third, a nuanced analysis focusing on normal Chromosomal Microarray Analysis (CMA) samples registered for both CMA and Next-Generation Sequencing (NGS) tests unveils a different trend. In this subgroup, the consanguineous group exhibits a higher diagnostic yield, particularly in the identification of pathogenic and Variants of Uncertain Significance (VoUS). Fourth, this study provides further evidence that NGS would be appropriate test for consanguineous individuals with normal CMA results. Finally, this highlights the importance of targeted genetic testing methodologies and appropriate counselling in our diverse populations.

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From HR Desk

Mastering Time Management

Dipti Manchanda
Head-HR

Dear MedGenome Team,

We hope the new year has started with a bang for you and your loved ones .

While we have all adjusted to the changes that have taken place in terms of our working structure in the past three years, time management remains a wide topic of discussion and how one can navigate through the same.

Time management is the process of **planning** and exercising **conscious** control of time spent on specific activities — especially to increase **effectiveness**, **efficiency**, and **productivity**. It involves demands relating to **work, social life, family, hobbies**, personal interests, and commitments.

Using time effectively gives people more choices in managing activities. Time management may be aided by a range of skills, tools, and techniques, especially when accomplishing specific tasks, projects, and goals complying with a due date. Initially, the term time management encompassed only business and work activities, but eventually, specially with today's scenario the term broadened to include personal activities as well.

In the fast-paced world that we live in, mastering time management is a crucial skill that can significantly impact our personal and professional success.

Here are a few tips to help you take control of your time and make the most out of each day:

Set Clear Goals

Define your short-term and long-term goals. Knowing what you want to achieve will give your time a purpose and direction. Break down larger goals into smaller, more manageable tasks.

Create a Schedule

Develop a daily or weekly schedule that allocates time for specific activities. Be realistic about how much time each task will take and stick to your schedule as closely as possible.

Use Time Blocks

Break your day into time blocks, assigning specific tasks to each block. This helps prevent multitasking and increases focus on one task at a time, making you more productive.

Prioritize Tasks

Not all tasks are created equal. Identify the most important and urgent tasks and tackle them first. Prioritizing helps you focus on what truly matters and avoids the stress of last-minute deadlines.

Learn to Say No

While it's important to be open to opportunities, it's equally crucial to recognize your limits. Politely decline tasks or commitments that don't align with your priorities or overwhelm your schedule.

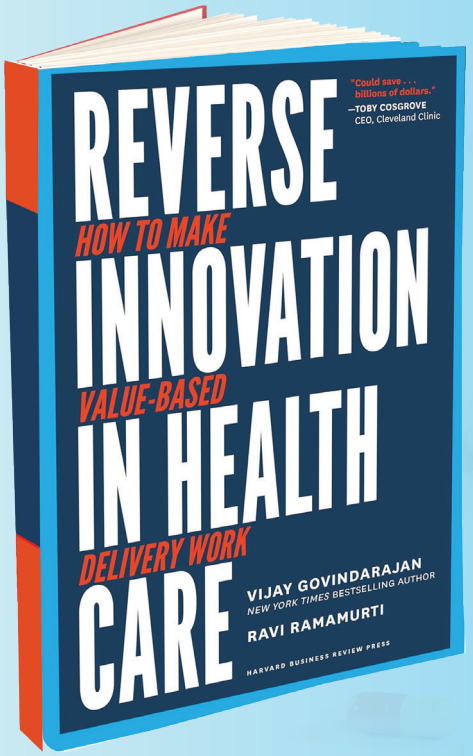
Invest in Self-Care

Remember that time management is not just about work; it's also about maintaining a balanced and fulfilling life. Prioritize self-care, including adequate sleep, exercise, and downtime, to sustain your energy and focus.

By incorporating these practices into your daily routine, you can take charge of your time, boost your productivity, and pave the way for personal and professional success.

Once again, I wish you the best with our career goals at MedGenome and hope the effectiveness of **Time Management** will play a significant role in the same.

