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# Beknowe

Internal Quarterly Newsletter

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# WORDS FROM THE MANAGEMENT

#### Dr. Shankar Sikri Vice President – Corporate Development

#### Dear Colleagues,

As many of you may be aware, I have recently joined MedGenome as Vice President, Corporate Development, based in the Electronic City office. I have met some of you in person and look forward to connecting with as many of you as possible in the US, India and Singapore over the coming weeks.

Prior to joining MedGenome, I worked as an investment banker for 11 years, most recently as Managing Director in the Healthcare team at Evercore, based in London. During my time as an investment banker, I was primarily focused on advising healthcare companies on M&A opportunities, IPOs, fund raisings and overall company strategy. Prior to banking, I qualified as a doctor from Imperial College, London and worked as a physician in the National Health Service in the UK.

I am delighted to have joined MedGenome at such an exciting time in its development. Genomics is now the cornerstone of diagnostics and drug discovery and MedGenome is a unique company in this area. MedGenome is continuing to transform the genomics diagnostics landscape in India and is increasingly well-positioned to leverage its unique understanding of the Indian genetic landscape to discover and develop novel treatments for healthcare conditions globally.

My role at MedGenome will be focused on driving forward the company's fundraising efforts as well as increasing the Company's visibility amongst pharma companies and other corporate entities, with a view to developing revenue generating partnerships. MedGenome is poised to achieve several crucial milestones in its growth story over the coming months, which should allow it to further raise its profile with all stakeholders, including doctors, investors and of course patients. It goes without saying that MedGenome's future success is dependent upon the continued excellent work and collaboration of the whole MedGenome family and I personally am very much looking forward to working with all of you to help achieve the best outcome possible for the company.

# HIGHLIGHTS

#### Most talked about MedGenome News MedGenome connect 05 CMEs, symposiums and events conducted by MedGenome to engage with clinicians, researchers and thought leaders Making a difference 06 CMEs, symposiums and events conducted by MedGenome to engage with clinicians, researchers and thought leaders From our US office 07 MedGenome engagements, participation in events, symposiums etc. Sneak peek into the world of science 08 Optimized run-plan designer for Illumina NGS sequencing systems using Constraint Programming From our colleague • Women's Health – it matters! • Art meets Science • Our employee's little Picasso :) Macro Photography **Employee connect** New loinees Crossword Puzzle Celebrations Photo feature

Celebrations

# Most Talked About



# MedGenome connect



The first lap of FY 2019-20 was an exciting and productive one for Claria, as we participated in numerous doctor events. Overall the participation was in 7 CMEs and a conference at Chandigarh. With these, we could touch base with more than 500 clinicians.

Claria team is determined to intensify promotion and scale up business in the new financial year through continued participation in such doctor events, and conduct many doctor engagement activities.

The key agenda for Claria in FY 2019-20 will be to establish business in Tier 2 & 3 markets, and drive growth from key tests including NIPT, CMA, KT & FISH. This will be coupled with enhanced prescriber base though KOL engagement programs in Metro and Capital cities.



Mega CME on role of genetic testing in prenatal practice at FETOMAT Patna.

#### Prima Cancer Genetics



Dr Ramprasad being felicitated at SGPGI Lucknow

The period between 1st Apr 2019 to 30th June 2019 was exciting as we had few but quality and important scientific events for Team Prima. We organized 5 important CME's/standalone Meetings

- 1. Standalone CME at SGPGI Lucknow
- 2. Muzumdar Shaw Cancer Hospital Oncology Department Doctors visiting MedGenome Lab and CME
- 3. Surat Paediatric Association CME
- 4. KIMS BIBI Hospital CME at Hyderabad
- 5. Paediatric Haematology conference at Kidwai institute of Oncology, Bangalore

Our team of experts, Dr. Ramprasad and Dr. Vidya made our participation remarkable with their involvement.

The visibility and awareness on Prima and its offerings was boosted further by sales team across cities in India.

The major therapies touch-based through these engagement programs were Oncology, Haematology and Primary Immunodeficiency.

# ACTIA

The 1st quarter for the financial year 2019-20 was a special one in terms of participation in events. Overall Actia organized 10 CMEs and participated in 2 conferences, one at AIIMS and one at SGRH. The latter one witnessed the attendance from more than 500 clinicians from across India.

With key growth driver for Actia this financial year is to drive business in Tier 2 & 3 cities, and 6 out of the 12 CMEs were organized in these cities, enabling us reach more than 150 clinicians. With leads getting converted into conversions, the flow of samples from these places has kick-started.

