MEDGENOME

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Internal Quarterly Newsletter Vol 27 | Oct 2023

Genome Asia 100K

Sequencing Asian population to reduce global genomic disparity and improving human health

NON-INVASIVE PRENATAL TESTING FOR RHD GENOTYPING

WORDS FROM THE **FRONTLINE**

Praveen Bharamagoudar
Vice President - Oncology Sales and CDx

It has been an incredible journey spanning 6+ years with the MedGenome family from 2018. Through this time, my role has revolved around establishing and nurturing our footprint within India and International markets. Our goal has been to provide top-notch services in the realm of cancer genetics. The journey has been very successful as we have been able to bring some of the well-known customers to our fold like Novartis, AstraZeneca, Sanofi, Takeda, MSD, Roche, etc. for Companion Diagnostic (CDx).

As a member of the oncology sales team, I've had the honor of witnessing the astonishing growth of our portfolio over the years, we started with about 50 tests and are now offering 450 tests. It has been a phenomenal experience for me to introduce one of MedGenome's most groundbreaking offerings to the market — the launch of the first liquid biopsy test in India. This achievement has had a life-changing impact on improving the prognosis of the people suffering from cancer while also establishing MedGenome's image as an innovator and preferred partner in the minds of the doctors. I would like to extend my heartfelt gratitude to our CEO, Dr. Ram, whose unparalleled expertise and knowledge has been the driving force behind this remarkable milestone.

Our Prima team, which initially consisted of 15 individuals, has grown into a team of 80 dedicated and passionate professionals. This team has been the backbone which has driven an impressive growth in our sales by 35% YOY. We're seeing an increasing demand for genomics tests in cancer management. Recognizing this demand, we strategically partnered with premier organizations, laboratories, hospitals, and even ventured into new countries in the southeast Asia and to CAMCAR region.

I would like to say a heartfelt 'THANK YOU" to every member of our organization, across all the departments, be it technical, scientific, bioinformatics, commercial, lab operations, customer support, or management, for their unwavering support, without which none of this would have been possible.

My congratulations to each member of our Sales Team in recognition of your relentless efforts in fortifying our client relationships. We have high expectations for our Sales team to continue seeking out opportunities for collaboration at every level.

As we press on with our global expansion to provide top-tier genetic testing and genomic solutions, let's remain fuelled by the same passion that ignited MedGenome's inception. Together, let's be committed to growth, continuous learning, and the exploration of new horizons, all in our pursuit of reaching even greater heights.

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Most Talked About

MEDGENOME IN NEWS

July to September 2023

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

Quality genomic testing needs to be democratized: Dr Vedam Ramprasad

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Why do South Asian genes make you prone to Coronary Artery Disease?

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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. We also created test specific brochures and mailers like KaryoSeq and NIPT and social media posts. We have also posted videos on IVF to explain role of genetic testing.

Brochure- KaryoSeq

The objective is to create awareness about KaryoSeq offering through various collaterals

Social Media Post- IVF

The objective is to create awareness.

CME on Genetics on Clinical Practice

ACTIA
Inherited Genetics

Past quarter, the campaigns were focused on Nephro Genetics, Opthalmic Genetics and Cardio Genetics. On offline engagement perspective we had more than 25 CMEs, RTM spread across all locations including a large format CME conducted by us in Hyderabad.

CME on Genomics in Clincal practice, Hyderabad with over 80 participants

Nephro Genetics & Opthalmic Genetics Campaigns

Nephrotic Syndromes are characterized by excessive protein loss in the urine. Understanding the underlying genetic factors is crucial for personalized treatment strategies and disease management.

MedGenome offers NGS - based genetic test for Nephrotic Syndromes for precise diagnosis to empower the clinical decision-making process. It helps in prognostic, therapeutic & transplant decision making, estimating recurrence risk and facilitating informed reproductive options.

#MedGenome #Actia #NephroticSyndromes #GeneticTesting #NephroGenetics #OnlyWithMedGenome #PersonalizedMedicine #HealthcareInnovation #Precision #Accuracy #Leaders #Pioneers #Nephrology

MedGenome introduces its latest offering, Comprehensive Opthalmic Genetic Disorder Panel launched by **Dr Rajani Battu**, Medical Director, Centre for Eye Genetics and Research, Bangalore at the Foresight 2023 summit.

Comprehensive Opthalmic Genetic Disorder Panel covers Retinal Degenerations, Dysfunctions and Dystrophies, Developmental Diseases, Retinoblastoma and other Ocular Cancer.

#ophthalmology #MedGenome #Actia #GeneticTesting #GeneExperts #PrecisionTesting #PowerOfGenetics

World Heart day campaign was a great success as we touched upon various topic such as congenital heart diseases, hypercholesterolemia, cardiac channelopathy, cardiomyopathy amongst others.

On #WorldHeartDay, **Dr. Aditi Singhvi,** Consultant Adult Cardiology & Heart Transplant at Narayana Health, Bangalore, sheds light on Cardiomyopathy and its significant role in causing heart failure. Learn about the different types of Cardiomyopathy and why genetic testing is crucial if there's a family history. Protect your heart health with knowledge!

#WorldHeartDay #SkipTheSuspense #GeneticScreening #KardioGen #HeartHealth #CAD #Cardiology #Genes #Genessense #CardiomyopathyAwareness #GeneticTesting #StayHeartHealthy

As part of World Heart Day, **Dr. Neeraj Awasthy,** Director of Paediatric Cardiology at Fortis Escorts Heart Institute, New Delhi, sheds light on the importance of early detection and prevention of Congenital Heart Disease in infants and kids.

Did you know that many infants are born with #CongenitalHeartDisease? But there's hope! Genetic testing can be a powerful tool in identifying potential risks and taking proactive measures to safeguard their precious hearts. More details in the video.

#WorldHeartDay #HealthyHearts #GeneticTesting #MedGenome #ChildHealth #HeartHealth #EarlyDetection Dr. neeraj awasthy

Talking about a case study of one of his patient, Dr. Neeraj Awasthy, Director of #PaediatricCardiology at Fortis Escorts Heart Institute, New Delhi, sheds light on the importance of genetic testing in Congenital Heart Disease in infants and kids. He also says that Congenital Heart Disease should not necessarily be a defect in the structure of the heart by birth, but Channelopathies.

#WorldHeartDay #HealthyHearts #CongenitalHeartDisease #Channelopathies #GeneticTesting #MedGenome #ChildHealth #HeartHealth #EarlyDetection neeraj awasthy

Dr. Virendar Sarwal, Director Cardiac Surgery, Ivy Hospital, Mohali sheds light on the groundbreaking importance of Genetic Screening and the Polygenic Risk Score (PRS) in assessing your risk of cardiovascular disease.

Genetic Screening: By examining your unique genetic makeup, we can uncover hidden predispositions to heart issues, allowing for early intervention and prevention.

Polygenic Risk Score (PRS): This cutting-edge tool analyzes multiple genetic markers to calculate your individual risk. It's like having a crystal ball for your heart health!

Don't wait for symptoms to strike. Take control of your heart health today through Genetic Screening and PRS analysis.

#MedGenome #PolygenicRiskScore #HeartHealth #GeneticScreening #PRS #PreventionIsKey #HealthyHeart HeartiVillage an Initiative by Dr Virendar Sarwal "The Heart Surgeon "

Prima
Cancer Genetics

Past quarter, the campaigns were focused on blood cancer and liquid biopsy tests. We had an insightful case studies, animated contents and KOL videos which were promoted across all platforms. On offline engagement perspective, we had more than take down CMEs, RTM & tumor board meetings spread across all locations.

In this video, **Dr Niti Raizada**, Senior Director - Medical Oncology & Hemato Oncology, Fortis Hospital, Bangalore explains the various causes of Lung Cancer and the treatment.

She reiterates that lung cancer has been strongly associated with tobacco consumption. However, recent years have witnessed a puzzling surge in diagnoses among younger women who have never consumed tobacco. Dr. Niti indicates that the potential triggers which may cause lung cancer other than tobacco consumption could be indoor smoke, genetic predispositions, and lifestyle factors.

Talking about personalised treatment for Lung Cancer patients, Dr Niti says that one of the most promising breakthroughs in lung cancer management is the advent of liquid biopsy. This non-invasive technique empowers oncologists for better Lung Cancer management with precise and accurate diagnosis.

#MedGenome #WorldLungCancerDay #LungCancerAwareness
#EarlyDetectionSavesLives #DefeatLungCancer #PowerofGenetics

In this video, **Dr Sunil Chopade**, Consultant Medical Oncologist, Jaslok Hospital, Mumbai talks about Lung Cancer symptoms, diagnosis and treatment in detail. He also highlights the importance of detecting the mutations with the help of biopsy and says #LiquidBiopsy is a helpful method when it comes to Lung Cancer management.

We thank Dr Sunil for entrusting the MedGenome NGS Based Liquid Biopsy test for precise and accurate detection of mutations in Lung Cancer tumors.

He also reiterates the fact that prevention is better than cure.

