

Genotypic Technology Genomics Simplified

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Established in 1998, Genotypic Technology is the first Genomics R&D company in India. Genotypic Technology offers a customized “one-stop solution” to address complex questions in Genomics. They have pioneered Microarrays and Next Generation Sequencing Services, and are well equipped with cutting edge molecular biology and bioinformatics tools to handle large scale genomics projects. **The core strength lies in their ability to customize and develop new / non-standard applications.** This is made largely possible because of the unique blend of high quality scientists (comprised of 8 Ph.Ds and over 60 Masters), and proprietorship of cutting edge technologies. *The Microarray team has been the cornerstone of Genotypic's contribution to*

genomics applications in the last decade and has contributed to applications such as Gene Expression Profiling (including non-coding RNAs), Cancer genomics, miRNA and siRNA profiling, AgriGenomics, Alternative Splice Variants profiling, Bovine / Cattle Genomics, ChIP on ChIP & DNA Methylation, Toxicogenomics / Clinical genomics, aCGH (Comparative Genomics), Biomarker Discovery / Epigenetics, CNV(Copy Number Variations), Bacterial Biosensors, SNP Validation Arrays, InDELS (Insertions & Deletions), and Drug repurposing/ Drug target discovery.

Genotypic Technology is an ISO and Agilent certified facility, enabled with SAP business by design systems to effectively execute and manage large projects and

data sets with complex mandates with relative ease. The founder Dr. Raja Mugasimangalam, Ph.D, also known as M C Raja is a Scientist turned entrepreneur in the Genomics domain, helping scientists worldwide to apply Genomics in real life research projects. Armed with a PhD (1994) from Madurai Kamaraj Univeristy, Dr. Raja worked as postdoctoral scientist at Weizmann Institute of Science, Israel and Sidney Kimmel Cancer Center, San Diego and Argonne National Lab, on developing novel methods for DNA sequencing for Human Genome Project. He along with co-founder Dr. Sudha N Rao (Ph.D) who has PhD in Biotechnology from Madurai Kamaraj University with post-doctoral experience at Weil Medical School, New York, established Genotypic Technology in 1998, with the goal of simplifying complex genomics technologies by **“looking out for small changes that make a big positive difference”**. Together they have not only several patents and publications in peer-reviewed scientific journals but also a wealth of experience and knowledge which they bring forth to guide the company and indeed the rapidly moving world of genomics into the frontiers of the future.

Next Generation Sequencing: A revolutionary change

Next Generation Sequencing (NGS) has revolutionized biology and is now moving into pharma and clinical applications, sequencing of cancer genes, genes involved in drug metabolism, genetically inherited diseases has now been made possible at very low costs and a short turn around time.

DNA sequencing technologies have evolved considerably over the last decade. Innovation and technology have combined to generate Next generation Sequencing (NGS) which is the term given to modern technologies that generate large amounts of accurate sequence information in relatively short amounts of time at considerably lower costs than envisaged in the past. *Illumina Inc* is a forerunner of this technology, and uses a proprietary technology to generate massively parallel high throughput sequencing efforts. This technology in a pharmacogenomic context is to prove invaluable in the coming years.

In the last two years Genotypic Technologies has significantly embarked on the NGS approach to Genomic solutions. Armed with two “Illumina GAIIX” machines each capable of generating between 85-95Gb

of DNA sequence information in less than two weeks, the company has experience in executing many NGS applications with a great degree of success. NGS Technological applications such as Whole genome sequencing, Targeted Re-sequencing, SNP, Mutation identification, Transcriptome sequencing, Digital gene expression, ChIP sequencing, Methylome sequencing and Small RNA sequencing have been successfully conducted. **These applications have been executed under various popular NGS themes like** microbial sequencing- De-novo and Re-sequencing, Human Genetics- Disease Inheritance studies, Transcriptome/RNA sequencing, Metagenomics, Agrigenomics, Pathogen detection in host system, and Chromatin Immuno-precipitation Sequencing (ChIP Seq) combined with ChIP on ChIP microarrays. Importantly Genotypic Technology provides *state of the art* data Analysis facilities both for Microarray as well as NGS data, and has a proven track record for client satisfaction in providing genomics solutions and is the first choice genomics service provider in India and abroad. Some of Genotypic's clientele and collaborators include Unilever, Indian Institute of Science, Astra Zenca, Evogene, JNU, IMTECH, Biocon, Weizmann Institute, Quark Pharma, Novartis, Genzyme, Novartis, Adelaide University, Harvard University.

NGS and it's application in pharmaceutical industry

NGS has been amply validated in diagnostic, pre-clinical /in-vitro and research environments and have begun to demonstrate robust dependability in clinical contexts as well (E.g.; HybSelect). Pre-clinical studies lean on evidences produced *in-vitro* and animal testing to provide hope for future therapies. The role of “genomics” in the pharma industry is clearly ushering in the era of personalized medicine, more than ever before. The steady development of a vast published knowledge database and the exploitation of new technologies like Next generation Sequencing (NGS) attempt to realize these ambitions.

The overbearing responsibility and occupational hazard of Pharmaceutical companies world over is to *walk the talk* in translational medicine efforts. The current landscapes of new and exciting breakthroughs in the world of academic research and basic Science such as Genome-wide Association Studies (GWAS)



Dr Raja C Mugasimangalam
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You have a vast experience in genome sequencing from the first generation to the next generation. How do you see the strengths of the Illumina platform for NGS?

