MEDGENOME

Vol 03 | Oct 2017
www.medgenome.com

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Internal Quarterly Newsletter

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Management speaks

Dr. V.L.Ramprasad
Chief Operating Officer

Dear Colleagues,

Deepavali Greetings and best wishes to you and your near and dear.

It has been almost 4 momentous years since we established MedGenome. Our Company's growth will remain as one of the best success stories in Indian Genomics Industry. I still remember having a candid discussion over a tea with Sam in a restaurant in the suburbs of Chennai six years back about his plans/ vision for SciGenom and MedGenome which inspired me to jump on the bandwagon in the end of 2012. Rest is history...

I am grateful to my colleagues and team mates who worked with me as a team from the early days of the company. While we take pride in the success, as everyone knows there is no point in pondering about the past, we all look forward for a better future. In this context, I have 3 points to share:

Growth Opportunity: We are placed in a much better position than we were few years back in terms of financial resources, intellectual capabilities and human resources. Let us use these strengths to steer the company to the next level while consolidating and continuing our market leadership. We all need to have a belief that the company's growth also means individual employee's growth and they both go hand in hand. Let us grab this unique opportunity, build the team, increase the momentum of growth and I am sure we all will be part of the next growth story.

Make things happen: As the popular saying goes: There are people who make things happen, there are people who watch things happen, and there are people who wonder what happened. To be successful, you need to be a person who makes things happen.

Quality commitment: We are in the field of diagnostic genetic testing which touches patient lives whether it is a new born or a cancer patient. Every assay we do, analysis we perform and report we generate will have an implication in the disease treatment and management. So let us keep this in mind in every bit of work we do and commit for the highest quality of work as per our quality policy.

Wishing the best of things to come. Cheers - Ram

Highlights

Most talked about

MedGenome in news

1

1 lakh Asians to be genetically screened for clinical diseases

OUR BUREAU

Chennai, July 18

Bengaluru-based Medgenome Labs Pvt Ltd, a genomics-based research and diagnostics firm, will undertake diagnostics of clinical diseases of close to one lakh South and South-east Asians in association with South Korean biotech firm Macrogen Inc and Singapore-based Nanyang Technological University.

The company has already sequenced the genomes of 2,500 people from India, Singapore, South Korea, Indonesia, Vietnam and Laos.

Focus on specifics

Speaking to *BusinessLine* at the launch of the second phase of the research project on cardiovascular diseases in partnership with Madras Medical Mission hospital here, VL Ramprasad, Chief Operating Officer, Medgenome, said the process is on to narrow down the area of focus to select medical conditions such as diabetes, cancer, select cardiovascular diseases and rare genetic diseases.

The objective of the project is build a database that could be cessed by academics, hospitals, ph maceuticals and government age cies. Ramprasad said the databa will help spread awareness about netic conditions, give insights a aid doctors to design precise cou of treatment and intervene early the data collected will be diverse. will also aid in policy-making, added.

Investment

Each of the three partners has inv ted $10 million for the project th will take another 4-5 years to co plete.

Talking about the project wi MMM, Ramprasad said the compa will be the technological partner the project on cardiac diseases su as myocardial infarction, hyperte sion and sudden cardiac deaths, collaboration with Glasgow Univ sity.

The project will have 600 patie and MedGenome is spending clo to $300 per patient.

2

MedGenome Labs Gets ₹192 crore in Series-C Round

THE NEXT CHAPTER

Varsha.Bansal
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Hyderabad: Genomics research and diagnostics startup MedGenome Labs has secured $30 million (₹192 crore) in series-C funds from a clutch of investors led by Sequoia India

provides genetic tests for a range of ailments like cancer, metabolic diseases, eye diseases, neurological and prenatal disorders. The company, which is present in both India and the US, claims to operate the largest next-generation sequencing (NGS) lab in Southeast Asia, and a CLIA-certified, CAP-accredited sequencing

3

MMM, MedGenome join hands, open lab

❑ *To take up research on cardiac diseases* ❑ *'Cardio-Vascular Diseases deaths in India accounts for 25% of total population'*

NT Bureau

Chennai, July 18:

The Madras Medical Mission (MMM) and MedGenome, a genomics based diagnostics and research company, have collaborated for research on cardiac diseases and inaugurated the second phase of the state-of-the-art Genomic laboratory.

Addressing mediapersons here on Monday, MMM director, Cardiology, Dr Mullasari Ajit S said, 'We are happy to associate with Glasgow University to realise our mission of providing world-class healthcare and engaging state-of-the-art technologies. We are at an advantage to have the most updated NGS tech-

Madras Medical Mission director, Cardiology, Dr Mullasari Ajit, Glasgow University, Cardiology and Imaging professor Dr Colin Berry and MedGenome COO Dr V L Ramprasad addressing the media at MMM campus, Mugappair in Chennai on Monday.

nologies required for this research, in vicinity through MedGenome. The ... e are keen to bring the ... evidence based ... research ... here in Ind ... ogy direct ... 'We Med ... collaborati ... diac disea ... Artery Dis ... cardial in ... pulmonary ... cardiomy ... cardiac de ... year, we b ... art genon ... serve for a

research purposes at the hospital premises. In the second phase II, we are taking this association one ... notch up by undertaking research

determinants, and the complex dynamics underlying their interaction including the genetic factors.' The research and diagnostic lab

4

20kg at 1: Family genes to blame

Shimona Kanwar
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Chandigarh: The genetic tests report of **Chahat**, a one-year-old baby girl from Amritsar weighing 20 kg, has found the cause of her early onset of obesity to a rare mutation in the leptin gene. This gene is involved in the regulation of body weight. This implies that this has been passed on to her from the family. Also, the treatment is genetic therapy which is not easily available in the country. Chahat turned one year old on Monday.