#MedGenome #WorldLungCancerDay #LungCancerAwareness
#EarlyDetectionSavesLives #DefeatLungCancer #PowerofGenetics

In this video, **Dr. Vikas Talreja**, Medical Oncologist from Regency Hospital, Kanpur says Lung cancer may seem challenging, but today's medical science has evolved in remarkable ways and with the access of cutting-edge technologies, treatment options for lung cancer at every stage is possible.

He also highlights that the battle against lung cancer starts with awareness and early detection. Regular check-ups and screenings can make a world of difference. Dr. Vikas Talreja emphasizes the importance of proactive health management, helping you catch potential issues before they escalate.

Let's raise awareness, detect early, and ultimately, conquer lung cancer – together!

#MedGenome #WorldLungCancerDay #LungCancerAwareness
#EarlyDetectionSavesLives #DefeatLungCancer #PowerofGenetics

On World Lung Cancer Day, **Dr Javvid Muzamil,** Medical Oncologist, Super Specialty Hospital, Srinagar shares his view on Lung Cancer incidence and management of Lung Cancer with the help of MedGenome LungTrack Advance (NGS based Liquid Biopsy test).

To know more, please watch the video.

MedGenome urges you to take care of your health by making healthy choices. #HealthyLungsHealthyLife

To know more about Liquid Biopsy, please visit https://lnkd.in/gBdkeKUJ

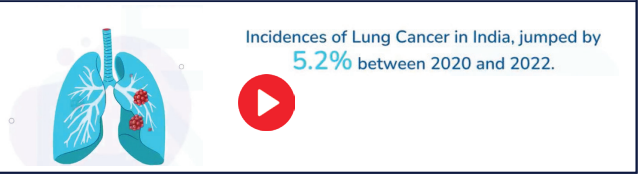
#WorldLungCancerDay #MedGenome #LungCancerAwareness
#EarlyDetection #GeneticTestingIndia #Precision #Pioneers #Leaders

Today is World Lung Cancer Day, and at MedGenome, we stand united in the fight against lung cancer. Together, let's raise awareness about this devastating disease and take steps towards early detection and prevention.

Lung cancer is a global health challenge, affecting millions of lives every year. As a leading genomics and diagnostics company, MedGenome is committed to advancing lung cancer research and providing cutting-edge genetic solutions to improve patient outcomes.

MedGenome urges you to take care of your health by making healthy choices. #HealthyLungsHealthyLife

#WorldLungCancerDay #MedGenome #LungCancerAwareness #EarlyDetection #GeneticTestingIndia #Precision #Pioneers #Leaders



Discover the Power of Molecular Tests for Blood Cancer with MedGenome.

With the Advanced technologies like Karyotyping, FISH, Flow Cytometry, RT-PCR, NGS & Fragment Analysis we utilize extensive bioinformatics to analyze multiple genetic markers and gene variations at a molecular level for precise diagnosis of blood cancer.

Why choose Molecular Tests for Blood Cancer by MedGenome?

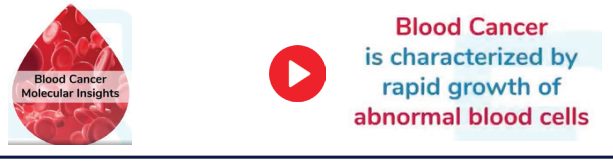
- Comprehensive Analysis
- Accurate Diagnosis
- Identify Targeted Therapies
- Monitor Disease Progression

Comprehensive reports deliver vital information that paves the way for personalised treatment approaches.

At MedGenome, we are committed to harnessing the power of molecular testing to revolutionize blood cancer diagnosis and treatment.

To book Free Genetic Counseling, visit https://lnkd.in/gnsMXw3u or call 1800 103 3691

#MedGenome #WorldLungCancerDay #LungCancerAwareness #EarlyDetectionSavesLives #DefeatLungCancer #PowerofGenetics

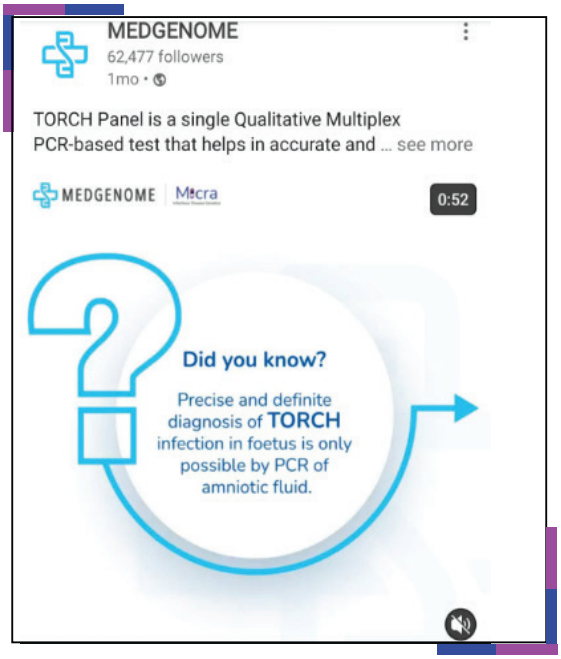


The past quarter was very encouraging and has been a highly active one for Micra with a focus to engage more clinicians with CME, conference participation, test specific mailers and social media posts. We have also posted video on TORCH Panel on all social Media Platforms. 5-Day training was conducted for sales team on Micra Portfolio.

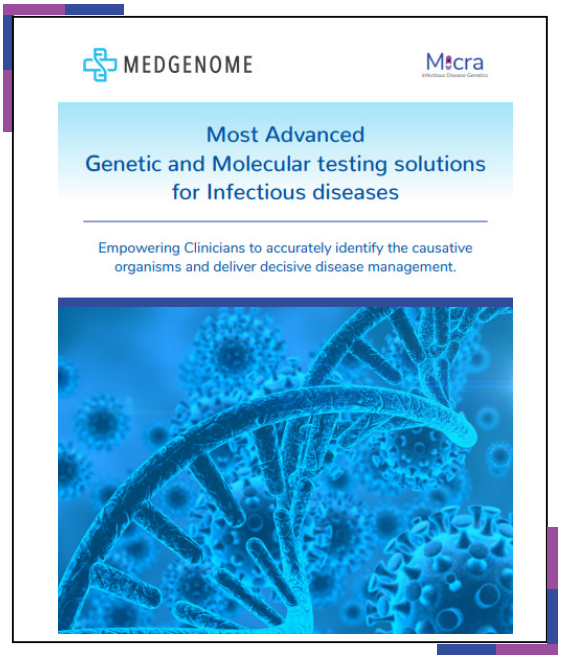
We have organized a webinar for clinicians on Sepsis by Gunisha Pasricha PhD, Associate Director, Research Services and Infectious Diseases. The team also completed a comprehensive Micra Brochure which contains in depth information about all the tests along new tests launched in Micra.

Participation at CME on Fungal Infections (CIDS)

Social Media Post- TORCH Panel



Micra Comprehensive Brochure



Social Media Post-Testimonial Video by Dr. John Paul on Tropical Fever Panel

GENESSENSE

Powered by MEDGENOME

We continued to evolve the various tests being offered under the Genessense portfolio in this quarter. We initiated a campaign on World Heart Day for Kardiogen with various KOLs testimonials and awareness videos on social media. We focussed on forging partnerships with a few aggregators & conversations were initiated with some of the major players in this space. We have also completed Comprehensive Genessense, Kardiogen, Curegen, Diabetogen, Hypersense, Neurosense, Visigen, Carriergen and Oncogen brochure and myTrueAge brochures and reports were created, and the test was made available for internal testing with a prospective partner organisation. We are also revamping our Genessense Website with packages details, Scientific Insights on staging.

World Heart Day- KARDIOGEN- Social Media Posts

myTrueAge Report

VISIGEN launch at the Opthal CME, Bangalore

What's new

Research Publications

Detection of 22q11.2 deletion syndrome by single-nucleotide polymorphism based non-invasive prenatal test Read more

Journal : *Indian journal of Obstetrics and Gynecology Research*

Tests launched

- HER2/neu for Colonic Carcinoma by IHC (Onco)
- Familial Erythrocytosis Panel (benign Hematology)
- VisiGen-PRS Screening for genetic risk prediction of AMD

Another notch in the belt

NovaSeq X Plus, Illumina's most powerful sequencing system has been added in MedGenome's state-of-the-art lab facility to offer an advanced genomics services in South Asia.

With the ability to generate more than 20,000 whole genomes per year – 2.5 times the throughput of prior sequencers at shorter turnaround time, this latest sequencer is aimed at making genomics more sustainable and accessible to more people globally.