Book Review



Book

"Reverse Innovation in Health Care: How to Make Value-Based Delivery Work"

Author - Ravi Ramamurti, Vijay Govindarajan

Book review by

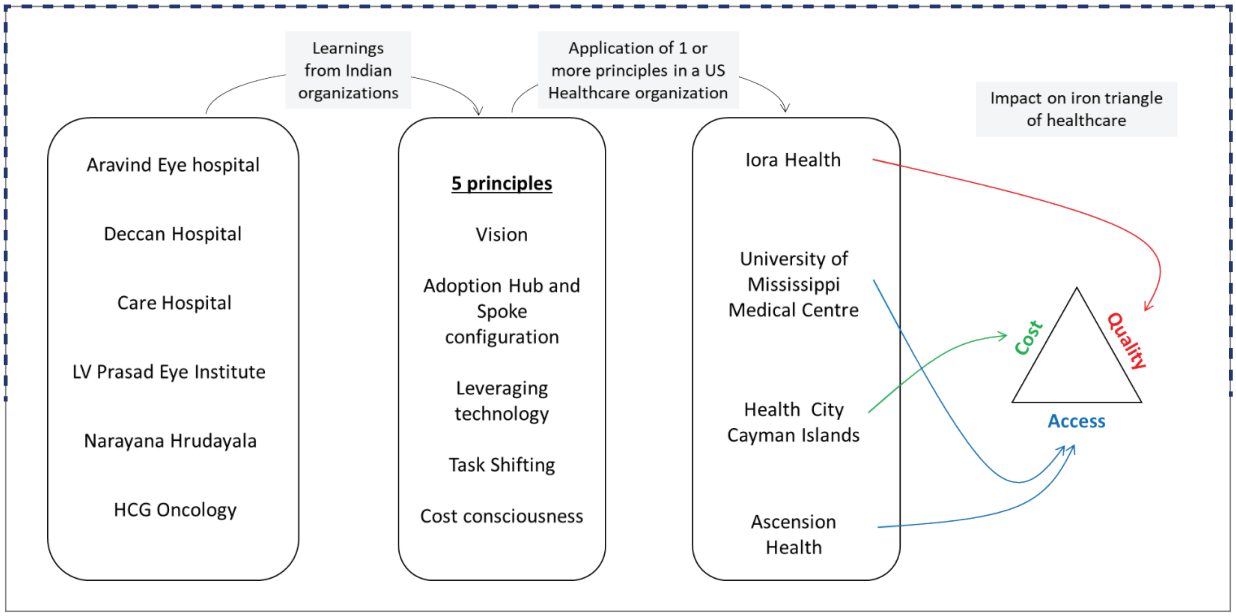
Arvind Venkatesan, Ph.D
Associate Director, Strategic Initiatives and Partnerships

"Reverse Innovation in Health Care: How to Make Value-Based Delivery Work',' a book authored by Ravi Ramamurti and Vijay Govindarajan discusses the potential for advanced countries to adopt innovations made by low- and medium-income countries in their healthcare delivery systems. Having spent time across healthcare systems in the US and in India, and having reviewed these both operationally and commercially, I enjoyed how the authors have brought out specific actionable ideas and have provided examples of Indian healthcare groups that are implementing such ideas effectively. This book stems from the idea that necessity is the mother of invention. Unlike the western world, countries like India aim to provide high quality healthcare at ultralow cost with limited resources. Obviously, innovations to address these challenges also originate in these countries. On the other hand, Western healthcare, although high in resources have been highly flawed warranting disruption in the sector. With this context, the ideas in the book seem plausible.

The authors have presented the book in 3 parts. In the first part, the authors discuss innovations in Healthcare Delivery systems by healthcare organizations in India and globally. Each innovation that is mentioned impacts one or more vertices in the iron triangle of healthcare, i.e. cost, access & quality. I am summarizing the innovations and impact on these factors below:

Country of Origin	Name of the Organization	Impact on Cost	Impact on Quality	Impact on Access
India	Deccan Hosptial	Dialysis for end stage kidney | patients is $4,000 whereas it is $70,000 in the US	5-year survival rate is 50% as compared to only 40% in the US	NA
	Aravind eye care	Contract surgery is $150 as compared to the US where it is $3,750	Complications after surgery is 1% as compared to the UK where is is 2.46%	Use of technology along with hub and spoke model to serve rural sectors
	HCG onoclogy	Cancer treatmentis $2,000 whereas it is 8-12 times more in the US and UK	5-year survival rates for |breast cancer (89%), which isthe same as the US	Use of technology to set up a hub and spoke model to provide oncoclogy services to rural sectors
	Narayana Hrudayalaya	Open heart surgery costs $2,000 whereas it costs$150,000 in the US	Mortality rates after 30 days is 1.4% as comapred to 1.9% for US hosptials	Hub and spoke model
	LV Prasad Eye insutute	Very similar to Aravind eye care system		
	Life Spring Hosptials	Vaginal delivery costs $120 ($8000 in the US) and C-section costs $3000 ($16000 in the US)	Higher % of natural birthing than other hosptals represents better quality	NA
US	University of Mississippi Med Centre	NA	NA	Use of technology along with hub and spoke model to serve rural regions in Mississippi
	Iora Health	Reducing healthcare costs byreducing the need to visit hospitals	Implementing health coach (Task shifting) concept toreduce patient numbers- 40%drop in hospitalizations & ER visits leading to 15-20% dropin healthcare costs in 5 years	NA
	Ascension Health	NA	NA	Increase healthcare access to the uninsured using:- Hierarchy model like Aravind where the insured pay for the uninsured - Utilize frugality concept by increasing effectiveness and cost efficiency
Dubai	Core Hospitals	Knee and hip transplantsfor $3,000 where itis $30,000in the US- Angioplasty costs $2,000whereas in the US it costs$150,000	1 in 200 angioplasty patients in the US require emergency surgery and half of those patients will die on the table whereas 2 out of 40,000 angioplasty patients atCARE Hospitals requiredemergency surgery and only 1 died since 1997	NA
British Overseas Territory	HealthCity Cayman Islands (also owned by NH's Dr.Shetty)	25-40% of the costs of US hospitals	Expect it to be similar to NH	NA

In the second and third part, the authors provide 5 key principles that have been the backbone for the above-mentioned innovations and have provided a framework for healthcare organizations elsewhere to adopt them. The authors follow this up with examples of certain US-based organizations where some of these innovations have been successfully implemented.



The best part of this book is that it provides an eagle's eye view of the different issues and possibilities in healthcare delivery systems globally. The authors have written the book in such a style that learnings on cross utilizing innovation can be ignited for sectors beyond primary healthcare. I am penning down some thoughts that crossed my mind as I was reading the book:

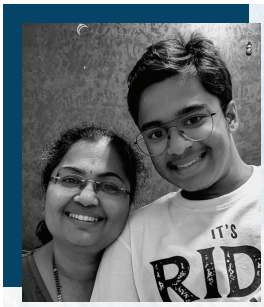
- Intuitively, we always consider an inverse relationship between volume and quality. The book offers a counterintuitive perspective idea for healthcare. For example, the book discusses the idea of better treatment outcomes for several disorders in India as clinicians in third world countries have larger real world evidence as they treat much larger volumes. This helps with the individual clinician's learning curve, but more broadly can help improve treatment paradigm for specific diseases.

- Healthcare does not have to geographically restricted if planned well. Opening up of a tertiary care centre by Narayan Hrudalaya in Health City Cayman Islands to provide treatment to US citizes was a big success due to the geographical proximity. This not only opens us opportunities for emerging economy healthcare systems to explore the advanced economy markets but through competition will force healthcare organizations in developing countries to rethink their business and operating model.

