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Genomics special Issue

BIOTECH EXPRESS

Top Company - Indian:
Genotypic Technologies- Forerunners in Indian Genomics

Top Company - Global:
Oxford Nanopore - Game Changer in Genomics

Scientific Leader Profile:
Short Living Biography
Dr B K Thelma

Editorial: Genomics – Origin Evolution and Future

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Next Generation Sequencing *in* Clinical Genomics

Applications and Advances

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Editorial

Genomics – Origin Evolution and Future

by Kamal Pratap Singh

Introduction

Genomics is the study of the genomes of organisms. Its main task is to determine the entire sequence of DNA. However one cannot go far in genomics unless they know about genetics. The main difference between genomics and genetics is that genetics scrutinizes the functioning and composition of the single gene whereas genomics addresses all genes and their inter relationships in order to identify their combined influence on the growth and development of the organism.

The term Genomics was coined by Tom Roderick, a geneticist at the Jackson Laboratory (Bar Harbor, Maine). Today Genomics has revolutionize the understanding of biological entities in many ways like personalized medicine, creation of modified crops as per the need and environment, etc.

Genetics- Mother of all creations

A short timeline of discoveries and development

The discoverer of genetics is Gregor Mendel, a late 19th-century Monk and plant scientist who by simple observation of progenies discovered the laws of inheritance in 1865, but the importance of Mendel's work did not gain wide understanding until 1900, after his death, when Hugo de Vries and other scientists rediscovered his research.

In some other part of science fraternity some work was going when in 1869, Swiss physiological chemist Friedrich Miescher first identified what he called "nuclein" in the nuclei of human white blood cells.

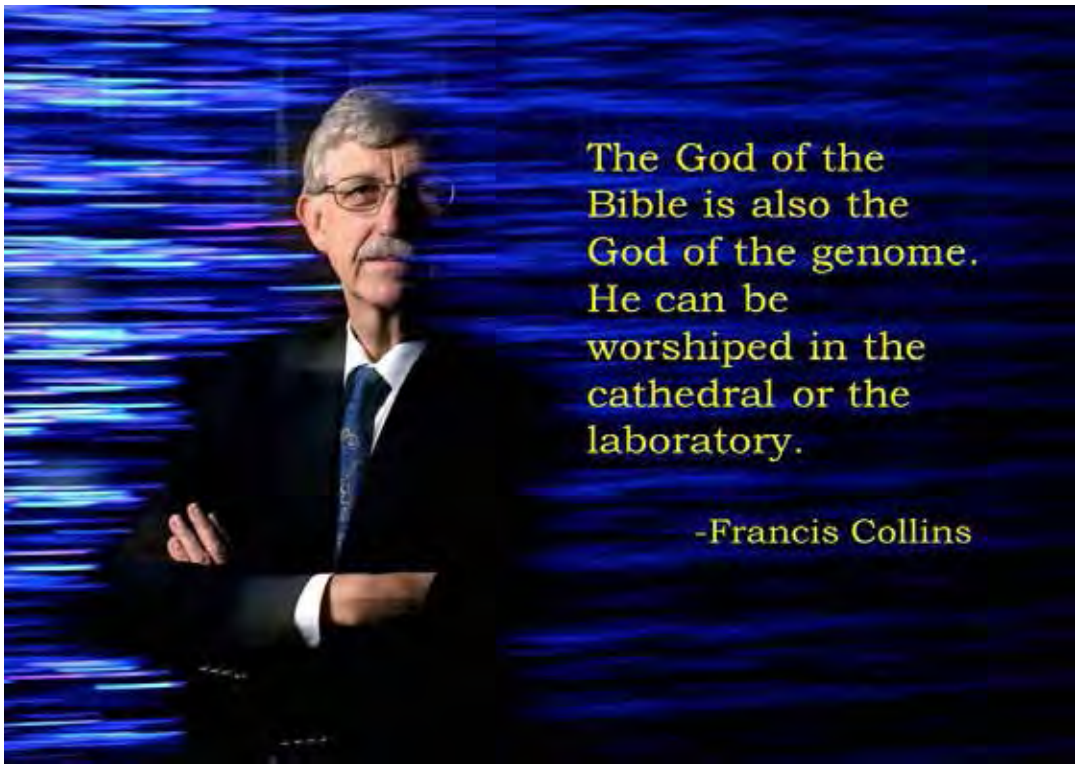
Column: Har Gobind Khorana

Har Gobind Khorana (9 January 1922 – 9 November 2011) was an Indian American biochemist. While on the faculty of the University of Wisconsin, he shared the 1968 Nobel Prize for Physiology or Medicine with Marshall W. Nirenberg and Robert W. Holley for research that showed the order of nucleotides in nucleic acids.

He was successful in constructing the first ever artificial gene in 1972. A few years later he made the artificial gene function in a bacteria cell. Genetic engineering has been made possible only due to the ability to synthesize DNA.

After the rediscovery of Mendel's work, scientists tried a long to determine which molecules in the cell were responsible for inheritance until 1944 when DNA was shown as Genetic determiner.