Proud Moment

We are extremely proud to announce that **Dr T Rajkumar, Director of Research (Oncology) at MedGenome Labs,** has been honored with the prestigious

"Legends of Medical Oncology – Lifetime Achievement Award"

by the Indian Society of Medical and Pediatric Oncology (ISMPO). This award recognizes his outstanding contributions to the growth of the medical oncology specialty and his dedication to the care of patients

This Award was conferred during the **Indian Cancer Congress 2023 on Thursday, November 2, 2023, Mumbai**

Dr Sudeep Gupta, President-ISMPO | **Dr Govind Babu,** Past President- ISMPO | **Dr T Rajkumar,** MedGenome | **Dr Maheboob Basade,** President Elect-ISMPO

Dr T Rajkumar, was the Best outgoing student in MBBS (1982) and MD (General Medicine - 1985) from Madras Medical College. He completed his DM (Medical Oncology – 1988) from Cancer Institute WIA, Adyar, Chennai and joined the Institute as Assistant Professor in Medical Oncology and was in charge of solid tumors. He developed chemotherapy protocols for ovarian cancer and osteosarcoma (an aggressive bone cancer). In 1991, he was awarded the Commonwealth Scholarship which he used to do his PhD in Molecular Oncology from ICRF Molecular Oncology laboratory in Hammersmith hospital. On successful completion of his PhD, he returned back to Cancer Institute and with support from Dr Krishnamurti, founder of the Institute established the Department of Molecular Oncology and moved his focus to Translational research.

The first comprehensive hereditary cancer detection and prevention program (comprises hereditary cancer clinic, and laboratory for mutation detection in important genes) in the country, under funding from DBT and later from DST and Cancer Institute was established by him. He was the first to develop, characterize and conduct the Phase 1 clinical trial for Dendritic cell vaccine in recurrent/ metastatic cervical cancer (funded by DBT). Subsequently, a phase 2 trial was conducted in stage IIIB cervical cancer which was funded by DST. Under funding from DST, he and his team identified biomarkers for early diagnosis of Cervical cancer (based on p16 and cytokeratin ELISA); Ovarian cancer using blood based assays for 5 proteins; Breast cancer early detection using 3 methylated genes in cell free DNA in blood. All the 3 assays have patent application done. The team also developed a therapeutic peptide as well as a monoclonal antibody to CD99 which is overexpressed and is a target for the treatment of an aggressive bone cancer called Ewing's sarcoma and a patent has been awarded for the peptide. Work is progressing to use Biosensor based protein detection in ovarian cancer to increase sensitivity further and preclinical work to evaluate the efficacy of the recombinant CD99 Antibody against Ewing's sarcoma is in progress, both with collaboration with IIT Madras and funded by DST.

Having Dr. Rajkumar join us at MedGenome is a great honor, and we are excited to tap into his wealth of knowledge and experience. His contribution will be instrumental in our quest for excellence in the realm of oncology genetics.

From Our US Office

The past quarter was a fruitful one with some new initiatives and solutions. We had attended the AGBT conference and presented a good poster titled "MedGenome's genomics solutions for precision medicine" – the poster explored advanced sequencing and bioinformatics solutions offered by MedGenome. The AGBT meeting is attended by prominent speakers and explores cutting-edge research across the broad landscape of genomics. Our Poster was well received at the event.

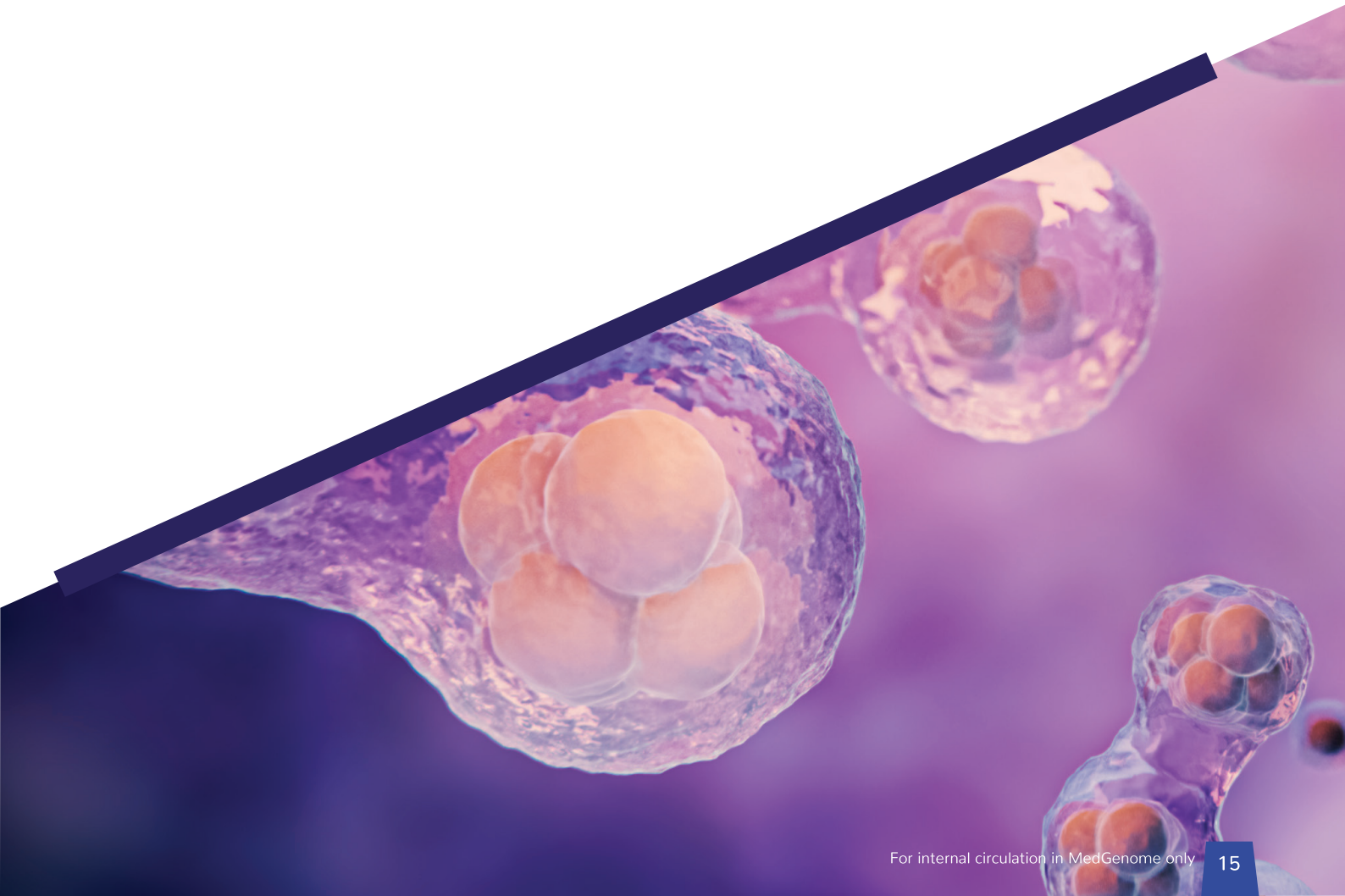
We are also happy to share the news that even this year we were selected as the

"Best Biotechnology Company in Foster City 2023"

We have recently published new articles on **https://research.medgenome.com/blog/**

1. Advanced Bioinformatics Solutions for Single Cell Research
2. Next generation cytogenomics: Optical genome mapping (OGM) for detection of chromosome structure variations

We encourage you to share your viewpoints and articles of interest at **mgus-blog@medgenome.com**



Genome Asia 100K – Sequencing Asian population to reduce global genomic disparity and improving human health

Ravi Gupta, PhD
VP, Bioinformatics

The Human Genome Project completed in 2003 and published the first draft of the human genome. However, the project did not represent the complete human catalogue as it primarily used the European population. The lack of diversity in data collection reduces the opportunity to detect distinctive features in different populations. In a study published in 2019 (Mills & Rahal) it was shown that approximately 88% of samples in genome-wide association studies (GWAS) were of European ancestry. Due to this the Europeans have more accurate and reliable diagnoses and the non-Europeans receive more false and ambiguous clinical diagnoses. Each population group carries a different combination of genetic variants so it important to catalogue more and more diverse genomes to improve the human health and promote better understanding of human biology.

Despite recent small improvements in non-European representation in genomic study, the diversity of the population in genomics remains dismally low. Failure in bringing and putting together a more diverse genome has already had and will continue to have huge ramifications. Geographical bias also limits diversity in genomic research as most of the genomic studies are conducted in the United States and Europe.

Asians which comprise more than 40% of the world's population are among the significantly underrepresented genomes in the world. Among the many initiatives taken all over the world to reduce genome data diversity, the GenomeAsia consortium was formed to facilitate and coordinate sequencing efforts of the Asian population. The overall goal is to sequence 100K individuals from Asia covering as many region groups as possible. MedGenome is one of the founding partners of Genome Asia with primary focus on sequencing diverse Indian population groups.

The GenomeAsia Pilot (GAsP) project published the whole-genome sequencing data of 1,739 individuals from 219 population groups across Asia (GenomeAsia100K Consortium, 2019). This includes 598 genomes from India. In the pilot study, the consortium focused on understanding the population structure, history, and disease-associated loci and the differences between populations. The study included several groups with small population size which was expected to have endogamy and hence high IBD (identical by descent) scores.