"The other family members need to be tested for the mutation," said a doctor in PGI, where the baby is undergoing treatment. Although the baby's parents are lean, her 14-year-old uncle is obese. "We suspect that he also has this gene mutation and the same has been

▶Continued on P 4

What is leptin

The LEP gene provides instructions for making a hormone called leptin. Involved in regulation of body weight. Normally, the body's fat cells release leptin in proportion to their size. As fat accumulates in cells, more leptin is produced. This rise in leptin indicates that fat stores are increasing. Mutations in this gene cause severe obesity.

inherited by her. As the obesity is due to genetic mutation, there is hardly any treatment," said a senior doctor at the institute.

The blood sample of the baby was sent last month at Medgenome Laboratory at Bengaluru and CSIR Institute of Genomics and Integrative Biology (IGIB), New Delhi. The Bengaluru report has found leptin gene mutation.

PGI to take sample of baby's uncle

▶Continued from P 1

Presently, Chahat is on a diet as recommended by PGI doctors. "We have been called to the hospital next week. The sample of my brother will ... taken. Chahat is not ... since the pa... cess," said ... ther Chahat's ... operate and ... more than ... month. The ta... with normal w... er, she started ga... after she turned ... old.

The Punjab and ... high court had take... to notice of this ... news reports stated ... was allegedly not ... ing as far as her ... was concerned. Ben... court had sought a re... the Union ministry ... and family welfare in... tion with her treatm... serving it is the prime ... sibility of the govern... provide medical treatm... citizens so that no one ... Chahat remains untreated

1 **Story on Genome Asia in The Hindu Business Line**
http://www.thehindubusinessline.com/news/1-lakh-asians-to-be-genetically/article9776023.ece

2 **Funding news in The Economic Times**
http://economictimes.indiatimes.com/small-biz/money/medgenome-labs-gets-rs-192-crore-in-series-c-round/articleshow/60273642.cms

3 **Announcement of Phase 2 collaboration with MMM hospital, Chennai**
https://diagnostics.medgenome.com/pdf/2017/19thNewsToday2017.pdf

4 **20kg at 1:Family genes to blame**
https://diagnostics.medgenome.com/pdf/2017/19thNewsToday2017.pdf

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• SCIENCE

It's all in the genes

Bengaluru-based MedGenome is spearheading the genetic testing field in India.

By Aishaar Khan

IT WAS DURING A workshop at the turn of the previous decade, with Professor Jeremy Lipschultz at the University of Nebraska in Omaha, that I first chanced upon outfits like 23AndMe. Among other services, these personal genomics and biotechnology companies allow you to take an ancestry test — which essentially lets you find out what per cent of your DNA comes from populations around the world, if you have relatives across continents, and also how much of your ancestry can be traced down to the Neanderthal species that mated with Homo Sapiens around 50,000 years ago.

Though obviously excited by this information, I unfortunately didn't have the time (or money — it cost $999 back then) in America to take up the test, and no such service existed in India for the longest time. Thus my eyes lit up when I learned about MedGenome, which set up shop in India not too long ago. Unfortunately, they don't offer ancestry tracing in the country at the moment, as I was informed when I contacted the genome testing company.

But though the continuously rolling wheel of the Bengaluru-based firm might currently not comprise that cool cog, it certainly does impress with the critical and significant ones, which lay the foundation for genome research and diagnostics for ailments like cancer, metabolic diseases, neurological disorders, prenatal disorders and eye diseases. My of parents-to-be and their coming generations.

What exactly does MedGenome offer? The company's chief operations officer, Dr VL Ramprasad, said: "Our range of genetic testing across various disease areas provides useful insights to clinicians for better diagnosis, treatment and management of diseases. It presents Next-Generation Sequencing based genomic solutions in cancer immunotherapy. Its unique access to genomics data with clinical and phenotypic data provides insights into

complex diseases at the genetic and at molecular level, and facilitates research in personalised health care."

How are the masses to make the most of this? "The genetic testing is suggested by a doctor if either he or the patient feels the need for it, on the basis of a lot of factors, like family history, hospitals for diagnostics and 10-plus research collaborators across the country, we get samples from all over. And based on the patient location, we suggest to them the nearest sample collection centre," said Dr Ram.

A total of 400 tests are presently offered by MedGenome, covering various disease areas like neurology, oncology, cardiology, autoimmune, rare inherited diseases, endocrinology, haematology, ENT, metabolic disorders, prenatal and population genomics. But what catches the eye is the exclusive set of non-invasive prenatal tests (NIPT), which were introduced by the company to India for the first time, in 2015.

NIPT examines foetal DNA in the mother's blood, to assess whether a developing baby is at high risk for assess and treat various forms of cancer. Another such examination, the Claria Carrier Screening Test, provides vital information of "Carrier" status to couples, and their risks of passing down recessive diseases (a condition where a person has two copies of an abnormal gene) to their child. In addition, the Sequoia Capital-backed firm also offers PGS (pre-implantation genetic screening) to check for chromosomal disorders in an IVF embryo, by checking the number of chromosomes.

"With awareness increasing and more people opting for such tests, the costs are expected to come down further. This will help even the marginalised sections of society to avail of such tests. Currently, the cost is such that not everyone can opt for it, as insurance doesn't cover them. With the government's help, it can be covered under insurance and certain tests can be made compulsory, which will benefit all sections," Dr Ram added.