In 1902, Sir Archibald Edward Garrod became the first person to associate Mendel's theories with a human disease. In 1905, Wilhelm Johannsen introduced the term 'gene' and William Bateson that of ‹genetics'. In 1910, Albrecht Kossel is awarded the first Nobel Prize in Physiology or Medicine for his discovery of the five nucleotide bases- adenine, cytosine, guanine, thymine and uracil. In 1911, Thomas Hunt Morgan argued that genes are on chromosomes, based on observations of a sex-linked white eye mutation in fruit flies. In 1913, his student Alfred Sturtevant used the phenomenon of genetic linkage to show that genes are arranged linearly on the chromosome. However, it wasn't until 1944 that deoxyribonucleic acid (DNA) was identified as the 'transforming principle' when Oswald Avery's team proves that DNA, not protein, is the genetic molecule. In 1944, Maclyn McCarty and his colleagues, Colin MacLeod and Oswald Avery published their landmark paper on the transforming ability of DNA. In 1950, Erwin Chargaff summarised his two major findings regarding the chemistry of nucleic acids: first, that in any double-stranded DNA, the number of guanine units is equal to the number of cytosine units and the number of adenine units is equal to the number of thymine units, and second that the composition of DNA varies between species. These discoveries are now known as 'Chargaff's Rules'. In 1952 - Rosalind Franklin crystallized DNA fibres.



In 1953 - James Watson and Francis Crick discover the double helix structure of DNA, Using available X-ray data and model building, they were able to solve the puzzle that had baffled scientists for decades. They published the now-famous paper in Nature in April, 1953 and in 1962 they were awarded the Nobel Prize for Physiology or Medicine along with Maurice Wilkins.

In 1953, Theoretical physicist and astronomer George Gamow decided to make the race more interesting - he created an exclusive club known as the "RNA Tie Club", in which each member would put forward their ideas about how nucleotide bases were transformed into proteins by the body›s cells. He handpicked 20 members - one for each amino acid - and they each wore a tie carrying the symbol of their allocated amino acid. Ironically, the man who was to discover the genetic code, Marshall Nirenberg, was not a member.

1959 - An additional copy of chromosome 21 linked to Down's syndrome In 1961, the pair performed an experiment which showed that a chain of the repeating bases Uracil forced a protein chain made of one repeating

amino acid, phenylalanine. This was a breakthrough experiment which proved that the code could be broken.

Finally, in 1965, Marshall Nirenberg became the first person to sequence the code. In 1968, his efforts were rewarded when he, Robert W. Holley and Har Gobind Khorana were jointly awarded the Nobel Prize.

1977 - Frederick Sanger develops a DNA sequencing technique which he and his team use to sequence the first full genome – that of a virus called phiX174. In 1980, Frederick Sanger shares the Nobel Prize for Chemistry with Wally Gilbert and Paul Berg, for pioneering DNA sequencing methods.In 1983, a genetic marker linked to HD was found on Chromosome 4, making it the first genetic disease to be mapped using DNA polymorphisms. However, the gene was not finally isolated until 1993.

In 1990, Human Genome Project was launched. The project was aimed to sequence all 3 billion letters of a human genome in 15 years.

Year 1996 revolutionize the idea behind Science because The world famous Dolly the sheep was first cloned from an adult cell to complete mammal. The feat was ground-breaking - whilst animals such as cows had previously been cloned from embryo cells, Dolly demonstrated that even when DNA had specialised, it could still be used to create an entire organism.

Evolution of Genomics - Early Sequencing Efforts

In 1964, Robert W. Holley and colleagues published the first nucleic acid sequence ever determined, the ribonucleotide sequence of alanine transfer RNA. Extending this work, Marshall Nirenberg and Philip Leder revealed the triplet nature of the genetic code and were able to determine the sequences of 54 out of 64 codons in their experiments. In 1975, he and Alan Coulson published a sequencing procedure using DNA polymerase with radiolabelled nucleotides that he called the Plus and Minus technique.

These could be fractionated by electrophoresis on a polyacrylamide gel (called polyacrylamide gel electrophoresis) and visualised using autoradiography. The procedure could sequence up to 80 nucleotides in one go and was a big improvement, but was still very laborious. Nevertheless, in 1977 his group was able to sequence most of the 5,386 nucleotides of the single-stranded bacteriophage φX174, completing the first fully sequenced DNA-based genome.

The refinement of the Plus and Minus method resulted in the chain-termination, or Sanger method, which formed the basis of the techniques of DNA sequencing, genome mapping, data storage, and bioinformatic analysis most widely used in the following quarter-century of research.

In the same year Walter Gilbert and Allan Maxam of Harvard University independently developed the Maxam-Gilbert method (also known as the chemical method) of DNA sequencing, involving the preferential cleavage of DNA at known bases. For their groundbreaking work in the sequencing of nucleic acids, Gilbert and Sanger shared half the 1980 Nobel Prize in chemistry with Paul Berg.