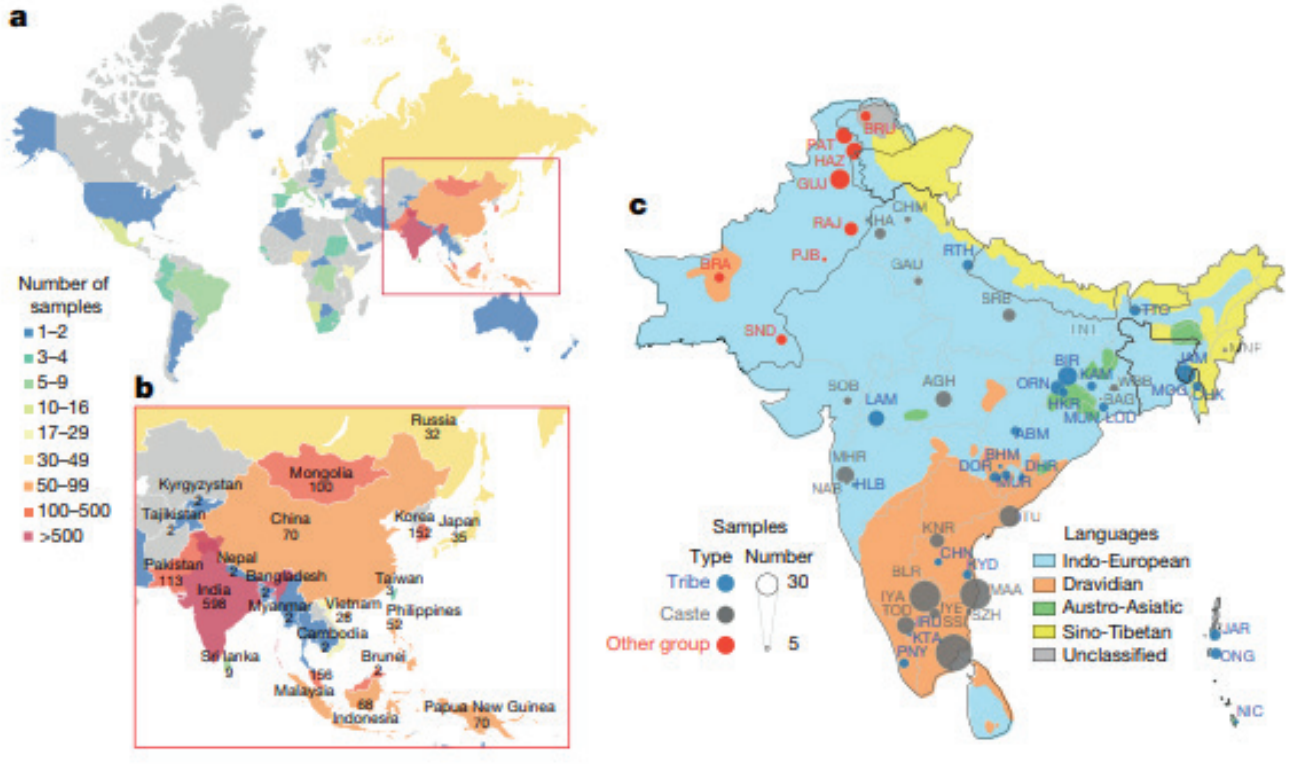


Figure 1. Sample sizes, location, language and social hierarchy associated with samples from South Asia. (GenomeAsia Consortium, nature 2019)

IBD in short measures whether the segments of genomes have the same ancestral origin in individuals from the same group. The study showed that the indigenous and tribal groups had IBD scores as compared to non - tribal groups. Interestingly, several indian groups with large urban populations have high IBD scores. For example, samples from Chennai, a city with a census size of 9 million, had an IBD score that was approximately 1.3 times greater than the score for the Finnish group. The Finnish population group is used as a reference control for IBD studies. The study also found that the Austronesian groups (~`400 million individuals) have increased risk for carbamazepine sensitivity. This includes most of the people living in Indonesia, Malaysia and the Philippines.

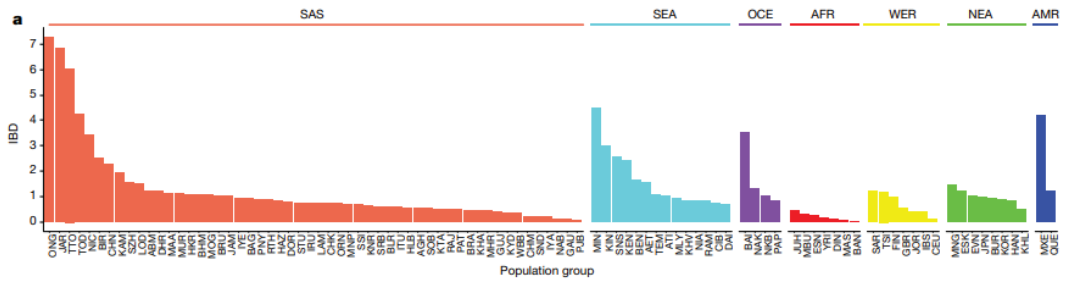


Figure 2. IBD scores across different population groups are shown for 96 ethnicities (1,417 samples) across global regions. The scores given in the figure are relative ratios compared to that of the Finnish group (GenomeAsia Consortium, nature 2019)

The second study (GenomeAsia consortium, nature comm. 2023) from GenomeAsia describes whole genome sequence (WGS) data from 6442 high-coverage genomes (average 25X) including 5734 genomes were of South Asian ancestry with medical cohort sizes of 1810, 1362, and 1634, respectively, for the Pakistani (PKN), South Indian (SOI), and Bengali (BNG) groups. Population structure analysis of South Asian genomes shows a clear distinction between Bengali, Pakistani, and South Indian groups that roughly mirror geography (Figure 3).

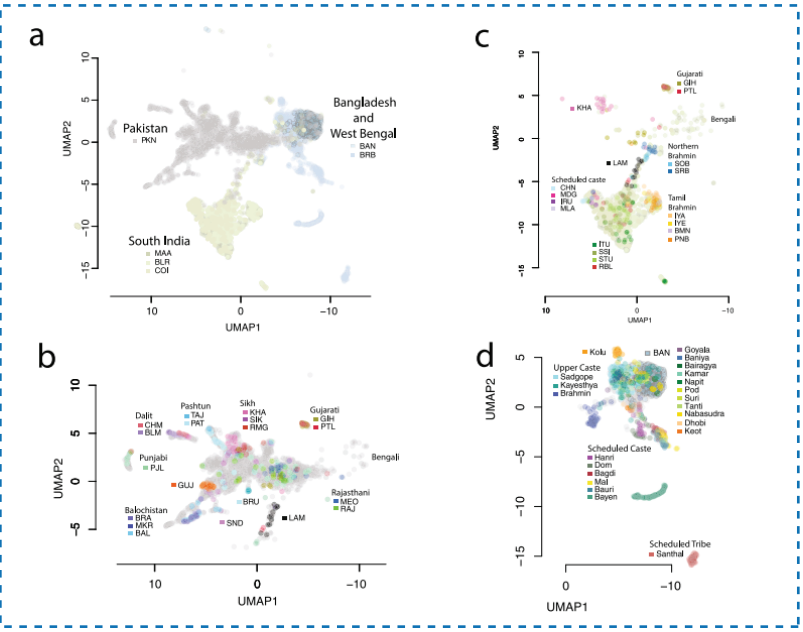


Figure - 3

Figure 3. Fine-scale population structure in the healthcare delivery system reflects the geographical locations of the sample sources. **a.** In the South Asian subset, samples cluster into three major groups by sample origins: Pakistan, South India, and West Bengal and Bangladesh. **b. c.** Samples with detailed locations or self-reported group memberships are shown to segregate within Pakistan and South India clusters. Among the samples from Pakistan and South India, some segregate with recent immigrants (e.g., Bengalis and Gujaratis) and historical immigrants (e.g., Lambadas), reflecting the metropolitan nature of the recruitment centers. **d**. Samples from Birbhum District, West Bengal, have detailed self-reported group membership information. Upper castes, scheduled castes, and scheduled tribes clearly segregate, reflecting the historical reproductive isolation between these groups. Bayen and Santhal are two notable population isolates.

To understand the functional impact of the high levels of endogamy and consanguinity found within South Asia, the putative loss of function (pLoF) variants was also studied. The predicted loss-of-function (pLoF) variants (nonsense, frameshift, essential splice site) lead to early terminal of protein. Some individuals (human knockouts) naturally miss the working copy of a gene due to LoF which can result in a range of phenotypes from no effect at all to severe phenotypes such as very low cholesterol or congenital insensitivity to pain. The extreme phenotypes and their underlying genetic causes represent experiments of nature. These extreme phenotypes can potentially uncover powerful new drug targets. Studying human gene knockouts gives scientists a means to identify potential new therapeutic targets and better understand safety concerns of therapies in development. Our study found many pLoF and a large majority of pLoF genes are not shared across all three South Asian medical cohorts and is consistent with the idea that SOI, BNG, and PKN are distinct population groups. pLoF mutations are widely studied because they often have phenotypic effects. The study looked at the impact of pLoF in three genes (PCSK9, ANGPTL3, CETP) and its impact on serum lipid levels (Figure 4). It was very interesting to observe that the individuals that carry pLoF variants in these genes have expected impact on LDL, triglyceride, and HDL levels in the body.