The other important growth driver is the focus on new tests, which will add to the growth of Actia business.

With the momentum generated in business during this period, the 2nd quarter is expected to further propel our growth in Tier 2 & 3 markets.



MedGenome's session received an overwhelming response at rare Disease conference, Gurgaon

# Making a difference

How genetic diagnostics provided an affected couple with an alternative method to start a family

In August 2016, a couple came to MedGenome Centre for Genetic Health Care (CGHC) who were married for 18 years with no children. Their reason for infertility was straight forward. The male was 47 years old when he came to our clinic, had obstructive azoospermia and underwent assisted reproductive technique to have a child. The couple underwent ICSI (Intra Cytoplasmic Sperm Injection) to retrieve sperms from his testis, since the obstruction was due to congenital absence of vas deferens and inject it inside his wife's egg in vitro. After successful fertilization of the same, embryo was formed and a full term normal delivery was achieved and the couple was blessed with a daughter. However, their daughter could not survive and was affected with very severe infection and died within 8 days after birth.

- By the time, the couple came to us, the wife was 40 years old and they had 3-4 failed ICSI cycles. No investigation was done to assess the cause for male infertility. The accumulated symptoms of the male, along with cause of death of their daughter pointed the case towards Cystic Fibrosis.
- Cystic Fibrosis is known to cause respiratory problems, sweating, infection, etc. and easily diagnosed with those set of symptoms. However, 80-90% of Cystic fibrosis mutation in males also causes Obstructive azoospermia due to congenital absent Vas deferens. Thus, when genetic evaluation of the husband was done in MedGenome Bangalore for CFTR gene, it was found out that the male was affected with an uncommon likely pathogenic homozygous mutation **c.712G>C (p.Ala238Pro) in exon 6 of CFTR gene** responsible for Cystic Fibrosis.
- Literature review says that it is not uncommon for male CFTR affected male patients to be infertile even if other symptoms are absent, but lot of clinicians miss this. This could have probably also caused their daughter's death which was due respiratory complication, although this could not be confirmed.
- CFTR mutation analysis was done only on husband who was affected and his wife was not tested, however due to her advanced maternal age (40 years old when she came to the clinic), her eggs were not available in abundance, in fact they were almost exhausted thus making the conceiving itself challenging. Even if that could be achieved, it was necessary to check the status of the
- fetus to prevent any complications in future, not just regarding the CFTR mutation but also for chromosomal aneuploidies which had a higher prevalence in such advanced maternal age.
- Thus, to reduce the complication, the couple was suggested to opt for egg donor. They choose an egg donor almost after a year in July 2017 and she was screened for CFTR mutations which was negative. Thus, this gave out a ray of optimism for the patients.
- This case was one representation of why genetic evaluation is necessary in various scenarios with respect to pregnancy planning and child birth in India and thus there is an increasing need to do more genetic screening in the reproductive space.

# From our US office



June 17-20, 2019 Boston, MA Seaport World Trade Center

This quarter we attended the World Pharma Week and also presented a poster titled "Applications of TCR repertoire analysis for biomarker discovery and beyond".

World Pharma Week brings together a unique and international mix of large and medium pharmaceutical and biotech companies, CROs, leading universities and clinical research institutions, emerging companies and tool providers—making it a perfect meeting-place to share experience, foster collaborations across industry and academia, and evaluate emerging technologies.

Recently, we organised a symposium on genomics where four distinguished scientists presented a talk on recent trends in Sequencing technology. Dr. Sarah Taylor, Staff Scientist, 10x Genomics, spoke about "High Resolution Profiling of the Antigen-Specific T Cell Response", Dr. Mark White, Sr. Director, Scientific Affairs at Berkeley Lights, Inc., spoke about "Stuck on function? Analyze the function of individual T cells in 1 day", Dr. Rikhia Chakraborty spoke about "Terrible T's in LCH", while Dr. Sampathkumar Rangasamy presented a talk on "Importance of disease phenotype in rare and complex disorders" at the symposium.

Visit our "Scientific sessions" video section on the website to know more : https://research.medgenome.com/videos/



We are also at the upcoming Immuno-Oncology Summit 2019 event from August 05 - Apr 09, 2019, being held at Westin Boston Waterfront, Boston, MA. CHI's Immuno-Oncology Summit has become the leading annual meeting focusing on the latest applied research, providing comprehensive and in-depth coverage across all modalities and stages in the pipeline. Every year, CHI assembles an international mix of thought leaders and decision makers from industry and academia to bring out the latest developments in immuno-oncology.