The first complete genome sequence of an eukaryotic organelle, the human mitochondrion (16,568 bp, about 16.6 kb [kilobase]), was reported in 1981, and the first chloroplast genomes followed in 1986.

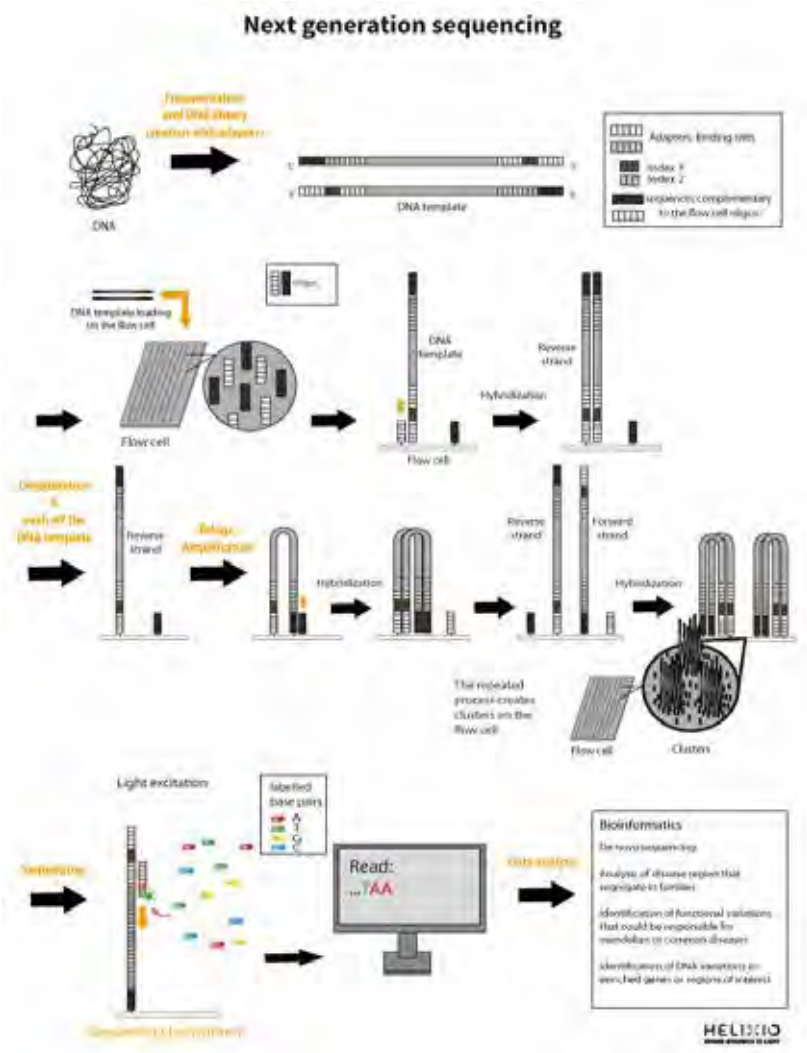
In 1992, the first eukaryotic chromosome, chromosome III of brewer's yeast *Saccharomyces cerevisiae* (315 kb) was sequenced. The first free-living organism to be sequenced was that of Haemophilus influenzae (1.8 Mb [megabase]) in 1995.

Steps underlying genomics

After an organism has been selected, genome projects involve three components:

- DNA in hand – extraction of DNA
- the sequencing of DNA
- the assembly of sequence to create a representation of the original chromosome a region or a network of genes
- and the annotation and analysis of that representation using bioinformatics.

DNA was first isolated by the Swiss physician, Friedrich Miescher, in 1869 while working in the laboratory of the biochemist Felix Hoppe-Seyler. The simple **DNA extraction** procedure involve the following steps:



Step 1. Breaking cells open to release the DNA

Step 2. Separating DNA from proteins and other cellular debris

Step 3. Precipitating the DNA with an alcohol

Step 4. Cleaning the DNA

Step 5. Confirming the presence and quality of the DNA

Once extracted, DNA can be used for molecular analyses including PCR, electrophoresis, sequencing, fingerprinting and cloning.

DNA Sequencing

The eight important methods used for DNA sequencing are:

(1) Sanger's Method (2) Maxam and Gilbert Method (3) Hybridization Method (4) Pal Nyren's Method/Pyrosequencing (5) PCR based sequencing (6) Slab Gel Sequencing Systems and (7) Capillary Gel Electrophoresis (8) Relatively new is Nanopore based sequencing.

Genome sequencing approaches fall into two broad categories, shotgun and high-throughput (or next-generation) sequencing.

Shotgun sequencing is a sequencing method designed for analysis of DNA sequences longer than 1000 base pairs, up to and including entire chromosomes. For much of its history, the technology underlying shotgun sequencing was the classical chain-termination method or 'Sanger method', which is based on the selective incorporation of chain-terminating dideoxynucleotides by DNA polymerase during in vitro DNA replication.