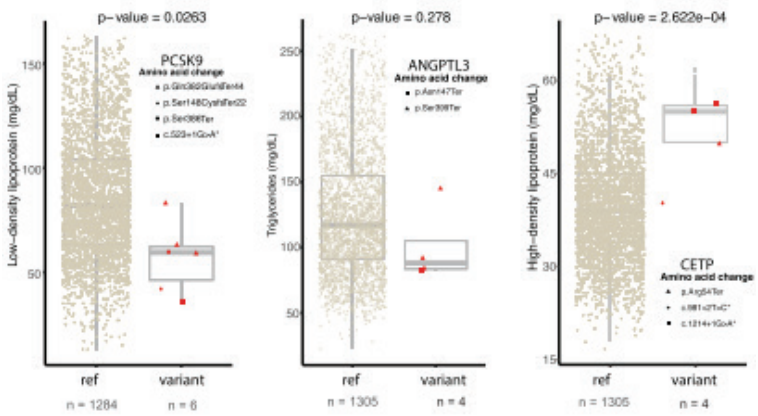


Figure 4. Effects of pLoF variants on blood lipid markers replicated the known biology: PCSK9 pLoFs associated with decreased LDL, ANGPTL3 pLoFs associated with decreased triglycerides, and CETP pLoF associated with increased HDL.

An important outcome of GenomeAsia study is the design of SARGAM (South Asian Research Genotyping Array for Medicine) array and imputation reference panel. Comparison of Global Screening Array (GSA, Illumina Inc) with South Asian population showed that ~22% of genotypes are never seen in the SAS individuals while 90% of functional variants found in SAS are not present in these arrays. To address the lower imputation performance and the lack of SAS genotype coverage, SARGAM array was designed. We compared the imputation accuracy of simulated SARGAM and GSA3 arrays. We found that both the SARGAM array and the GAsP2 reference panel contribute to higher imputation accuracy (Figure 5). Our study also showed that the improvement in genotyping and imputation can lead to a more accurate polygenic risk score (PRS). We imputed CAD patient dataset using the 1000 Genomes and GAsP2 reference panels and applied the ancestry-adjusted genome-wide PRS. The results showed a significant improvement in the predictive power of the PRS, with an improved AUC (0.638 for GAsP2 vs. 0.595 for 1000 Genomes).

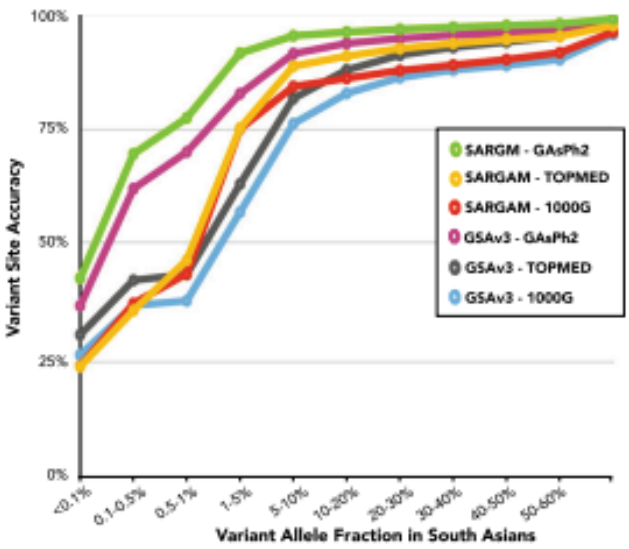
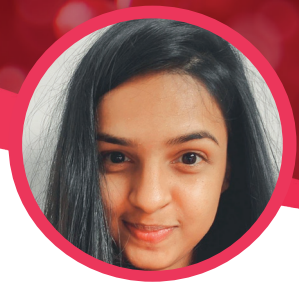


Figure 5. Accuracy of non-reference allele imputation expressed as the concordance rate and plotted versus South Asian minor allele frequency.

The South Asian populations have been largely unexplored. The GenomeAsia study is an attempt to reduce global genome disparity and open up opportunities to explore population and genetic diseases which were difficult to do earlier. With several population specific variants, the GenomeAsia database will provide a better resource to evaluate disease associations more accurately. A large amount of unique pLoF alleles with frequencies >0.1% found in South Asians provides an opportunity to drug companies to study human knockouts and correlate with extreme phenotype. The SARGAM genotyping array platform and GAsP2 imputation reference will allow the community to genotype the South Asian population more accurately than the existing commercial array and will lead to better discoveries through GWAS and other studies. The large and diverse dataset of GenomeAsia presents a powerful set of opportunities for genetic discovery which will further improve healthy life span around the globe.

NON-INVASIVE PRENATAL TESTING FOR RHD GENOTYPING

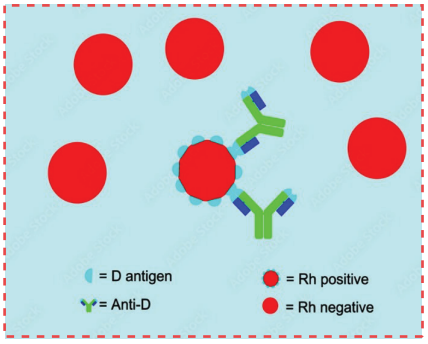


Shwetha
Senior Genome Analyst &
Genetic Counsellor

Hemolytic diseases in fetus and new-born (HDFN) can be caused due when the maternal alloantibodies are directed against the fetal red blood cells due to incompatibility of maternal-fetal blood group. One such situation arises due to incompatibility between a RhD negative pregnant mother and RhD positive fetus. Anti-D alloantibodies are produced in the mother that attacks the fetus red blood cells leading to severe fetal anemia that leads to fetal heart failure, fluid retention and swelling (hydrops), hyperbilirubinemia, kernicterus, and sometimes perinatal death.

This alloimmunization may increase with gestational age of the pregnancy, and most commonly occurs during delivery (15-50% of the cases). It may also occur during spontaneous and induced abortions, ectopic pregnancies, and certain obstetric procedures such as chorionic villus sampling, and amniocentesis. Routine antenatal anti-D immunoglobin is administered to all Rh-negative pregnant women who have given birth to Rh-positive baby or women having abortion/miscarriage or invasive procedure during pregnancy as a prophylactic measure. This reduced the risk of maternal immunization from 15% to 1-2%. Later antenatal prophylaxis was administered in two doses to all RhD negative pregnant women during pregnancy at the gestational age of 28-34 weeks along with a post-natal dose. This reduced the risk further from 1-2% to 0.4-0.1%.

The prevalence of RhD negative population can vary depending on the ethnicity. It is considered 1-3% for the Asian population and ~5% of the Indian population. However, not all Rh-negative pregnant woman will carry a Rh-positive child. Theoretically, 50% of the RhD negative pregnant women are expected to carry a RhD negative fetus if the father is a heterozygous carrier, however the empirical evidence may suggest different percentages depending on the ethnicity and race. Disha Parchure et *al* 2022 described in their study RhD negative fetus observed in 13.79% of the studied Indian population.



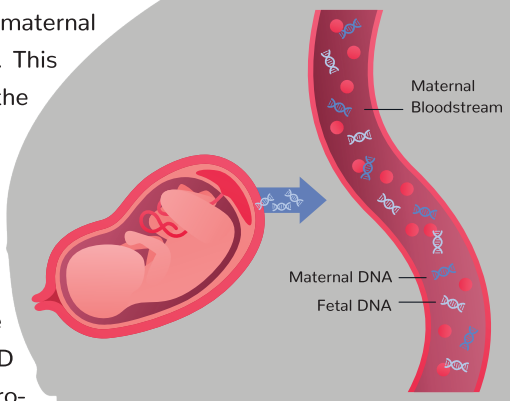
Anti-D immunoglobulin is a biological product which has limited availability. Thereby lack of donors and limited supply can pose a shortage. Anti-D immunoglobulin can also cause allergic reactions in some people. Apart from this, there is also a small risk of transfusion-transmitted infections while implementing anti-D immunoglobulin. Thus, an effective screening modality for detecting the status of RhD status in the fetus and implementing the anti-D only in RhD positive pregnancy will reduce such auxiliary risks and may aid in better pregnancy outcome.

At least 1% of the Rh-negative pregnant women may still develop anti-D after receiving the post-natal prophylaxis. The failure of prophylactic treatment can be due to late administration of the treatment, administration of anti-D before 28 weeks or the quality of anti-D used. Thus, the fetal screening of RhD may also aid to increase the preparedness of pregnancy care in case of history of alloimmunization in the pregnant woman. There can be a need for interventions that require tertiary healthcare centers for appropriate management.

There are limitations to existing tests of prenatal RhD testing due to its invasive nature or lesser sensitivity. Genetic tests can be more accurate in establishing the phenotypic status. To understand this, we must know the molecular basis of RhD antigen. The RhD antigen is a surface protein on red blood cells. The absence or presence of this antigen determines the blood group of the person. The molecular mechanism behind the phenotypic expression of the RhD protein is, however, more complex. There are two major genes involved – RHD and RHCE producing D antigen and C, c, E, and e antigen respectively. Other antigens or variations such as frameshift mutations, deletions, or missense mutations may be involved in molecular events leading to weak, partial, or complete absence of the RhD antigen. Thus, the determination of RhD gene status can help in determining the blood group as well in predicting the pregnancy outcome in prenatal scenarios.