# Sneak peek into the world of science

Optimized run-plan designer for Illumina NGS sequencing systems using Constraint Programming



Vivek Gopalan Associate Director, Clinical Bioinformatics

#### Introduction

In MedGenome, Illumina-based Next Generation Sequencing (NGS) systems are used for sequencing thousands of clinical and non-clinical samples every month. This article is a walkthrough on a customized solution that we are planning to provide for the NGS sequencing team to reduce their errors and to improve sequencing throughput. Two challenges are faced by bioinformatics team while providing informatics support to the lab team - formulating a clinical-lab operation challenge as mathematical problem and converting back the raw results from mathematical applications to reports that are comprehensible to the clinical lab team members.

#### Background

Blood or saliva samples from patients that we receive for molecular genetic tests (NGS tests) are converted to DNA libraries and then sequenced in Illumina NGS sequencing systems. DNA libraries, usually referred to as libraries, obtained from samples are not sequenced individually but are collated and sequenced together in batches or runs. Each sample library is tagged with unique 8 or 6 nucleotide barcode sequences during library preparation so that mixing of samples do not have any impact during sequencing. De-multiplexing of the mixed data to individual sample data is performed during downstream bioinformatics analysis. A typical run of Illumina NGS HiSeq machine generates 300 to 1000 giga-base pairs (Gbps) of sequencing read data in 3 to 4 days of time in eight-lane flow cell. This allows batch-wise sequencing and analysis of 80 to 200 clinical exomes [~8300 genes panel; 100X read depth] data simultaneously.

In an Illumina NGS system sample libraries are loaded to small specialized glass slide coated with DNA templates called flow-cell in which the sequencing chemistry happens. Typically a flow-cell contains 8 independent fluidic channels called lanes where the sample libraries are loaded. Each lane supports a specific maximum amount of DNA for sequencing based on type of Illumina NGS machine model.

Run plan design is the process of assigning sample libraries to the specific lanes of the run. This is performed by the NGS sequencing scientist based on all the backlogs of sample libraries available for sequencing. The run-plan document becomes the basis for sequencing and downstream bioinformatics analysis.

NGS sequencing scientist needs to fulfill the following requirements, for planning and loading sample libraries to the lanes of NGS flow-cell (Fig. 1a-c)

- 1. Barcodes of all the sample libraries in a lane should not "clash" with other samples in the sample lane. Barcodes should at least differ by 2 nucleotides to accommodate sequencing errors in the index sequences. Barcodes that do not satisfy this condition cannot be differentiated uniquely after sequencing.
- 2. Sample pooled together during library preparation should be sequenced together in a lane.

- 3. Total expected data size (Giga-bases) of the samples sequenced in each lane should be approximately equal to the amount recommended by Illumina for a specific machine (e.g. 50 Gbps for HiSeq 2500; 70 Gbps for HiSeq 4000). This is controlled by the amount of DNA content loaded into each lane.
- 4. Samples marked as urgent priority must be loaded in the planned run. Fetal and emergency clinical samples are marked as urgent and these samples should be loaded in the imminent run.

For a typical run, NGS sequencing scientist takes more than 10 hours to manually prepare a run-plan design document. The high volume of samples (thanks to the sales and the marketing team), a limited set of barcode sequences, a different type of Illumina systems and grouping of samples as pools makes it challenging to continually prepare run-plan manually.

Poorly prepared run plan document significantly increases the cost and time required for sequencing of samples. Barcode clashes of samples in lanes result in re-sequencing of the samples and non-optimal amounts of DNA in lanes results in more number of runs. NGS sequencing process is one of the most expensive and time-consuming steps of the NGS assay. Any challenge on this step has direct impact on the business such as delay in releasing the genetic reports to the doctors and mixing or swapping of samples.

#### Solution

#### **Results and Summary**

We developed an automated system for the NGS team to generate optimal run plans for sequencing hundreds of sample libraries in the NGS machines fulfilling all the constraints required to load libraries in flow-cell lanes. We used constraint optimization (CO) paradigm to solve NGS run plan since it is the industrial standard for solving scheduling problems. CO is the process of optimizing (maximizing or minimizing) an objective function with respect to some variables in the presence of constraints on those variables. There are Constraint Programming Languages (CPL) available to define and perform CO specific problems. Developing application using Constraint Programming Languages (CPL) instead of the standard programming languages reduces the development time significantly.

**Objective function:** Maximize the amount of data to load in all the lanes in a flow cell (i.e. minimize the difference between the total expected and obtained data size from all the lanes).