High-throughput sequencing specifically refers to sequencing techniques like Illumina that allow you to sequence massive amounts of DNA at once (hundreds of thousands of strands), as opposed to older techniques such as cloning the cDNA in plasmids, followed by sequencing.

Any high-throughput technique tries to measure several variables simultaneously. The examples include, other than the Next Gen DNA sequencing, RNA sequencing, protein identification and quantification by mass spectrometry (LC-MS), lipid profiling by GC-MS etc.

There are also medium-throughput techniques that can measure several variables but much less than high-throughput techniques. Many low-throughput techniques can be converted to medium-throughput by some level of automation and experimental planning. Example would include real-time PCR.

Sequence assembly

After sequencing the work left for data analysis is job of a bioinformatics specialist who read out the machine language and interpret the results. Because Bioinformatics has emerged as a whole new discipline, we have secured a special issue for this and will discuss more about data analysis and other associated things in the concerned issue. To Just understand the next steps, we are giving an introduction here:

Assembly can be broadly categorized into two approaches: *de novo* assembly, for genomes which are not similar to any sequenced in the past, and comparative assembly, which uses the existing sequence of a closely related organism as a reference during assembly.

Genome annotation is the process of attaching biological information to sequences, and consists of three main steps:
- Identifying portions of the genome that do not code for proteins
- Identifying elements on the genome, a process called gene prediction, and
- Attaching biological information to these elements.

Development of genome sequencing platforms

The First Generation of Sequencing

Gel electrophoresis was first used to separate the fragments according to their length. By knowing which terminator base is associated with which fragment on the gel, the base sequence was constructed.

Commercialization of the first DNA sequencer - "Direct-Blotting-Electrophoresis-System GATC 1500" by GATC Biotech, was intensively used in the framework of the EU genome-sequencing programme, the complete DNA sequence of the

Photo: First automated DNA sequencing machine. Credit: Lloyd Smith.

yeast *Saccharomyces cerevisiae* chromosome II.

Leroy E. Hood's laboratory at the California Institute of Technology announced the first semi-automated DNA sequencing machine in 1986. This was followed by Applied Biosystems' marketing of the first fully automated sequencing machine, the ABI 370, in 1987 and by Dupont's Genesis 2000.

In 1987, scientists at DuPont published details of a system for rapid DNA sequencing using fluorescent chain-terminating dideoxynucleotides (Prober, J.M. *et al. Science* 1987). Developed by George Trainor and colleagues, the instrument was named the Genesis 2000 DNA Analysis System and featured a 12-lane gel and an argon laser to read the fluorescently labeled DNA fragments. The major advance was to label the dideoxynucleotide terminators rather than the oligonucleotide primers. Because of this and the emission characteristics of the dye set, the instrument was able to combine the four labeled deoxynucleotides into a single lane. DuPont briefly marketed the instrument but subsequently sold the license to Applied Biosystems.

The Second Generation of Sequencing

Sanger and Maxam-Gilbert sequencing technologies were the most common sequencing technologies used by biologists until the emergence of a new era of sequencing technologies opening new perspectives for genomes exploration and analysis. These sequencing technologies were firstly appeared by Roche's 454 technology in 2005 and were commercialized as technologies capable of producing sequences with very high throughput and at much lower cost than the first sequencing technologies. These new sequencing technologies are generally known under the name of "Next Generation Sequencing (NGS) Technologies" or "High Throughput Sequencing Technologies".