NIPT can determine the genotype of the fetus from the circulating fetal DNA in the maternal blood. There are several techniques developed to determine the RhD status in fetus. This includes determining the presence of a combination of exons validated that predicts the phenotype of the fetus.

At MedGenome, we currently use a kit that uses a real time PCR technique with sequence specific primers (SSP) to detect the presence of three exons – Exon 3, 5, and 10 of the RHD gene along with an internal amplification control and fetal marker. The test is performed on human cell free fetal DNA isolated from maternal plasma. The primers are designed for the selective amplification of specific sequences of the RHD alleles and a fetal marker. The amplicons are detected with fluorescent dye-labelled hydrolysis probes. A fluorescence signal is thus generated and measured, and the data is analyzed to determine the RhD status in the fetus.



NON-INVASIVE PRENATAL TESTING (NIPT)

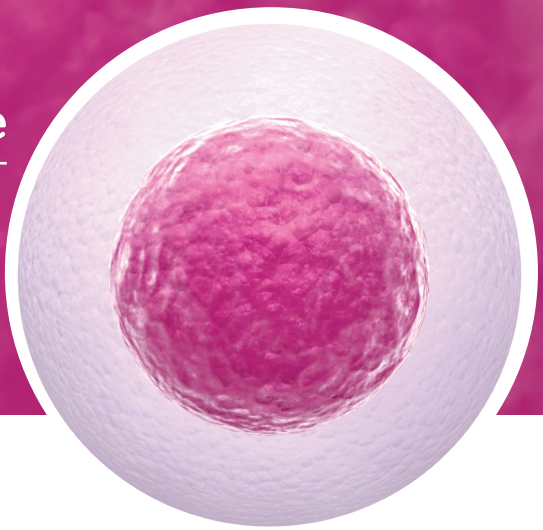
Since the launch of this test in August 2022, we have received over 100 samples. The expected outcome of the test includes 'Fetal RhD gene present' or 'Fetal RhD gene absent'. The presence of other antigens or genotypic variations due to RHCD gene expression can lead to inconclusive results in a small percentage of cases (~6% in Indian population according to Disha Parchure 2022 et al). Our laboratory experience over the past year shows fetal RhD gene was present in 88.29% of the samples, 9.01% showed absence of RhD gene and ~2% were reported as inconclusive.

With NIPT, this screening can be implemented as early as the first trimester or early second trimester of pregnancy, however, a repeat sampling may be requested in case of a RhD negative result before 20 weeks of gestation for confirmation. A non-invasive screening of RhD positive fetus will reduce the redundancy in administration of anti-D immunoglobulin and reduce its adverse effects. This will also ensure rapid implementation of anti-D immunoglobulin reducing the risk of alloimmunization and its related adverse outcomes early in pregnancy.

Sneak Peek into the World of Science

Single Cell Sequencing New Insights

By MedGenome Inc., Scientific Affairs



The advent of single cell sequencing technologies has enabled us to understand and study the complexities of biological systems at a finer resolution. Traditional bulk sequencing methods provide an average representation of gene expression across a population of cells, masking the inherent heterogeneity that exists within a tissue or organism. However, single cell sequencing allows us to capture the maximal transcript diversity in a given cell and allows for a multi-model analysis strategy to generate meaningful insights.

Single Cell Technologies

In recent years, technological advancements have improved the efficiency, throughput, and accuracy of single cell sequencing methods.

To achieve single cell resolution, various technologies have been developed, each with its own strengths and limitations. One commonly used approach is droplet-based sequencing, which encapsulates individual cells into tiny droplets along with a unique barcode. This barcode allows for the identification and quantification of transcripts originating from each cell. Droplet-based technologies have the advantage of high throughput, enabling the profiling of thousands to millions of cells in a single experiment. However, they may suffer from certain technical constraints, such as limited sensitivity and the inability to capture full-length transcripts.

Another approach is plate-based sequencing, where single cells are sorted into individual wells of a microplate. This method allows for more precise control over cell capture and is particularly useful when studying rare cell populations. Plate-based technologies also enable the isolation of intact cells for downstream functional assays, such as cell culture or transplantation experiments. However, they are generally lower throughput and require more extensive manual handling.

Regardless of the specific technology used, scRNA-seq data analysis is a critical step in extracting meaningful insights from the vast amount of information generated. Computational methods have been developed to handle the unique challenges posed by single cell data, such as high dimensionality, sparsity, and batch effects. These tools allow researchers to identify differentially expressed genes, perform clustering and trajectory analysis, and visualize the resulting data in a biologically interpretable manner.

Here we explore three broader areas of single cell research that helps us to discover novel insights:

Single Cell RNA Sequencing

One of the key advantages of scRNA-seq is its ability to capture the transcriptomes of individual cells, allowing for the identification of cell types, subpopulations, and rare cell states that may have been overlooked in bulk analyses. By profiling the gene expression patterns of thousands or even millions of single cells, researchers can gain unprecedented insight into the dynamic nature of cellular heterogeneity and its impact on development, disease progression, and therapeutic response.

Moreover, scRNA-seq has shed light on the existence of transitional cell states that occur during cellular differentiation processes. By capturing the gene expression profiles of cells at different time points, researchers can construct lineage trajectories and decipher the molecular events that drive cell fate decisions. This newfound knowledge has the potential to transform regenerative medicine, as it provides a blueprint for generating specific cell types in the laboratory for transplantation or disease modeling purposes. This has led to significant progress in various fields, such as cancer research, immunology, neuroscience, and developmental biology.

Single Cell Immuneprofiling

In recent years, single cell sequencing has also made significant contributions to the field of immunology. By profiling the transcriptomes of individual immune cells, researchers can gain a deeper understanding of the complex interactions between different cell types and their roles in immune responses. This approach, known as single cell immuneprofiling, has the potential to revolutionize the development of immunotherapies and personalized medicine.

For example, scRNA-seq has revealed the existence of rare subsets of immune cells that have distinct functional properties and play crucial roles in disease pathogenesis. By characterizing these rare cell types, researchers can identify novel therapeutic targets and develop more effective treatments. Additionally, single cell immuneprofiling has shed light on the mechanisms underlying immune evasion in cancer and autoimmune diseases, providing new avenues for therapeutic intervention.Furthermore, scRNA-seq has enabled the study of immune cell dynamics in response to infection or vaccination. By capturing the gene expression profiles of immune cells at different time points, researchers can decipher the molecular events that drive immune activation and memory formation. This knowledge can inform the development of vaccines and adjuvants that elicit robust and long-lasting immune responses.

Single Cell Epigenetics

In addition to gene expression analysis, single cell sequencing has also opened the door to studying the epigenetic landscape of individual cells. Epigenetic modifications, such as DNA methylation and histone modifications, play a crucial role in regulating gene expression and cellular identity. Traditional bulk sequencing methods provide an average measurement of these modifications, masking the cell-to-cell variability that exists within a population. However, with single cell epigenetics, researchers can now explore the dynamics of epigenetic regulation at a single cell resolution.

Single cell DNA methylation sequencing allows for the identification of cell-specific DNA methylation patterns, providing insights into cell lineage relationships and developmental processes. By comparing the methylomes of different cell types, researchers can unravel the epigenetic mechanisms that drive cell fate decisions and contribute to disease states.

Furthermore, single cell chromatin accessibility assays have enabled the characterization of cell-type-specific regulatory elements and the identification of transcription factor binding sites, shedding light on the transcriptional regulatory networks that underlie cellular diversity.

Novel techniques, such as spatial transcriptomics and multiomics approaches, are also being used to further enhance, gain holistic understanding of gene and protein expression in the tissue microenvironment. This opens the way to high resolution spatial analysis of cells and tissues without introducing biases in cell recovery.

Overall, single cell sequencing has provided a powerful toolkit for dissecting the complexities of biological systems at an unprecedented level of resolution. By profiling the transcriptomes, immune repertoires, and epigenomes of individual cells, researchers have gained new insights into the mechanisms that govern development, disease, and therapeutic response. As single cell technologies continue to evolve and improve, we can expect even greater discoveries and advancements in the field of genomics and beyond. Therefore, it's important to stay updated with the latest developments and breakthoroughs gained through single cell sequencing.

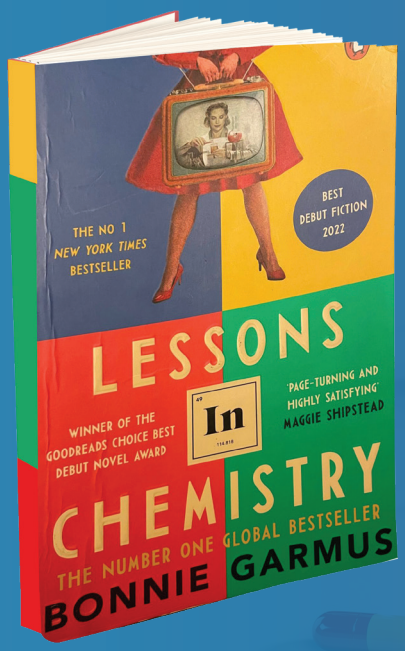
MedGenome's Powerful Single Cell Bioinformatics Analysis Pipeline

To support the single cell research, MedGenome has created highly specific single cell advanced analysis pipelines for different data modalities. Our pipelines can analyze all of 10X Genomics data outputs using well adopted tools in the industry. Our PhD level team can perform sample integration and comparisons, customized analysis, integration of ad hoc tools, project specific visualizations and final customized reporting to support your scientific publications.