In current times, when medical science has progressed by leaps and bounds, genomic analysis could add another dimension to research and prevention of critical ailments. Prenatal testing has advanced to a stage where it's possible to differentiate and check the cell-free DNA of a foetus from the mother's blood. Similarly, by testing for circulating tumor DNA in the blood stream of cancer patients, we can better understand the present status, expected prognosis and even the response to different forms of IVFs), which can help a couple have a healthy baby.

In this air of excitement, however, Dr Ram cautions that through genetic testing, some might be trying to infer too much from genetic data, and extrapolating correlation to causation. "There may be certain gene variants that may confer a higher risk, but not necessarily enough to cause a disorder. This is especially true for polygenic disorders, such as diabetes and hypertension. And though numerous strides have been taken in identifying the underlying genes for such traits, currently a one-is-to-one correlation between the gene and the disorder is not possible," he concluded, but

Dr VL Ramprasad

ASIAN DATABASE

MedGenome has joined hands with South Korean biotech firm Macrogen Inc and Singapore-based Nanyang Technological University (NTU) to sequence the whole genome of 1,00,000 people in Asia. The within India highlights the genetic heterogeneity of the Indian population and the enormous potential for leveraging this diversity for genetic research.

LIVES MATTER

CASE STUDY 1

Just two months old, a male baby was brought to a hospital in Guntur, Andhra Pradesh, with complaints of a coloboma in the right upper eyelid, ocular hypertelorism, a bifid nose, a small nasal alar, omphalocele, renal agenesis, anorectal anomalies and bilateral undescended testis. In order to investigate the aetiology of this disorder and thereby console the distraught consanguineously married parents with at least an answer, genetic testing at MedGenome was advised. Testing confirmed a genetic diagnosis of Manilstia-ciliis-tricho-anal (MOTA) syndrome, an extremely rare disorder that is predominantly confined to

CASE STUDY 2

A seven-year old girl presented with severe fatigue and malaise and was referred to a leading cancer centre in Kolkata. Clinicians, after examinations, suspected the disease to be Myelodysplastic Syndrome (MDS) (myelo- = bone marrow; dysplastic = abnormality), which is a result of bone marrow failure to produce healthy blood cells. At MedGenome, further testing led doctors to pinpoint the exact disease - Diamond-

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For Indian Doctors, It's Written in the Genes not Stars

Doctors are now asking patients to take genetic tests to identify 'faulty' genes which helps them diagnose and treat genetic diseases better

Nilesh.Christopher
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Bengaluru: When five-year-old Chathura Corea from Sri Lanka landed in India for cancer treatment, his physician Sachin Jadhav got a genetic test done on his blood sample before starting any kind of treatment. Corea had been diagnosed with a very rare form of blood cancer called Juvenile Myelomonocytic Leukaemia (JMML). After a genetic test, Jadhav concluded that a "simple chemotherapy would not suffice and the kid needs a bone-marrow transplant".

"The (genetic) test helped me identify what line of treatment to give providing maximising the chance of cure and in planning treatment better," says Jadhav, who has partnered with Bengaluru-based MedGenome Labs which provides genetic tests for a range of ailments like cancer, metabolic diseases, eye diseases, neurological and prenatal disorders.

Increasingly, doctors like Jadhav are asking patients to take genetic tests to identify 'faulty' genes in treating genetic diseases better.

MedGenome has seen the number of samples triple for genetic tests in the last one year.

"We now get about 600-800 samples a month," said VL Ramprasad, COO of MedGenome Labs. "The uptake is primarily due to increased awareness among clinicians in India who see a scope for better results and efficient treatment," he said.

Another lab, Stand Life Sciences has also seen a similar spike in the number of samples received. "Strand has seen a 250% growth in the number of samples last year, and we have done about 5,000 samples this year," said cofounder Vijay Chandru. The science behind these tests is straight forward: everything about us — the length of our hair, the colour of our eyes, the complexion of our skin is coded onto the DNA — which also has hidden hints of the possible disease one might get. Scientists analyse the genetic code and figure out what mutation causes a specific disease. As the awareness among doctors increases, revenues have been surging. MedGenome revenues have doubled every year. The lab's revenues have grown from $4 million in 2015 to $16.5 million in 2017.

"At this point, we are just scratching the surface," says Chandru of Strand life sciences, adding, "The addressable market is 500,000 people according to India Council of Medical Research (ICMR) report. Say, 20% people can afford the tests... 100,000 people could be tested. Right now, only 5,000 people are being tested."

These genetic tests cost about ₹30,000 - 40,000 for a single test. "Only 2% of Indian population is covered by insurance. Hence, affordability is another bottleneck in the widespread adoption of genetic tests," said Chirantan Bose, VP of Clinical services at Medgenome.

Aside from providing insights to clinicians for better diagnosis, the milestone for genetic tests is 'targeted therapy' for specific diseases. For instance, precision medicine in the treatment of cancer when the drug hits only the cancer cells and not the entire body (like in chemotherapy). Genetic testing paves way for precision medicine. Consumers too want to dig into their genes to know more about their family history, lifestyle tendencies and information about their ancestry. Mapmygenome provides a report on 100 different conditions including inherited and acquired genetic health risks. The firm's product, Genomepatri, has found massive traction and the number of samples "have tripled over the samples we received last year," says Anu Acharya, co-founder of Mapmygenome, adding that demand was not just coming from metros but even from tier-II towns across India.