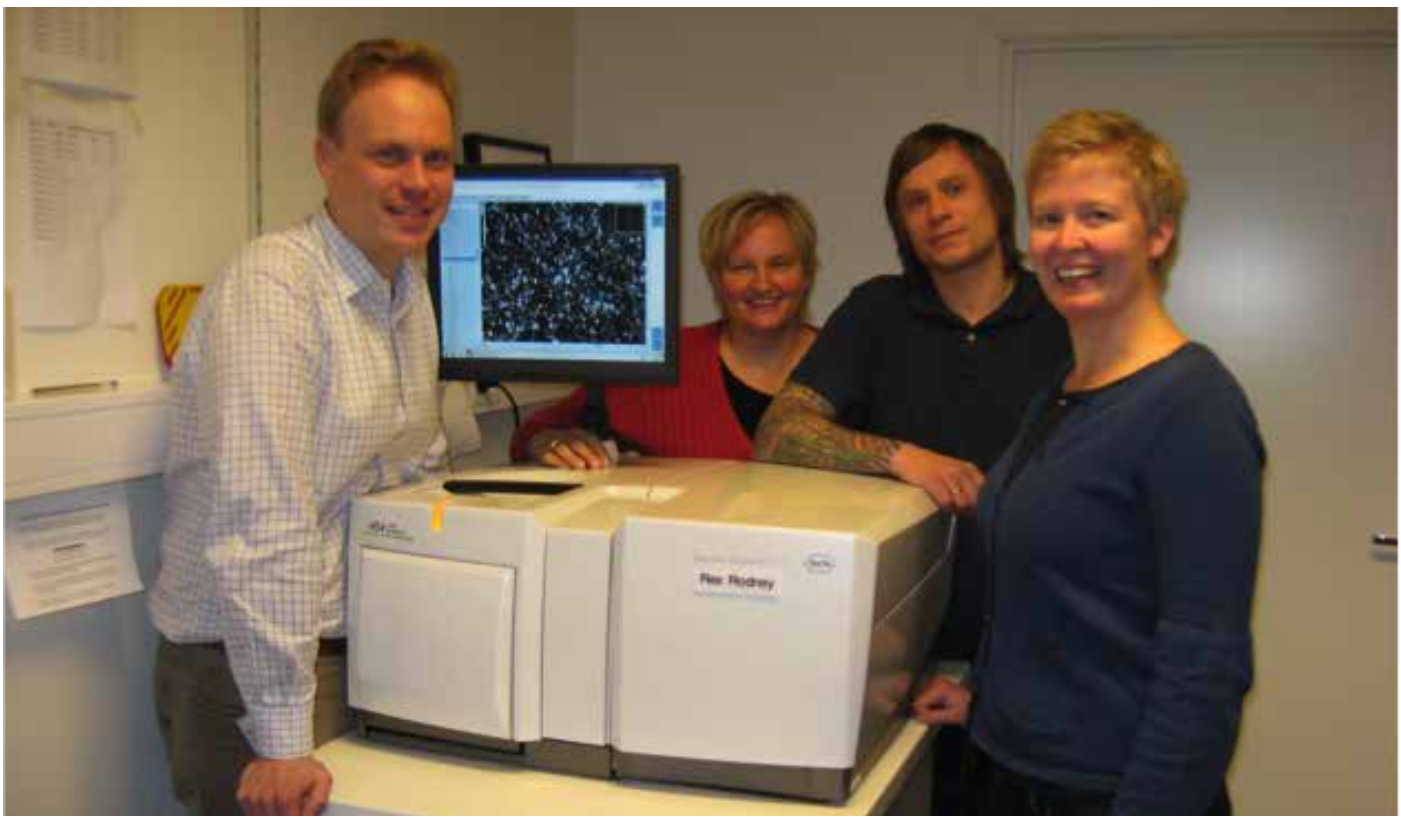


Photo: The author (left) with colleagues showing off their 454 GS FLX
Credit: https://flxlexblog.wordpress.com

Roche/454 sequencing appeared on the market in 2005, using pyrosequencing technique which is based on the detection of pyrophosphate released after each nucleotide incorporation in the new synthetic DNA strand (http://www.454.com). The pyrosequencing technique is a sequencing-by-synthesis approach.

Life Technologies commercialized the Ion Torrent semiconductor sequencing technology in 2010 (https://www.thermofisher.com/us/en/ home/brands/ion-torrent.html). It was similar to 454 pyrosequencing technology but it does not use fluorescent labeled nucleotides like other second-generation technologies. It was based on the detection of the hydrogen ion released during the sequencing process.

The Solexa company developed a new method of sequencing. Illumina company (http://www.illumina.com) purchased Solexa that started to commercialize the sequencer Ilumina/Solexa Genome Analyzer (GA). Illumina technology is sequencing by synthesis approach and is currently the most used technology in the NGS market.

ABI/SOLiD sequencing Supported Oligonucleotide Ligation and Detection (SOLiD) is a NGS sequencer Marketed by Life Technologies (http:// www.lifetechnologies.com). In 2007, Applied Biosystems (ABI) has acquired SOLiD and developed ABI/SOLID sequencing technology that adopts by ligation (SBL) approach.

The Third Generation of Sequencing

The second-generation of sequencing technologies previously discussed have revolutionized the analysis of DNA and have been the most widely used compared to the first generation of sequencing technologies. However, the SGS technologies generally require PCR amplification step which is a long procedure in execution time and expensive in sequencing price. These third generations of sequencing have the ability to offer a low sequencing cost and easy sample preparation without the need PCR amplification in an execution time significantly faster than SGS technologies. In addition, TGS are able to produce long reads exceeding several kilobases for the resolution of the assembly problem and repetitive regions of complex genomes.

There are two main approaches that characterize TGS: The single molecule real time sequencing approach (SMRT) that was developed by Quake laboratory and the synthetic approach that rely on existing short reads technologies used by Illumina (Moleculo) to construct long reads. The most widely used TGS technology approach is SMRT and the sequencers that have used this approach are Pacific Biosciences and Oxford Nanopore sequencing (specifically the MinION sequencer).

In 2014, Oxford Nanopore Technologies released the MinION device that promises to generate longer reads that will ensure a better resolution structural genomic variants and repeat content. It's a mobile single-molecule Nanopore sequencing machine which measures four inches in length and is connected by a USB 3.0 port of a laptop computer. MinION can provide very long reads exceeding 150 kbp which can improve the contiguity of the *denovo* assembly.