Illumina after they picked up Solexa vastly improved the quality, quantity and length of the sequencing output. 454 might have started NGS era, but the NGS revolution was indeed brought out by Illumina strongly. We see Illumina playing a much bigger role in the future NGS and personal genome sequencers among other players.

The data output from these Illumina sequencers being quite high what sort of client projects do you cater to?

Leading research institutes in India and abroad like IISc, JNU, JNCASR, NCBS, NCCS and companies like AstraZeneca, Bharat Biotech, Serum Institute, Wiermann Institute, Volcani Centre, Yale University. We are working with more than 250 scientists in India. The size of projects starts from sequencing small viral genomes to large scale sequencing of dozens of human exomes, whole plant genomes, etc.

On the topic of throughput please tell us how many samples you process on an average?

We have completed 250 next generation sequencing projects in the last one year. We are running the instrument continuously back to back over the last several months. From short reads for applications like Chip Seq, Small RNA Seq to long paired end reads for applications like de-novo sequencing, all types of applications are covered at Genotypic.

Out of those 250 projects would you highlight some successful project/s for the benefit of Cutting Edge readers?

We sequenced Indian clinical isolate of “*Candida Albicans*” in collaboration with Prof. Parag Sadhale from IISc, which will be published soon. We are pleased to be involved in the recent publication from Prof. Niyaz Ahmed “*Genomes of Two Chronological Isolates (Helicobacter pylori 2017 and 2018) of the West African Helicobacter pylori Strain 908 Obtained from a Single Patient*” (<http://www.ncbi.nlm.nih.gov/pubmed/21515762>).

The other successful projects include several projects like chickpea sequencing (Prof. Mukesh Jain, NIPGR), Human whole Exome sequencing projects for ACTREC and other scientists.

How do you see the NGS services market evolving in India?

Scientists tend to outsource rather than optimize genomic technologies on their own. In our understanding their first priority is to get high quality data and useful interpretations rather than generate the NGS data in-house.

What are your plans to expand your Illumina NGS services offerings?

We now have got our second Illumina sequencer with an aim to provide very short turn around time with high quality data. We are also going to specialize on paired-end long reads with different insert lengths (more than 300bp total) to replace the expensive long read technologies. We are in the process of expanding and concentrating more in the field of non-standard / novel NGS applications, amplicon sequencing, use of microarrays for SNP / InDel validation and validation of NGS data. We are very pleased to inform you about the co-authored publication “*Genome sequence of the pattern forming Paenibacillus vortex bacterium reveals potential for thriving in complex environments.*”

(<http://www.ncbi.nlm.nih.gov/pubmed/21167037>) in which microarrays were used to validate NGS data.

We at Spinco Biotech started marketing and supporting Illumina products since mid-January this year. What has been your experience so far?

Thank you for your excellent support. We look forward to continuing and improving the relationship in various fronts



and Next Generation Sequencing (NGS) technologies provide renewed impetus for *Pharmaco-genomic* explorations on the path to Personalized Medicine. The adage, thus far wholeheartedly applied to avid consumerism, “*Whats good for you.....need not be good for me*”, now seems to ever-increasingly be apt in the realm of disease treatment.

The number of clinical trials being conducted in India is growing at a rapid rate, and the reason for this have been variously attributed to (i) population size, (ii) genetic diversity, (iii) socio-economic and cultural diversity, etc., among other reasons.

Regulation, documentation and database management (both for drug efficacy as well as toxicity) in transparent and politically secure environments are vital ingredients to aid the success of these efforts. While the availability of high quality scientists/talent and India's CRO capabilities are world renowned and acknowledged its access to Next generation Technologies is only recently being addressed. While the Government of India in particular the Department

of Biotechnology (DBT) embarks on ambitious mandates of empowering India's scientists with these technologies, companies like Genotypic Technology have taken pioneering steps towards harnessing new technologies and indeed excelling in their execution.

The convergence of personalized medicine efforts, with careful and safe cohort selection for clinical testing and trials requires that the Pharma companies and CRO's conducting Pharma research reach out to these new technologies now available quite literally “...in their backyard”.

Genotypic's contribution to Genomics:

Genotypic is involved in technology and assay development/optimization of projects in collaboration with leading reagent suppliers like Diagenode and Agilent. RNA & DNA extraction and QC from challenging tissues and the major contributor to RIN dB. Genotypic takes an active part in developing and testing newer applications, it has co-authored a recent “most accessed” publication with a land mark application of **microarrays in validating NGS data** (Sirota-Madi et.al BMC Genomics 2010). Genotypic is also undertaking research and development in the areas of sequencing Indian medicinal plants, quality control of NGS data

Seq QC : A Simple desktop application for rapid quality control, Reporting of NGS Data and Processed sequence files has been developed by Genotypic, which can be accessed at below link : www.genotypic.co.in/SeqQC.html

Genotypic also manages its largest genomics group in Linked-in : “Genomics: Next Generation DNA Sequencing (NGS) and Microarray” which provides a platform for NGS and Microarray users across the globe to discuss and share their ideas. To join our group visit: www.linkedin.com/groups?about=&gid=1907871&trk=anet_ug_grppro

Apart from the above, Genotypic conducts frequent seminars and workshops (Lab and Informatics) in the areas of Microarrays and NGS. Our recent workshop was “Hands on NGS Workshop” held in January 2011, where participants not only got an in-depth training but also could sequence their own samples. For more details about this workshop visit www.nextgenseq.com/blog and to register for future workshops visit www.nextgenseq.com/register ■■■