FIGHTING FIT

SANDOR BORTNYIK, *The Twentieth Century*

₹30,000 - 40,000
Cost of a single genetic test

- As the awareness of genetic testing increases among doctors, revenues have been surging

The uptake is primarily due to increased awareness among clinicians in India who see a scope for better results and efficient treatment,
VL RAMPRASAD,
COO, MedGenome Labs

MedGenome

- Sample numbers for genetic tests have tripled in the last one year
- Revenues have doubled every year

Revenue

2015 — $4 million

2017 — $16.5 million

5 **MedGenome story in Man's world magazine**
https://www.mansworldindia.com/features/pre-natal-tests-for-cancer-and-more-bengaluru-based-medgenome-spearheading-genome-testing-in-india/

6 **Industry story on genetic testing in India in The Economic Times**
https://economictimes.indiatimes.com/industry/healthcare/biotech/healthcare/for-indian-doctors-its-written-in-the-genes-not-stars/articleshow/59857052.cms

CAP Audit

We recently had CAP audit in our lab, can you please share the experience with us?

It has been an enriching and a great learning experience I would say not just for the technical teams but also for the entire organization. Infact, this experience has reiterated that Company-wide quality initiatives and compliance is of paramount importance to ensure seamless precise quality diagnostic testing.

The audit was rigorous which involved lab processes, documentation, HR/Admin, IT/Bioinformatics, Logistics and other aspects that could affect patient safety. The auditors were very experienced and constructively critical while citing the deficiencies. Though our team was well prepared, the audit made us learn some new nuances of documentation, test validations etc. which moving forward will help us in subsequent audits.

The audit concluded successfully with very few deficiencies cited and the team is working to close these in 30 days.

What are the key learnings from the audit? What is the scope of improvement for us?

Some of the key aspects that we learnt were:

It's not just enough to implement a quality plan, but equally important is to document the processes, policies and SOPs.

We got to know some new aspects of test validations and the importance of quality processes in diagnostics testing. The audit also made us aware that Quality program is a continuous process and I hope we improve day by day.

How do we prepare ourselves for the next audit?

We are planning to implement and be compliant to the quality plan and program (Processes, policies, SOPs, Procedures) on a day-to-day basis. A separate quality team led by Dr. Venkataswamy will set up a daily, weekly, monthly and quarterly quality program and plan for all departments to ensure that every employee is aware of the program and is aligned to the quality policy/plan and processes that will help MedGenome deliver highest possible quality Diagnostics testing and aid patients/clinicians.

NGBT

The 7th "NextGen Genomics, Biology, Bioinformatics and Technologies (NGBT)"

The NGBT conference was held successfully by SciGenom Research Foundation (SGRF) at Bhubaneswar from Oct 2nd -4th 2017. The Conference featured exciting developments in genomics technologies and their applications in life sciences including human, plant and animal biology, drug discovery, cancer immunology, genome engineering using CRISPR/CAS9, medical applications and personalized therapy. Featuring accomplished national and international speakers, thinkers and thought leaders that shape the course of scientific discovery, the Conference saw about 80 talks and 13 keynote lectures delivered. Speakers and delegates representing leading universities and research institutions from India and abroad were at the meeting.

At the conference, SGRF presented the 2017 Lifetime Achievement Award to Dr Partha Majumder, NIBMG, Kalyani, India. Dr. K. Thangaraj, CCMB, Hyderabad was awarded the 2017 SGRF Excellence in Science Award. They both have done pioneering work in the field of human genomics. SGRF awarded scholarships and travel awards to 140 students to enable their participation at the meeting. SGRF also announced the winners of its 2017 Genomics Project Grants at the meeting.

Around 100 employees from MedGenome attended the NGBT conference. We had close to 25 poster presentations and 5 session speakers.

MedGenome connect

CLARIA

FETALMED conference, 1st-3rd September in Leela Ambience

Between July and September 2017, we conducted 7 CMEs across 5 cities in India. These CMEs covered latest introductions in prenatal testing offered by MedGenome. How these offerings can help their patients to plan their pregnancy in a hassle freeway.

In all the CMEs latest update like microdeletions and Pre-implantation genetic testing for IVF pregnancies were introduced by MedGenome Speakers-Dr Gaurav Verma, Dr Sam Balu and Dr Priya Kadam.

To aggressively launch microdeletions, speaker session from International speaker Dr Herman L Hedriana was conducted in Rainbow hospital in the month of August which was attended by 23 key FMS and Obstetricians/Gynecologists. During the talk, he presented several cases through which early detection of most prevalent microdeletion 22q11.2 is established across all ages of pregnancies. We also participated in national level conference i.e. FETALMED through stall and speaker session. Overall MedGenome presence was highly visible through standees, product brochures and Sales & Marketing team.

ACTIA


Nephrogenetic Meet , MedGenome, Bangalore

Between July and September this year, we conducted 11 CMEs and relationship meetings in 8 cities across India. These events covered various aspects of Neuro and Nephrogenetics to promote our services among KOLs (Key Opinion Leaders) and clinicians.

The aim was to reach out to nearly 700 clinicians with special focus on Genetic Renal, Neurological Disorders and how genomics have helped patients with these disorders. Dr. Sheetal Sharda and Dr. Gaurav Verma were the speakers for these CMEs.

Taking a leap forward in Nephrogenetics, a Focus Group Meeting of 12 of the eminent Pediatric Nephrologists also was organized on 21st July at the Bangalore office. Many important points like current scenario of nephrogenetic disorders in India, its prevalence and awareness, and also the key requirements of clinicians with respect to genetic testing and current offering gaps were discussed. The session was moderated by Dr. Anil Vasudevan, one of the noted names in Pediatric Nephrology. This meet also saw active involvement of our MedGenome colleagues, i.e. Mr. Sanjay Sharma, Mr. Anil KC, Dr. Prasanna, Dr. Sakthivel, Dr. Sheetal, Mr. Saurabh Budhiraja, Mr. Jayan Kondan, Ms. Krithika and Mr. Jason D'Silva. With more such events queued up for the next quarter, visibility of MedGenome, and connect with key clinicians is expected to gain lot of impetus.