- Most organizations in the specialty business predominantly focusses on improving its core process. Therefore, the focus on operational processes that may not be core to the company but may have larger opportunity of improving revenue or reducing costs. While the authors have provided specific examples for innovations in healthcare that can be lifted and shifted to other economies, they seemed very optimistic about implementing these. A few issues that I thought were not addressed are:
    - **Scalability of innovations in the Indian healthcare sector:** The authors have not investigated why these innovations that were developed in India have not been successfully implemented in other organizations in the same country. Understanding what these challenges are will be fundamental to applying these innovations elsewhere.
    - **Governance structure:** The authors have not examined any unique governance structure in the mentioned organizations that have made such innovations possible. It is possible that such innovations require doctopreneurs or a management team that is well versed with clinical, operational as well as commercial concepts? Will any type of organizational change be necessary to implement such innovations?
    - **Assessment of the target market:** The target market i.e., the patients in the developed nations such as the US are different from those in India, especially the ones that most of the mentioned Indian organizations target. 70-80% of the volumes that these organizations treat are low-income groups from the rural sector who have no access to healthcare. Any mis-happenings in treatment due to ideas such as task shifting or due to fatigue by treatment of larger volume may be forgiven in the Indian context owing to poor regulations and legal systems and the patient's financial inability and lack of awareness. However, in developed nations, patient's are highly aware and suing hospitals in a common phenomenon. While most organizations have shown better clinical quality, this aspect should have been inspected more deeply by the authors.
    - **Economies of scale problem in developed markets:** The population density in countries such as the US may not help organizations in the US attain as much volume as achieved by organizations such as Aravind. In such cases, where economies of scale cannot be achieved, will the above-mentioned innovation fall apart is a question that is not addressed.

From our Colleagues

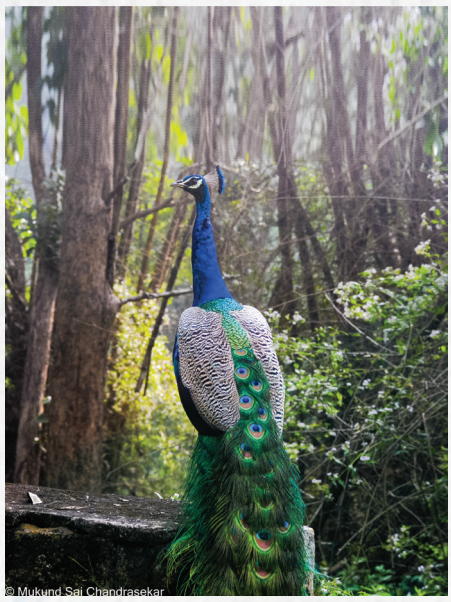
Our employee's little Photographer:)



By:

Mukund, 16 years

DNA of Malini Ayathu Venkata, Genomic Medicine dept.



From our Colleagues

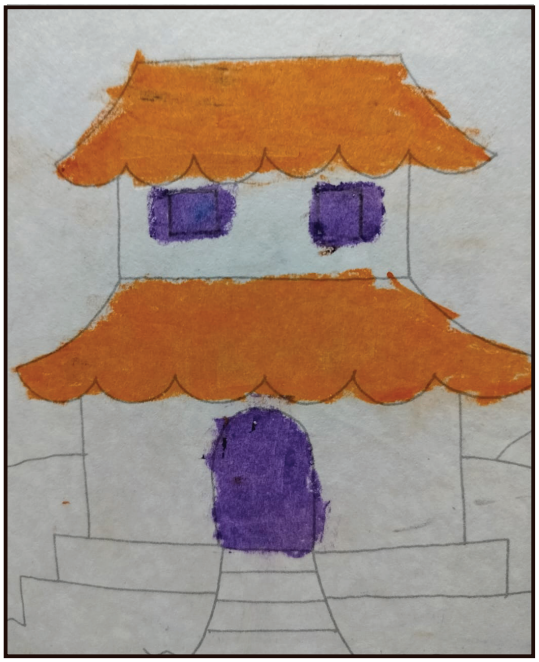
Our employee's little Picasso:)

By:
Vaidehy Sreejesh, 3 years
DNA of Sreejesh Damodaran, Sales Dept.

From our Colleagues

Our employee's little Picasso:)

By:
Vihaan V Bharadwaj, 5 years
DNA of Venu Seenappa, Lab operations.