- Single 3' and 5' Gene Expression
- Single Cell Multiome: ATAC + Gene Expression
- CITE-seq: Cell surface protein expression + Gene Expression
- Single cell immune profiling: VDJ expression for paired B-cell or T-cell receptors (possible coupling with GEX data)
- Visium spatial transcriptomics: GEX analysis on sectioned tissue layer

#Single Cell Sequencing, #Single Cell Technologies, #Single Cell RNA Sequencing, #scRNA-seq, #Single Cell Immuneprofiling, #Single Cell Epigenetics, #Single Cell Analysis

Book Review



Book

Lessons in Chemistry

Author - Bonnie Garmus

Book review by

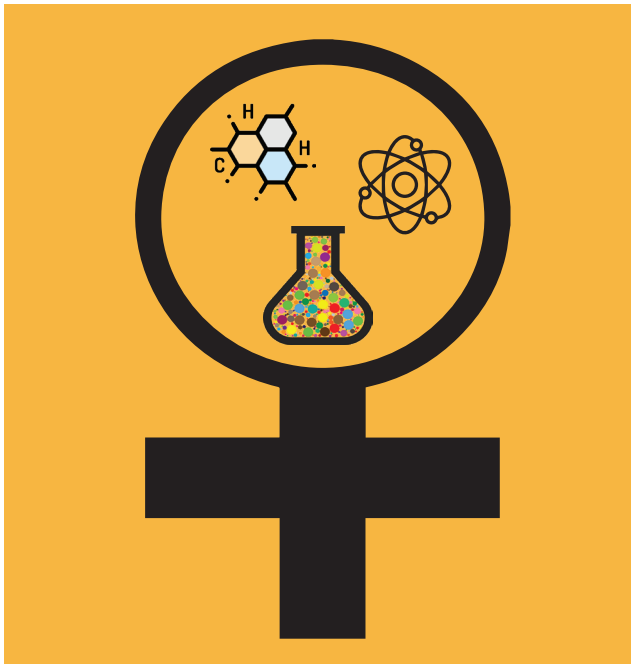
Gunisha Pasricha, PhD
Associate Director, Research Services and Infectious Diseases

Why I chose this book.

More recently, I choose a book based on the recommendation given by few set personalities whom I admire either for their work or the opinions they keep. This book was recommended by Nigella Lawson, the world-renowned celebrity chef and Twinkle Khanna, an author and columnist herself, who is known for being fearless, forthright and funny. Another obvious reason to choose the book was the reference of 'Chemistry/Science',- as if we scientist do not already have enough of science to deal with!!

Review

"Lessons in Chemistry" is a thought-provoking novel that seamlessly intertwines feminist themes with the world of science. This captivating work of fiction, authored by Bonnie Garmus, explores the struggles and triumphs of a brilliant but overlooked female scientist in the 1960s, highlighting the gender biases and systemic obstacles that women in STEM fields faced during that era. Bonnie Garmus is an American writer and 'Lessons in Chemistry' is her debut work.

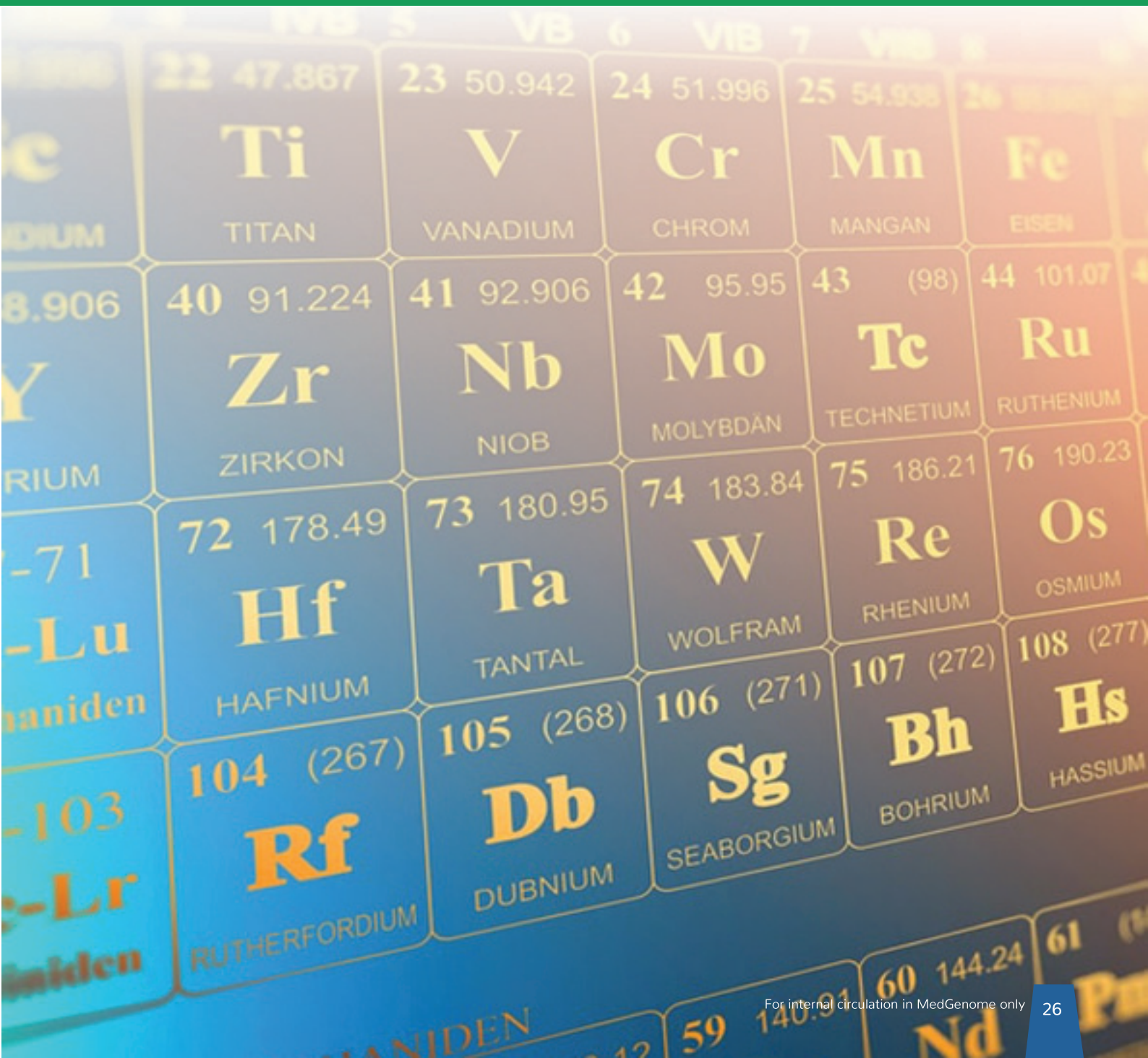


The protagonist, Elizabeth Zott, is a remarkable character who embodies the resilience and determination of countless women who dared to challenge societal norms and pursue their passion for science. Through her journey, the novel emphasizes the importance of recognizing and rectifying the historic lack of recognition for women's contributions to science. Elizabeth is a chemist who is a postgraduate from UCLA but was denied a PhD degree because of gender inequalities and biases. Her research interest is 'Abiogenesis' or the origin of life which is the natural process by which life has arisen from non-living matter, such as simple organic compounds. She is not your average woman; she is a gifted scientist, and she does not give up on her pursuit of science.

Chemist Elizabeth Zott works in all-male team at Hastings Research Institute, where her work is neither appreciated nor recognized by her supervisor. Another main character of the novel is Calvin Evans; the lonely, brilliant, Nobel–prize nominated scientist who falls in love with the protagonist. But like science, life is unpredictable, wherein Calvin dies in a freak accident. Elizabeth Zott finds herself not only a single mother, but the reluctant star of America's most beloved cooking show Supper at Six. Elizabeth's unusual approach to cooking ("combine one tablespoon acetic acid with a pinch of sodium chloride") proves revolutionary. She takes the TV gig to pay the bills after being fired from her research institute. Elizabeth initiates a quiet revolution, using her platform to speak directly to millions of housewives who follow her show religiously. But as her TV show becomes increasingly popular, not everyone is happy since she was not only teaching women to cook, but she was daring them to change the status quo and the norms. Her atheism cuts her a lot of flak too.

'Lessons in Chemistry' also has its flaws wherein the protagonist comes across as one-dimensional and lacking depth. Her struggles sometime felt forced, with less room for subtlety. Few characters were not developed well, while there is little too much mention of the brilliance and vocabulary of the dog named 'Six thirty' who apparently is the only character in the novel who is based on real being.