MinION - A pocket frirndly DNA Sequencing Machine

Available Genome Sequencers

Here is the list of most prevalent genome sequencers and their specifications, the more updated and elaborated version is available on next page:

Comparing metrics and performance of next-generation DNA sequencers.[36]

Sequencer	Ion Torrent PGM [5][37][38]	454 GS FLX [10]	HiSeq 2000 [5][10]	SOLiDv4 [10]	PacBio [5][39]	Sanger 3730xl [10]
Manufacturer	Ion Torrent (Life Technologies)	454 Life Sciences (Roche)	Illumina	Applied Biosystems (Life Technologies)	Pacific Biosciences	Applied Biosystems (Life Technologies)
Sequencing Chemistry	Ion semiconductor sequencing	Pyrosequencing	Polymerase-based sequence-by-synthesis	Ligation-based sequencing	Phospholinked fluorescent nucleotides	Dideoxy chain termination
Amplification approach	Emulsion PCR	Emulsion PCR	Bridge amplification	Emulsion PCR	Single-molecule; no amplification	PCR
Data output per run	100-200 Mb	0.7 Gb	600 Gb	120 Gb	0.5 - 1.0 Gb	1.9~84 Kb
Accuracy	99%	99.9%	99.9%	99.94%	88.0% (>99.9999% CCS or HGAP)	99.999%
Time per run	2 hours	24 hours	3–10 days	7–14 days	2–4 hours	20 minutes - 3 hours
Read length	200-400 bp	700 bp	100x100 bp paired end	50x50 bp paired end	14,000 bp (N50)	400-900 bp
Cost per run	$350 USD	$7,000 USD	$6,000 USD (30x human genome)	$4,000 USD	$125–300 USD	$4 USD (single read/reaction)
Cost per Mb	$1.00 USD	$10 USD	$0.07 USD	$0.13 USD	$0.13 - $0.60 USD	$2400 USD
Cost per instrument	$80,000 USD	$500,000 USD	$690,000 USD	$495,000 USD	$695,000 USD	$95,000 USD

Fig, The picture does not include Oxford Nanopre sequencers which we will discuss in separate article in this issue. Source: Wikipedia

Genome databases

Genome databases are an organized collection of information that have resulted from the production or mapping of genome (sequence) or genome product (transcript, protein) information. The process of making a genome database involves taking information that researchers have generated and organizing it into a database so that biological inferences can be made.

The available sequencing platforms has resulted in the generation of enormous amount of data which has placed into different sets of databases like according to the organism, product of sequence or any specific regions of genome(transcript). Here is a list but it it is likely that this list would miss out one or more database name as the list is very long at present. We will discuss more about this in Bioinformatics special issue of this magazine in some next issue.

1000 Genomes Project
Cancer Genome Atlas
Cold Spring Harbor Mammalian Promoter Database
ENCODE Project
Ensembl
Entrez-Gene
FlyBase
GenBank
OMIM
Reactome
RefSeq
TAIR - The Arabidopsis Information Resource
UCSC Genome Browser
Wormbase

Platform	Instrument	Reads per run	Avg Read length (pb)	Read Type	Error Type	Error Rate (%)	Data Generated per run (Gb)	Year
First Generation								
ABI Sanger	3730xl	96	400 – 900*	SE	NA	0.3	0.00069 to 0.0021	2002
Second Generation								
454	GS20	200	100	SE, PE	indel	1	0.02	2005
454	GS FLX	400	250	SE, PE	indel	1	0.1	2007
454	GS FLX Titanium	1M	450	SE, PE	indel	1	0.45	2009
454	GS FLX	1M	700	SE, PE	indel	1		2011
	Titanium+						0.7	
454	GS Junior	100	400	SE, PE	indel	1	0.04	2010
454	GS Junior+	100	700	SE, PE	indel	1	0.07	2014
Illumina	MiniSeq	25M (maximum)	150	SE, PE	mismatch	1	7.5 (maximum)	2013
Illumina	MiSeq	25M (maximum)	300	SE, PE	mismatch	0.1	15 (maximum)	2011
Illumina	NextSeq	400M (maximum)	150	SE, PE	mismatch	1	120 (maximum)	2014
Illumina	HiSeq	5B (maximum)	150	SE, PE	mismatch	0.1	1.5Tb (maximum)	2012
Illumina	HiSeq X	6B (maximum)	150	SE, PE	mismatch	0.1	1.8Tb (maximum)	2014
SOLiD	5500 W	3B	75	SE	mismatch	–0.1	160	2011
SOLiD	5500xl W	6B	75	SE	mismatch	–0.1	320	2013
Ion Torrent	PGM 314 chip v2	400.000-550.000	400	SE	indel	1	0.06 to 0.1	2011
Ion Torrent	PGM 316 chip v2	2M - 3M	200	SE	indel	1	0.6 to 1	2011
Ion Torrent	PGM 318 chip v2	4M - 5.5M	400	SE	indel	1	1.2 to 2	2013
Ion Torrent	Ion Proton	60M - 80M	200	SE	indel	1	10	2012
Ion Torrent	Ion S5/S5XL 520	3M - 5M	400	SE	indel	1	1.2 to 2	2015
Ion Torrent	Ion S5/S5XL 530	15M-20M	400	SE	indel	1	03 to 05	2015
Ion Torrent	Ion S5/S5XL 540	60M - 80M	400	SE	indel	1	NA	2015
Third Generation								
PacBio	RS C1	432	1300	SE	indel	15	0.54	2011
PacBio	RS C2	432	2500	SE	indel	15	0.5 to 1	2012
PacBio	RS C2 XL	432	4300	SE	indel	15	0.5 to 1	2012
PacBio	RS II C2 XL	564	4600	SE	indel	15	0.5 to 1	2013
PacBio	RS II P5 C3	528	8500	SE	indel	13	0.5 to 1	2014
PacBio	RS II P6 C4	660	13500	SE	indel	12	0.5 to 1	2014
PacBio	Sequel	350	10000	SE	NA	NA	7	2016
Oxford Nanopore	MinION Mk	100	9545	1D,2D	indel/mismatch	12	1.5	2015
Oxford Nanopore	PromethION	NA	9846	1D,2D	NA	NA	2Tb to 4Tb	2016