**Constraints:** limits or restrictions that are imposed (refer previous section)

We used MiniZinc<sup>1</sup>, a free and open-source constraint modeling language to model the problem and G12 Finite Domain (G12 FD) solver to optimize the model along with input data. The application takes approximately 30 seconds to allocate 150 sample libraries to a typical NGS run. The first optimized solution was used whenever there were multiple solutions obtained.

To make this optimized solution useable by the sequencing team, we developed a web-based application that takes inputs such as library identifier, index sequences, pooling groups, expected amount of data required for each libraries, sequencing priorities and lane capacity for a flow-cell. In the background it runs the analysis and returns the results as a sequencing-team friendly web report. Tables and images summarizing optimized lane allocations, unallocated libraries and amount of data allocated in each lane are showing the web report (Fig. 1c).

We have developed an optimized run-plan designer that will reduce the time taken by the NGS sequencing team for preparing run plan document from 10 hours to less than a minute. It also significantly improves the planning and reduces manual foot-print of NGS sequencing process.

#### Constraint optimization (CO)

CO is the process of optimizing (maximizing or minimizing) an objective function with respect to some variables in the presence of constraints on those variables. There are Constraint Programming Languages (CPL) available to define and perform CO specific problems.

The popular Sudoku solution can be formulated as CO problem to meet all the requirement of not having same single digit number in any rows, columns and sub grids. Sudoku problems can be solved using CPL using few lines of code.

CO is used widely in real-world problems such as minimizing trips for package deliveries by logistics companies, scheduling of aircrafts to reduce fuels and optimizing resource allocations in production operation processes. CO principles are used in bioinformatics domains in pathway modeling – Metabolic Flux Balance analysis<sup>2</sup>, protein structure folding and phylogenetic analysis.

#### References

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- 2. J.D. Orth, I. Thiele I, B.Ø. Palsson. What is flux balance analysis?. Nat Biotechnol.;28(3):245-8, 2010.



Figure 1. Run-planner workflow (a) Input requirements for Run-Planner tool (b) Program used to optimize the run-plan design problem (c) Optimized run-plan design document with predicted lanes and (d) Run-Planner web interfaces



# Women's Health – it matters!

Governed by natural laws there is no doubt that our body changes as we age. Especially, Women face different health issues at different stages of their life owing to hormonal and biochemical changes inside their body. It is but natural for humans to age and wither away like a dead leaf when the time comes. Death and Destiny is in nobody's hand, however, health is something one can always care about and a little attention to the body and a regular exercise regimen can push that dreaded lifestyle diseases a bit away.

#### Few tips here for women that can help them to take care of themselves:

If you are in your **20s and 30s, pump up the iron**. Iron prevents anaemia and related fatigue by helping your red blood cells transport oxygen to all of your tissues. And it's particularly important during your childbearing years.

If you are in your **40s and 50s, consume more calcium**. After age 40, your daily recommended intake of calcium increases from 1,000 to 1,200 mg per day.

If you are in your **60s and beyond, preserve muscle with protein**. As you age, the body becomes less efficient at processing protein and incorporating it into your muscles.

Also, get screened periodically for:

#### **Breast Cancer**

Some of the recent reports indicate an estimated 25.8 per 100,000 women in India have a high risk of breast cancer. It's projected that at least 17,97,900 women in India may have breast cancer by 2020. Mutation in genes BRCA1 or BRCA2 – significantly increase your risk of developing breast cancer and ovarian cancer. A genetic screen and a periodic mammogram can avoid any future complications

#### **Cervical Cancer**

Starting from age 21, it's always good to receive a Pap smear every three years until you're 65.

#### **Colon Cancer**

Always good to get a screening test done for the disease starting at age 50.

#### **High Blood Pressure**

Lookout on your cholesterol levels and blood pressure. Good to have it checked at least once a year.

#### Osteoporosis

A common issue as the body ages and screening is a must at the age 65 to make sure your bones are strong.