In conclusion, the book provides a poignant examination of the gender disparities in academia and research, shedding light on the injustices faced by female scientists. It underscores the importance of women's empowerment and equal opportunities in STEM fields, a message that remains relevant in today's world. Moreover, "Lessons in Chemistry" showcases the support and camaraderie Elizabeth finds among her female friends and illustrates Elizabeth's strength and grit not to be silenced or sidelined. The story is also about Elizabeth intelligent daughter who is in pursuit of her roots. Book is worth a read.

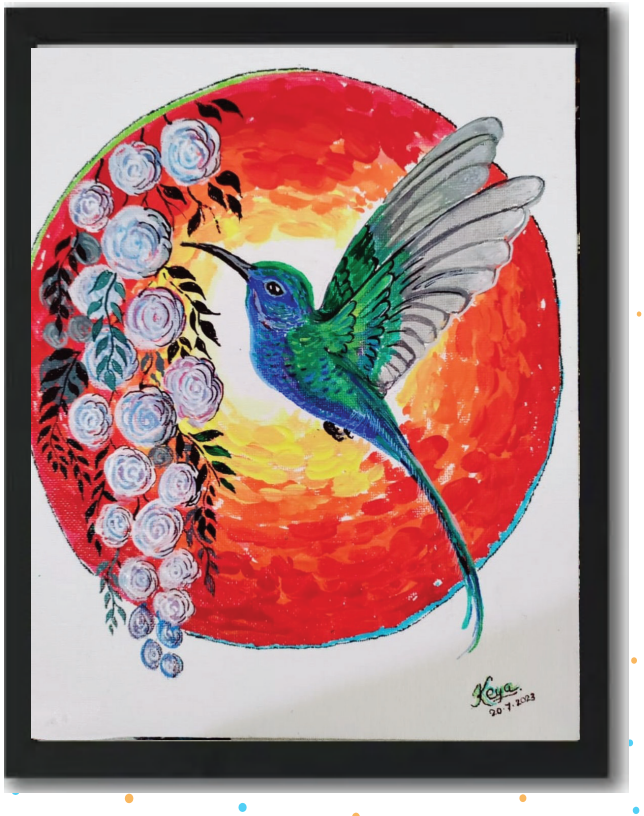


From our Colleagues

Art meets Science

The most beautiful thing we can experience is the mysterious. It is the source of all true art and science.
— Albert Einstein

By:
Keya Mukherjee
Lab Operations

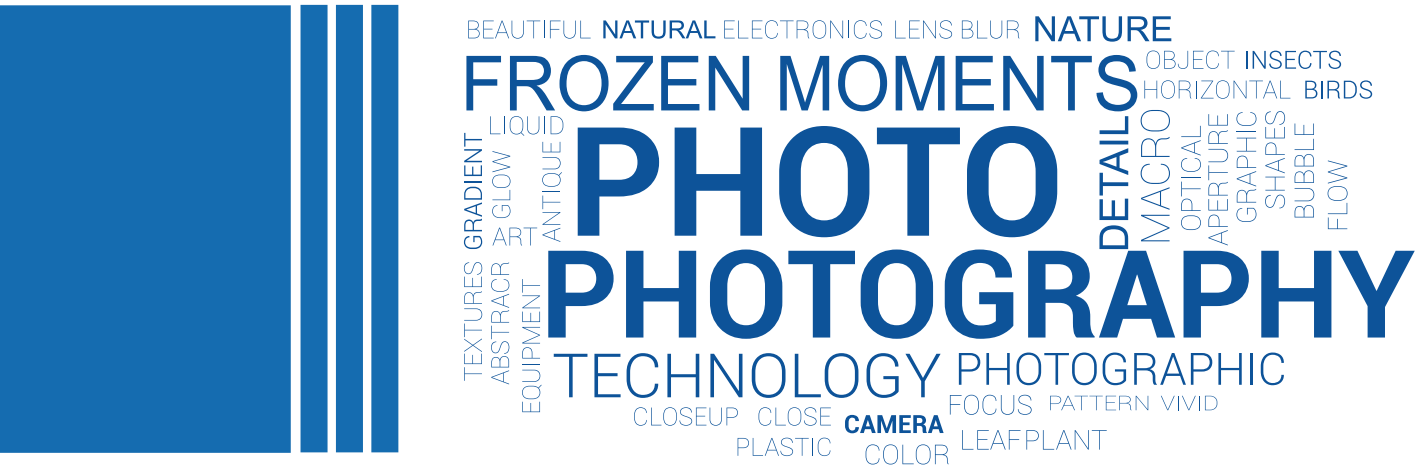


From our Colleagues

Our employee's little Picasso :)

By:
Neha S
Grade: IV
DNA of Aberami Seeneevasan, Lab Operations

From our Colleagues



Capturing the Heart of the Wild: A Journey through Lens

By
Dr Anjani Singh
Sr. Director – Lab Operation

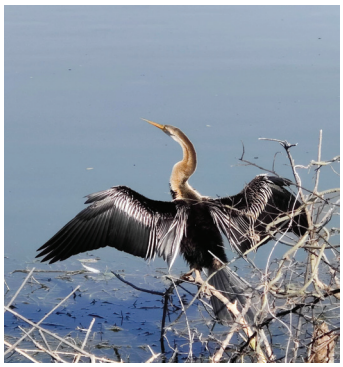
In the realm of photography, there exists a profound connection between the soul of an adventurer and the essence of the wild. It is a journey filled with love, passion, and an unquenchable thirst for the beauty that nature bestows upon us. As I embark on this incredible odyssey with my trusty phone and camera in hand, I am reminded of the magical bond that links my heart to the wild world, and how my lens serves as the translator of this extraordinary love story.

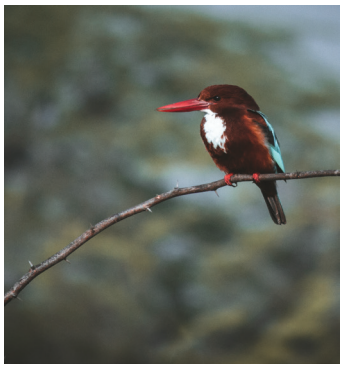
The allure of photography and nature first beckoned to me when I was barely a child, igniting a lifelong passion that has only grown stronger with the passing years. Each click of the shutter button is a testament to the bond I share with my subjects, whether they be the sprawling grass lands, forests and mountains of India, the dense rainforests of western ghats. Through my lens, I aim not only to capture the visage of these places but also the very spirit that resides within them.

My journeys, which spans counties and traverse diverse landscapes, are not mere sightseeing tours. They are expeditions born out of an innate wanderlust and a heartfelt devotion to the world's wildlife. It's as though I am tracing the footsteps of countless explorers who ventured into the unknown before me, leaving their own imprints on the history of our planet.

When I look at a lioness tenderly caring for her cubs, I am overcome with a profound sense of admiration for the intricacies of nature. The love and dedication she shows to her young ones mirror the kind of passion that fuels my own journey. There is a shared understanding between us, as if she knows that, like her, I too am bound by an unwavering devotion to my passion.

As I gaze upon a breathtaking sunset over the bay of Bengal, Arabian sea, I feel a deep connection with the earth beneath my feet. My love for travel, driven by a relentless curiosity, pushes me to explore the far reaches of our world. It is a love that knows no bounds and a passion that seeks to embrace every corner of this magnificent planet.





Each photograph that I present to the magazine carries with it a piece of my heart. It's not just a frozen moment in time; it is a story waiting to be told, a testament to the love I hold for the world and its inhabitants. Whether it's a playful otter by a tranquil stream or a regal eagle soaring through the mountains, these images are my voice, my way of sharing the love and passion that define my journey.

Photography, traveling, and wildlife are more than just my hobbies; they are the very fabric of my being. With every click of my phone's camera, I hope to convey the boundless beauty and the enchanting, untamed spirit of our planet. It is my hope that these images will inspire in others the same love, passion, and wanderlust that continue to drive me on this remarkable expedition through the heart of the wild.

Employee Connect

Our New-Joiners


A Elumalai


Aarushi Gajri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Avantika Srishti


Azmat Naseem


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Christine Elizabeth Cherry


Debadrita Ray


Debasish Kar


Deepak Kumar Sahu


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Nilesh Kumar Sharm


Pallabi Senapati


Pavithra

Phani Kumar Bathina

Prafulla Sharma

Pramod Kumar Pal

Rafiya Sultana R

Rahul

Ravi Kishor Vishwakarma

Rocky Singh Haojam

Roopakshi

Saikripa

Sakthi Vignesh M

Santhooshjayan Balamurugan

Saravanan Raj

Shalmali Sardesai

Shilpa Uday

Siddhesh Parag Karole

Sindhu D N

Souptik Bhattacharya

Sowjanya N

Srishtii S

Suman T V

Suryakant Dashrath Bangar

Swagath V

Vaibhav Golchha

Vishal Agarwal

Vishal

VORA DIVYA

Wajid Zahoor

Photo Feature

In the previous quarter, MedGenome's Engagement Squad organized and successfully carried out several enjoyable activities. They kicked off the season with vibrant Onam celebrations, complete with exquisite decorations and delicious snacks. The Independence Day festivities saw a thrilling pani-puri eating competition that left the office buzzing with excitement. Our dedicated colleagues and offices were beautifully adorned, and everyone dressed their best to partake in these fantastic events.

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