PRIMA

The Team Oncology conducted approximately 12 RTM's and 4 major CME events in the field of Oncology, the topics covered here were a mix of Haematological malignancies, Solid tumours with a special focus on Lung cancer, Colorectal Cancer and Breast Cancer. We also participated in 2 major AIIMS Breast Cancer Conference and Milan conference.

Making a difference

First case report of Manitoba Oculotrichoanal Syndrome

Just two months old, a male baby was brought to a Hospital in Guntur, Andhra Pradesh with complaints of a coloboma in the right upper eyelid, ocular hypertelorism, a bifid nose, a small nasal ala, omphalocele, renal agenesis, anorectal anomalies and bilateral undescended testis. In order to investigate the aetiology of this disorder and thereby console the distraught consanguineously married parents with at least an answer, genetic testing was advised. In lieu of this recommendation, the samples of the proband, his parents and his unaffected elder sister were sent to MedGenome in the hope that whole exome sequencing would shed some light onto the aetiology of this debilitating genetic disorder.

Tandem genetic analysis of the samples identified a homozygous nonsense FREM1 mutation in the proband. While this mutation was not present in the unaffected sister, the parents were found to be herterozygous carriers of the mutation. This was consistent with an expected autosomal recessive mode of inheritance and affirmed a genetic diagnosis of Manitoba-oculo-tricho-anal (MOTA) syndrome, an extremely rare disorder that is predominantly confined to the Oji–cree community of northern Manitoba, Canada.

This is the first case of MOTA syndrome to be reported from India. The report of this extremely rare disorder within India highlights the genetic heterogeneity of the Indian population and the enormous potential for leveraging this diversity for genetic research. Furthermore, the identification of bilateral undescended testis adds to the variable clinical spectrum of the disorder and highlights the potential of genetic testing within the clinical diagnostic framework.

From our US office

MedGenome US lab is expanding its operational capacity and we have recently installed Agilent Bravo Automation System and a new HiSeq 2500 for increased throughput. We are also building advanced capacity for generating cell-lines which has numerous applications in addressing research questions pertaining to cancer and other disease areas.

This quarter, we have been able to successfully engage some prominent research scientists with the Case Western University and it is hoped that we are in for a long-term fruitful collaboration in the coming days. Recently, we invited Dr. Vishwajit Nimgaonkar, Professor of Psychiatry and Human Genetics at the University of Pittsburgh for a symposium on "NeuroGenomics" at out Foster City Lab. He spoke extensively on "Gene mapping work among inbred populations".

ASHG2017
ORLANDO • OCTOBER 17-21, 2017
SHARING DISCOVERIES. SHAPING OUR FUTURE.

We have been active at the key conferences and are attending the upcoming 67th Annual Meeting of the American Society of Human Genetics being held at Orange County Convention Centre South Building in Orlando, Florida, from Tuesday, October 17 through Saturday, October 21, 2017. The ASHG Annual Meeting is the largest human genetics meeting and exposition in the world. This year's meeting is expected to attract over 6,500 scientific attendees, plus over 200 exhibiting companies.

We also attended the 53rd EASD Annual Meeting which was held in Lisbon where we have been successful in showcasing one of our lead product DIABETOME. Each year more than 15,000 delegates from over 130 countries attend this event.

EASD 2017
Lisbon – Portugal
53rd Annual Meeting of the European Association for the Study of Diabetes
11 - 15 September 2017

Sneak peek into the world of science

Healthy lifestyle can offset one's risk of heart attack

by SANGHAMITRA MISHRA, Senior Scientist

Coronary artery disease (CAD) is a condition where the blood vessel supplying blood to the heart is blocked due to a waxy deposit called 'plaque'. When the plaque completely blocks the blood vessel, a part of heart muscle dies due to lack of blood supply, commonly known as 'heart attack'.

Sometimes plaque in an artery can rupture and block the artery, leading to either a heart attack or stroke. A significant number of CAD patients have a case of Young Onset Myocardial Infarction (YOMI), who are below 40 years of age and experienced a heart attack due to a block in the arteries. Globally, CAD, along with stroke, is the leading cause of death and is predicted to remain so for the next 20 years.

Among Indians, there has been a recent rise of premature onset of myocardial infarction/ heart attack. Epidemiological studies from various parts of India indicate a prevalence of CAD to be between 7% and 13% in urban and 2% and 7% in rural populations. South Asian population is the only population in world where cardiovascular mortality is on the rise, while in the rest of the world it is declining.

We have the fatal combination of high risk of acquiring the disease and having a minimally accessible medical management. Lack of awareness only adds up the odds. Rapid urbanisation has led to stress and flawed lifestyle in individual like high fat diet, lack of exercise and poor daily routines.

We are partly blessed to be in the medical generation where cardiac disease management is available with new generation drugs and interventions. Affordability is still a challenge to many in spite of recent steps such recently subsidised stent prices. The other aspect of this disease is that prevention does not get adequate attention in case of CAD. It is only until an event occurs that we start worrying about the organ which works round the clock for us.

Genetic factors

Coronary artery disease results from a combination of multiple factors, partly genetic and partly lifestyle. Some people are more susceptible to get CAD due to their genetic makeup. Multiple genetic factors and a combination of these with the environmental factors lead to the disease condition. Discovery of genetic factors has helped improve management, especially early intervention in these patients. There has been a recent interest in using this genetic information as combinatorial risk assessment to predict a person's risk to develop CAD by scoring the disease causing and beneficial mutations. There is also evidence that individuals with high genetic risk can reduce their risk by adequately managing their lifestyle. If a person is aware that they may be more likely to get the disease compared to others in their age, they can be counselled to be careful about their lifestyle. This may prevent or delay any untoward coronary event.