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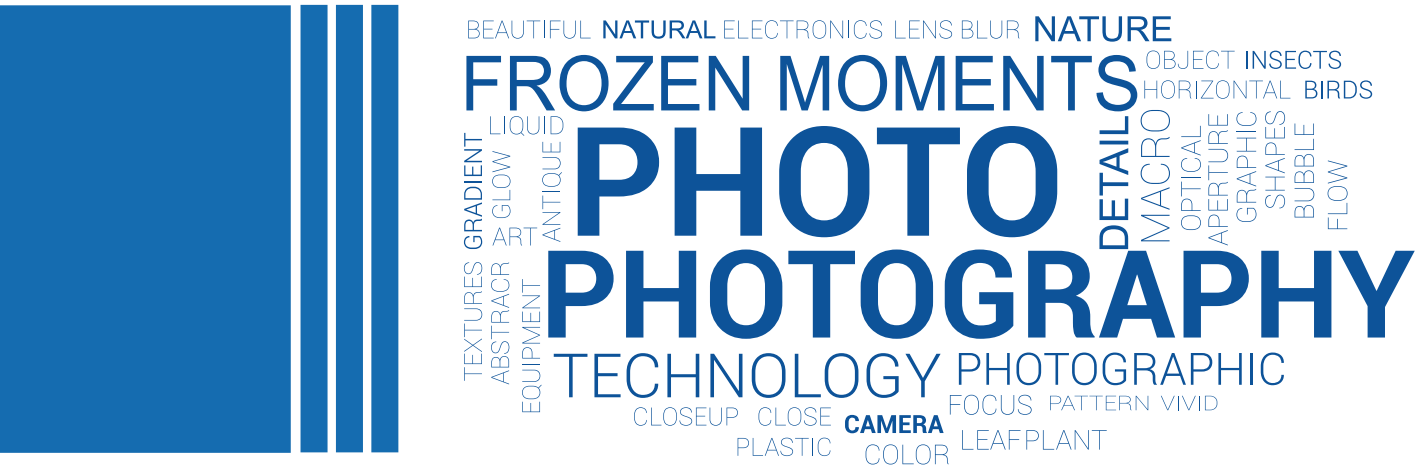

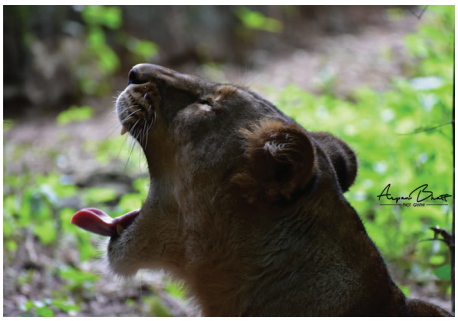

By:
Arpan Bhatt
Senior Manager
Lab Operations.

Employee Connect

Our New-Joiners


Abhishek Kumar Tripathi


Abhishek M P


Akshara M Nair


Amit Singh


Anand P S


Ancy Angelene K


Angeline Unni


Aswathi N


Babasaheb Digambar Jadhav


Bhavana Lakshmi C


Chinmayan P Raju


Ekant Tyagi


Gaurav Premsing Rathod


Gaurav Sharma


Godavarthi Raghu


Hridhya Jacob


Jahnavi R


Jenifer


K Bhargavi


Karingula Haritha Reddy


Kripa Saira Jacob


Lakshmi Priyankka Alagappan


Lava


MeganKumar M


Meghana P Raman


Nidhi Sanjay Shah


Nikhil Arjun C


Niranjan G V


Pavana K S


Prabhat Singh


Pradeep Kumar Pattanaik


Prathyusha Girish

Praveen Ramalingappa Kalloli

Preethi D S

Rajesh Rajan Nagarajan

Rajni Rawat

Ramwung Shimrah Huimiwon

Randeep Kumar Bhagat

Ratul Das

Ravi Mukundrao Barange

Sandeep S

Sandip Shankar Kamble

Sanika Sudhakar Avhad

Sarvanamma K S

Shailaja Pankaj Vernekar

Shajil O V

Shivam Dwivedi

Shri Poornima Rajaram

Shri Preethi Manikantan

Shubham K R

Soni Jha

Sreegowri P

Subhiksha N Iyer

SUMITHA

Sunil Bhujingrao Kalaskar

Ulaganathan

Varshitha A

Vignesh V

Vinodh kumar

Viveak Kumar

William Ignatius

Yash Agrawal

Photo Feature

Christmas & Diwali Celebrations

2023 Year end celebrations were filled with joy, gratitude and colors. We celebrated Diwali with our colleagues dressed in traditional/ethnic wear followed by Christmas celebration. We also conducted yet another successful 'Joy of Giving' activity, thanking our silent heroes (housekeeping, security, runner boys, etc.) with a token of appreciation (gift of their choice).

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