Human genome project

A rough draft of the human genome was completed by the Human Genome Project in early 2001, creating much fanfare. This project, completed in 2003, sequenced the entire genome for one specific person, and by 2007 this sequence was declared "finished" (less than one error in 20,000 bases and all chromosomes assembled). In the years since then, the genomes of many other individuals have been sequenced, partly under the auspices of the 1000 Genomes Project, which announced the sequencing of 1,092 genomes in October 2012.

Diversified Applications of Genomics

What we can do using data generated by sequencers and bioinformatics, this has numerous applications in all fields of biosciences like clinical agricultural industrial environmental, we are discussing some broad applications applicable to all above mentioned areas here.

1. Functional genomics uses genomic data to study gene and protein expression and function on a global scale (genome-wide or system-wide), focusing on gene transcription, translation and protein-protein interactions, and often involving high-throughput methods.

2. Structural Genomics aimed at determining the three-dimensional structures of gene products in an efficient and high-throughput mode.

3. Epigenomics is a method of analysis of DNA methylation, mapping of transcription factors, modified histones, and epigenetic regulators. Epigenomics studies differential gene expression triggered by chemical reactions or other stressors that do not alter the DNA sequence. An epigenome is a cell's full set of epigenetic modifications.

4. Metagenomics is the study of the collective genomes of the members of a microbial community. It involves cloning and analyzing the genomes without culturing the organisms in the community, thereby offering the opportunity to describe the planet's diverse microbial inhabitants, many of which cannot yet be cultured. The field of metagenomics has also been referred to as environmental genomics, ecogenomics, and community genomics. A primary aim of metagenomics experiments is to identify which genes and metabolic pathways are present

5. Genomic medicine NHGRI defines genomic medicine as "an emerging medical discipline that involves using genomic information about an individual as part of their clinical care (e.g., for diagnostic or therapeutic decision-making) and the health outcomes and policy implications of that clinical use." Already, genomic medicine is making an impact in the fields of oncology, pharmacology, rare and undiagnosed diseases, and infectious disease. Pharmacogenomics involves using an individual›s genome to determine whether or not a particular therapy, or dose of therapy, will be effective. Currently, more than 100 FDA-approved drugs [fda.gov] have pharmacogenomics information in their labels, in diverse fields such as analgesics, antivirals, cardiovascular drugs, and anti-cancer therapeutics. For example, Alexis and Noah Beery, a pair of Californian twins, were misdiagnosed with cerebral palsy, but DNA sequencing pointed to a new diagnosis, as well as a treatment, to which both children are responding well. Another patient who was misdiagnosed (for 30 years) with cerebral palsy was also found to have a treatable dopa-responsive dystonia thanks to whole exome sequencing. In another case, a young boy in Wisconsin, Nic Volker, was able to be cured of an extreme form of inflammatory bowel disease after his genome sequence revealed that a bone marrow transplant would likely be life-saving.

6. Synthetic biology is the design and construction of new biological parts, devices, and systems, and the re-design of existing, natural biological systems for useful purposes.

7. Conservation genomics is the application of genomic analysis to the preservation of the viability of populations and the biodiversity of living organisms. Genomic methods can be used to argue species identity, degree of hybridization, genetic diversity, demographic history and effective population size.

8. Precision Medicine precision medicine is "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person. Although the term "precision medicine" is relatively new, the concept has been a part of healthcare for many years. For example, a person who needs a blood transfusion is not given blood from a randomly selected donor; instead, the donor's blood type is matched to the recipient to reduce the risk of complications.

9. **Forensic Science** Targeted sequencing of the genes used for human identification can inform forensic DNA testing and deliver more conclusive results for criminal casework, missing persons cases, or disaster victim identification. Because of the complex nature and large numbers of biological samples at the heart of these applications, analytical capabilities must be robust, reliable, and scalable. Today, most forensic DNA testing utilizes PCR and capillary electrophoresis (CE)-based methods for the analysis of forensic samples. However, numerous limitations in that approach exist, including challenges presented by degraded DNA, low quantity DNA, or complex DNA mixtures, which can result in a forensic case going unresolved. Whole-genome sequencing (WGS) reveals all the allelic differences between individuals across the whole human genome, including variations that occur in coding, regulatory, and intronic regions.