Latest development

Also new mutations are being identified as potential therapeutic targets and existing medications are being validated for safe use, without increasing cardiovascular risk. Recently, a variant in the *GLP1R* gene encoding the glucagon-like peptide-1 receptor was reported to be associated with lower fasting glucose levels, lower T2D susceptibility, and with reduced risk for CAD. This information is useful in the light that agonists for this gene can be used for treating diabetes without increasing cardiac risk.

A cluster of lifestyle factors such as increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels also collectively known as 'Metabolic Syndrome' increases the risk of cardiovascular hazard. One of the causes of CAD is familial hypercholestremia, a condition where individuals have elevated LDL (low density lipoprotein) levels due to mutations in genes regulating lipid (fat) metabolism. All these are clinically manageable conditions and an appropriate predictive diagnosis can direct the patient to the clinic in time.

Plaque deposition in the arteries starts early at about the second decade of our lives, depending on one's family history and habits. Both the genetic and lifestyle factors can independently predict likelihood of a person developing the condition. A two pronged approach with knowledge about the risk and timely lifestyle and medical management can help avoid an unwanted trip to the cardiac surgeon.

Clinical Bioinformatics for diagnostics of hereditary diseases

by Vivek Gopalan, PhD, Senior Bioinformatics Scientist

Introduction

MedGenome offers NGS-based clinical tests for a spectrum of hereditary disease categories such as cardiac diseases, cancer, immune disorders, metabolic disorders, neurological and neuro muscular disorders, sensory disorders, pulmonary disorders etc. [1]

For many hereditary diseases, similar clinical symptoms are observed which makes it difficult for doctors to diagnose the disease using only the routine biochemical and laboratory tests. NGS-based clinical assay helps to specifically diagnose the disease based on simultaneous sequencing of thousands of genes and quantitatively identifying the underlying molecular level defects that are associated with the hereditary diseases. A genetic report is the final outcome of the clinical NGS assay.

Typical genetic report contains one or more genomic changes in the patients' DNA (genotype) and the clinical diagnosis (phenotype) that are associated with the clinical symptoms of the patient. This report is prepared for the doctors and it is used along with other biochemical and laboratory analyses of the patient for accurate diagnosis and effective treatment.

The entire process can be broadly divided into two types: analytical wet-bench process and dry-bench process (Figure 1). Wet-bench processes involve all the steps performed in the clinical laboratory setup such as storage and handling of patient samples, extraction of DNA, molecular indexing (barcoding), target enrichment, amplification, library preparation and generation of sequencing reads. The dry-bench process involves all the bioinformatics analysis processes performed on the raw sequencing reads generated by high-throughput state-of-the-art NGS sequencing machines.

In this article, we will briefly explain about the bioinformatics principles involved in processing the clinical samples focusing specifically on the hereditary diseases that are based on germline variants in the patient samples.