#### Move the body:

- 1. 150 minutes of vigorous exercise every week can keep most of the ailments away
- Keep your heart healthy by taking up some aerobic activity such as – dancing, brisk walking, skipping or jog
- 3. Take the stairs instead of lifts
- 4. Strength Train Keeps your muscle fibres active, flexible and strong
- 5. Count nutrition and not calories
- 6. Focus on Flexibility and not on the weighing scale
- 7. Exercise while watching TV

#### Sleep

- 1. A good night's sleep keeps you fresh for the next day challenges.
- 2. Use meditation or sleep relaxation techniques to get a good night's sleep.
- 3. Avoid alcohol and other stimulants.
- 4. Remove all computers, TVs, and other gadgets from the bedroom
- Use your bed only for sleeping and not for other activities such as reading, watching TV, or listening to music
- 6. Don't eat heavy food, keep it light and hit the bed after 2 hours of your dinner
- Repeat positive affirmations before you fall asleep (no matter how silly they may be) – remember your sub-conscious mind has more power than your wakeful mind

Incorporating few lifestyle changes into your daily routine can make a lot of difference to your body and mind. And finally always have a smiling and cheerful attitude both at personal and professional life. Keep a balance :)

#### Always wishing you good health Team HR



# Art meets Science

"Art and science have so much in common - the process of trial and error, finding something new and innovative, and to experiment and succeed in a breakthrough." - By Peter M. Brant



By: Sandesh Chavan, Admin and Operations

# Our employee's little Picasso :)



By: G.R Rithwik (10 Years) DNA of Raghunathan G, IT & Design



By: Srecharan (7 Years) DNA of Vivek Gopalan, Clinical Bioinformatics



By: Srecharan (7 Years) DNA of Vivek Gopalan, Clinical Bioinformatics



By: G.R Rithwik (10 Years) DNA of Raghunathan G, IT & Design

# <text>

Macro photography (or photomacrography or macrography is an extreme close-up photography, usually of very small subjects and living organisms like insects, in which the size of the subject in the photograph is greater than life size. The term photo-macrograph was proposed in 1899 by W. H. Walmsley for close-up images with less than 10 diameters magnification, to distinguish from true photo-micrographs. One of the earliest pioneers of macro photography was Percy Smith, born in 1880. He was a British nature documentary filmmaker, and was known for his close-up photographs.

Our colleague, Mr. Swarup from IT and design department is an amateur macro photographer and has clicked stunning photos of insects such as green house fly, horned treehopper, spider, mantidae, etc.



Green Housefly



Horned Treehopper



Pantropical jumping spider

# **Employee connect**





### Our New-Joiners



Abijit Umesh Hegde



Dipak Kumar Singh



Sharmila Selladurai



Priya Joshi



Karthik R



Neha Shrikant Ghorpade



Sanjib Kumar Das



Pratik Das



Prakash Nagarajan





G Arun Kumar



Jatin Rawat



Rajith Harimoorthy



Keya Mukherjee



Shraddha Raju Malagali



Sharoon Grace



Renjusha P T



Haripriya Gopalakrishnan





Swapneshwar Sahoo



Bharath Kumar Reddy

# **Employee connect**



Nikita Jain



Kritika Passi



Gayatri Krishnan



Avinash Pradhan



Sureshkumar Prajapati



Mohammed Faizal



Sameera Fatima



Archita Sharma



Nitesh Dattatray Bhalerao



Gulam Mohammed U



Sharada Sivaramakrishnan



Shweta Kannan Mahalingam



Priyanka Shrivastav



Rayees Ahmad



Ayaz Hussain



Naveen Milarusetti



Shankar Sikri



Gopal N



Surbhi Prajapati





Sangeeta Rani















# Employee connect

## Cross word puzzle



#### ACROSS

- 2 He inserted a gene from an African clawed toad into bacteria and birthed genetic engineering
- 4 These hormones allow cows to produce more milk
- 7 Industry that benefits from genetic engineering
- 8 The environment is unable to destroy these
- 9 Organism modified by introduction of foreign DNA
- 10 Dormant genes
- 11 Percent of genetic engineering is focused on promoting agriculture

#### DOWN

- 1 How to manipulate a genome to alter cell function?
- 3 The first genetic engineering company
- **5** A technique used in biological vectors
- 6 Small ring of DNA

#### **Previous Winners :**

Dr Malini Manoharan (Bioinformatics) Mrs Roopa Shanmuga Kumar (Human Resources) Ms Manjula Rama Vasan (Human Resources)

Kindly mail your answers by 15<sup>th</sup> August 2019 to editor@MedGenome.com. The first two people to answer the puzzles correct will be featured in the next edition of our newsletter.



# Photo feature

# Celebrations



























For internal circulation in MedGenome only



# A market leader in Genomics-based Diagnostics and Research



#### One-stop solution for all your Diagnostics and Research needs

Flow Cytometry	Microarray	Sanger	FISH	NGS	PCR	IHC	Fluidigm
			X10	HiSeq	MiSeq		



Bangalore Chennai Delhi Kochi Mumbai **US** Foster City SINGAPORE