Bioinformatics pipeline

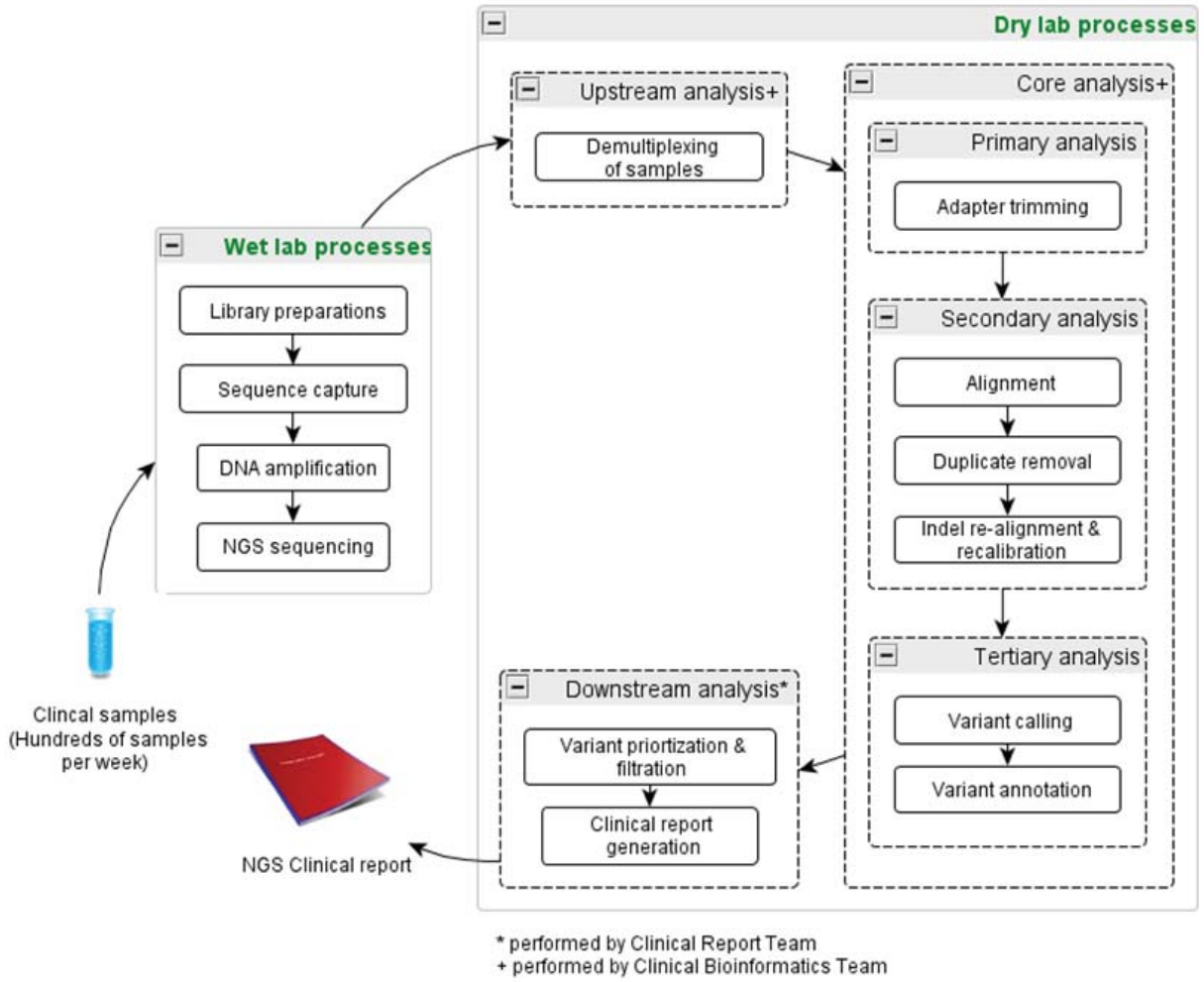

Figure 1. Wet and Dry lab processes to generate NGS clinical report from patient sample

The upstream analysis involves processing of binary format sequence data from Illumina's HiSeq NGS sequencing machine to computer readable sequenced reads. The primary analysis involves handling of the read data and pre-processing of the reads to remove poor quality reads and to trim adapter sequences used during library preparations. The secondary analysis involves aligning of adapter trimmed reads to human reference sequence (current version: hg19) and removing duplicate reads based on the aligned reads. The tertiary analysis involves identifying variants from the alignment based on the differences between the nucleotides from aligned reads and the reference genome and annotating them. We follow GATK best practices for Germline SNP & Indel discovery workflow for the core bioinformatics analysis [2].

The in-house variant annotation pipeline (VariMAT - Variation and Mutation Annotation Toolkit) is being used for annotations of variants. VariMAT integrates multiple clinical grade databases, variant class prediction and variants pathogenicity prediction tools for annotating the variants and mutation which rely on EnsEMBL's Variant Effect Predictor (VEP) [1]. VariMAT contains more than 170 attributes annotated for every variant to annotate in depth to understand their causal effect on associated disease or phenotype. Some of the annotated information by VariMAT are the population frequency, computational pathogenicity prediction, variant type and predicted impact of the variant on the protein (missense, loss of function, etc.). The total raw read in millions of records are reduced to tens of thousands annotated variants at the end of the tertiary analysis.

Downstream process involves preparation of the clinical report from the annotated variants and clinical symptoms provided in the TRF (Test Report Form). The tens of thousands of annotated variants are then prioritized to generate clinical report where only typically one or two clinically relevant variants are used. This step is done by the Clinical reporting team using in-house web-based Varminer application developed by MedGenome's software engineering team.

Clinical Bioinformatics Team: Roles and responsibilities

At MedGenome, all the dry lab processes related to clinical samples are performed by the clinical bioinformatics team. This team consists of bioinformatics analysts who have programming skills, NGS data analysis skills, Infrastructure knowledge for performing analysis and interfacing with IT team and biological knowledge to interface with the sequencing, lab and clinical interpretation and reporting team.

The clinical bioinformatics analysis and QC pipelines are automated and they are triggered and monitored in the analysis compute servers by the bioinformatics analysts. The progress of the analysis and the QC of the pipeline are monitored real time using in-house web-applications. The programs and SOP (Standard Operating Procedure) documents are locked and versioned. Clinical bioinformatics analysts strictly follow the steps in the SOPs for all the clinical samples.

The clinical bioinformatics team handles diverse scope of work in order to analyse clinical samples. This involves pipeline operations for day-to-day analysis of clinical samples (Arjun); annotations of variants by many population and disease databases using VariMAT (Sattibabu); developing, enhancing, and maintaining analysis pipelines (Rushiraj); Quality Assurance of analysis pipelines and results (Kaalindi); data sharing with customers in a secure manner (Dhanya); building and versioning the analysis pipelines (Inna); and compliance with policies and SOPs (Palani).

Typically, In a single run of Illumina's HiSeq NGS machine, 80 to 200 clinical samples are processed using MedGenome's Clinical Exome Panel (20 Mbps regions of the human genome containing protein coding regions of 6,883 hereditary disease related genes sequenced at the average depth of 100X) in 3 to 4 days. Each sample takes approximately 4 to 5 hours of analysis time and all the samples from a single run are processed by the clinical bioinformatics pipeline in approximately 2 days. Only QC-passed samples are shared with Clinical Report Team (CRT) for downstream analysis to generate clinical report.

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3. W. McLaren, L. Gil, S. Hunt, H. Riat, G. Richie, A. Thormann, P. Flicek and F. Cunningham, "The Ensembl Variant Effect Predictor," Genome Biology, vol. 17, no. 1, p. 122, 2016.

From our Colleague

All the king's horses and all the king's men couldn't bring Devasena back again!

by SHRADDHA EASWARAN, Scientific Communications

So I finally gave in a while back, and decided I had to watch Bahubali 2, the movie that India has been raving about. Of course, for that I had to first watch Bahubali 1. So I settled down, fully expecting to loathe it and ready to write a scathing review..but err..I loved it. And then, I watched the sequel, and I loved it more. The film has great casting and performances, amazing cinematography and stellar CGI, and has managed to garner over INR 1500 crore in box office collections in a mere 3 weeks after release. Further away from home, Game of Thrones (also a personal favorite) is a TV series that has fast become one of the most popular TV shows worldwide - dubbed and watched in multiple languages.

The commonality between these stories? Both chronicle life in an era long gone, both are set in historic times, and both have leading characters born into royalty. There are good kings who are protecting their subjects and fighting bad kings, and obviously in the end, good will triumph over evil.

What is this fascination with kingdoms and royalty and castles that we have? That transcends all barriers of nationality, culture, language and upbringing? Is it about the battle between good and evil? Or is it about the royalty, resplendent in its wealth and riches? I believe it is something very base - our fascination with power. Every single person, consciously or sub-consciously fantasizes about him or herself as being all-powerful and invincible. And these movies and TV shows, for that brief period of time, allow us our escape into this world full of possibilities and power, where no government or law, no judge or judiciary, no police or prison can put a crimp in our hero's (and therefore our) style.

Devasena and Baahubali

What do we believe we would achieve with this power? Greater good? Fighting for the suppressed? Or furthering our gains by amassing land and wealth? No matter which you choose - it is a manifestation of mamakaara -what Vedanta describes as "mine-ness" or "ownership". My kingdom, my subjects, my land, my wealth, my people and my family. Would any of these movie/TV characters have the motivation to be the glorious warriors that they are, had it not been for this mine-ness? While mamakaara isn't a desirable quality to have for those seeking to attain nirvana, it can be very well utilized for societal benefit for those of us who are still bound by our worldly restraints. So the next time you feel mine-ness for your religion or community and set out to fight those who critique it, step back and let that feeling pass. Instead, take a deep breath and feel that ownership for simple things like keeping your city and country clean, and showing basic courtesy and etiquette to your fellow human beings.

From our Colleague

All the king's horses and all the king's men couldn't bring Devasena back again!

Oh, and while we are on the topic of ancient India and its rulers - I noticed something unique and heartening. Be it the awe-inspiring archery partnership displayed by Devasena and Bahubali as they fight enemies side by side, or the valor shown by Jodha dueling with Akbar in a swordfight (in Jodha Akbar), or the skilled warfare that Mastani effortlessly engages in alongside Bajirao (in Bajirao Mastani), all our epics and sagas have depicted women to be as fierce and brave as their male counterparts. India has traditionally always respected its women and considered them equal to men.

Jodha and Akbar

Bajirao and Mastani

So people - if we ARE going to extol the virtues of a time gone by and envisage ourselves as part of that magical era, let's also try and imbibe some of those virtues, shall we ?

Employee connect

Our New-Joiners

Employee connect

Idea committee

As part of our employee engagement initiative, the Idea committee was formed to create a platform to gather employee suggestions at MedGenome.

The suggestions/Ideas could be related to making savings, simplification or speeding up processes or business. There is an Idea box placed at the Bangalore, Kochi, Chennai & Gurgaon offices. The ideas will be collated once in a month and evaluated by "The Idea Committee" at the end of every month. The prioritized ideas will go into approvals and implementation. Some of the ideas have been as specific as ensuring that there is appropriate signage in the lab areas and some like the need for a newsletter etc., Some of the ideas implemented were specific to certain office locations and there are certain ideas in the pipeline for approvals.

The upcoming idea committee meeting will be held on 24th October 2017, 22nd November 2017 and 20th December 2017.

Please do not forget to drop in your suggestions into the Idea box or reach out to the Idea committee members.

Employee connect

Cultural committee

The Cultural Committee at MedGenome adds that extra zing to our work life and makes work a fun place to be . It also makes office life more fun-filled, artistic and interesting. At MedGenome we provide a platform for employees to go beyond their regular work and explore their creative and artistic side.

This 9 member team along with the Management is responsible for keeping festive spirits alive in the office by organizing a multitude of cultural activities round the year. We make sure that every event lasts in your memory for a lifetime.

It requires a lot of effort and planning to organize events on this scale which needs a strong, dedicated and united team with a multitude of skills, selection of which is a big responsibility . A sneak peak of what we do round the year:

- Women's Day Celebrations
- Onam Celebrations
- Ethnic day Celebrations
- Christmas Celebrations
- Games (Indoor and Outdoor)

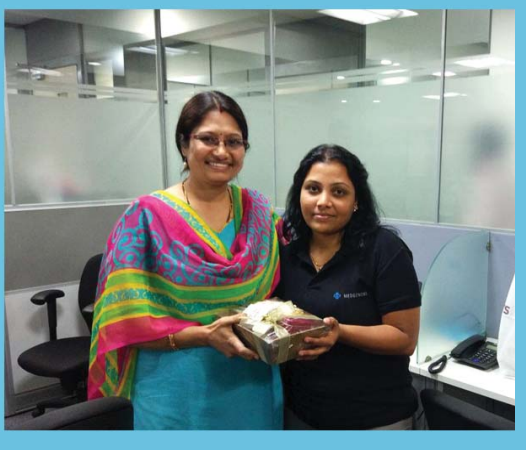
Photo feature

BIRTHDAY CELEBRATIONS

Bangalore Office

Kochi Office

EMPLOYEES RECEIVING DIWALI GIFTS



MEDGENOME

Onam Celebration At MEDGENOME *(Bangalore and Cochin office)*

MEDGENOME

Onam Celebration At MEDGENOME *(Bangalore and Cochin office)*

Wish you and your family
a Happy Diwali &
a Merry Christmas

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