10. Nationalised healthcare The Global Alliance for Genomics and Health (GA4GH) is an international, nonprofit alliance formed in 2013 to accelerate the potential of research and medicine to advance human health. Bringing together 500+ leading organizations working in healthcare, research, patient advocacy, life science, and information technology, the GA4GH community is working together to create frameworks and standards to enable the responsible, voluntary, and secure sharing of genomic and health-related data.

Jobs prospects for genome biologists

As a healthcare scientist (also known as a clinical scientist) working in genomics, you'll examine patient samples to identify genetic and genomic abnormalities, which may cause inherited or acquired (non-inherited) diseases.

You will work closely with other healthcare professionals such as clinicians to provide advice to patients about diagnosis and treatment, as well as help predict whether other family members or future generations are at risk from the abnormality.

Your work will typically fall into three main categories:

prenatal diagnosis - examining cells for possible abnormalities in the foetus

predictive testing - to identify patients who may be at risk from single or multiple gene disorders

confirmation of diagnosis.

Conclusion

Genomics the advanced study of Genetics involve studying whole genome and thus it gives a broader picture of Genetic constitution of an individual as well as the species as a whole. With the completion of Human Genome project many possibilities for Biomedical applications came through with time, and similar is the case with Plant Genomics.

Since the discovery of Mendel's work and after many criss cross we have now pool of Genome specialist, sophisticated instruments and Intelligent softwares. These all when work together generate applications which are revolutionizing the surrounding and making our lives more comfortable. For example Fragile X syndrome once a bane has now become less stressful because of earliest diagnosis and treatment. Today Genomics has become a whole new discipline both for academia and industry and gave rise to a whole new level of competition to find innovative uses using Genomics as a tool.

In India, many institutions and scientists are working in the area of genomics,, for example CSIR's autonomous institution IGIB has emerged as a specialist in research of Genomics. This is just a single example of institution but we cannot ignore other Genomic Scientists who are working in other institutions like in ICMR, DBT, DRDO and many universities.

Recently Indians as part of International collaborative project have helped to elucidiate Wheat Genome, which is a main crop around the world. This will have enormous applications like to develop high yielding varieties, to make stress tolerant crops etc.

Similarly, Indian Genomics Scientists are working toward Biomedical research and trying to include Genetic testing for prenatal or new born screening, which in future can help to reduce disease burden among Indian population.

Along with advancement in research industry has also adjusted with growing needs. Like OXFORD NANOPORE has emerged as the best sequencing service provider at lowest cost. With 12 years of continous hard work and evolutionary ideas they had made the world's smallest DNA sequencer and lowered the cost of sequencing which was once a dream. Now with their technology anyone can do sequencing.

Considering future, much is awaitng to come because of recent advances and data generation, so genomics provides limitless avenues to explore. Still we have many organism whose genetic informations are unexplored so one can go ahead to do the work that not been addressed yet.

TOP GENOMICS SCIENTIST

Short Living Biography

Dr B K Thelma

Dr. Bittianda Kuttapa Thelma

Fellow- IASc, INSA, NASI

Professor, Department of Genetics, University of Delhi- South campus

by Piyush Kumar

Prof B K Thelma, known as Thelma among the BioScience community is a well recognized leader in Medical Genomics Scientific research and among the few scientists who translated her research into application. Dr Thelma is an excellent example to understand how Genomics is done and how it is applied for the welfare of general public. Thus we are trying to write as much as possible about her for our readers who search for new avenues and career prospects in Genomics.

Early Life

Dr Thelma came from a pretty little town called Madikeri, situated in the hills and valleys of a heavenly place called Coorg, some three hours away from Mysore. She was raised by a very loving, caring and progressive family - which included her parents, grandparents and several aunts - in a small house with a large backyard. Her parents were busy state government officials. Her grandfather was a highly disciplined, gentle yet firm man who had served in the British army and was an art teacher in a government school. Thelma's father, B G Kuttapa, had a transferable job buther mother, Muthamma, also a government employee, chose to stay with her elderly parents and look after them and the extended family.

One of her aunts, who was the first woman to serve in the government office in Coorg, took on the role of her mother and teacher. In her household, there was no discrimination done between boys and

RESEARCH INTERESTS:

- Human molecular genetics and Medical genomics
- Genetics of complex brain and inflammatory disorders in humans (Schizophrenia, Parkinson's disease, Rheumatoid arthritis, Inflammatory bowel disorders, Celiac Disease)
- Pharmacogenetics of commonly used antipsychotic, anti-PD, anti rheumatoid drugs
- Identification of new gene(s) for Mental retardation and Parkinson's disease
- Population genomic architecture
- DNA Diagnostics

Notable Honors and Awards

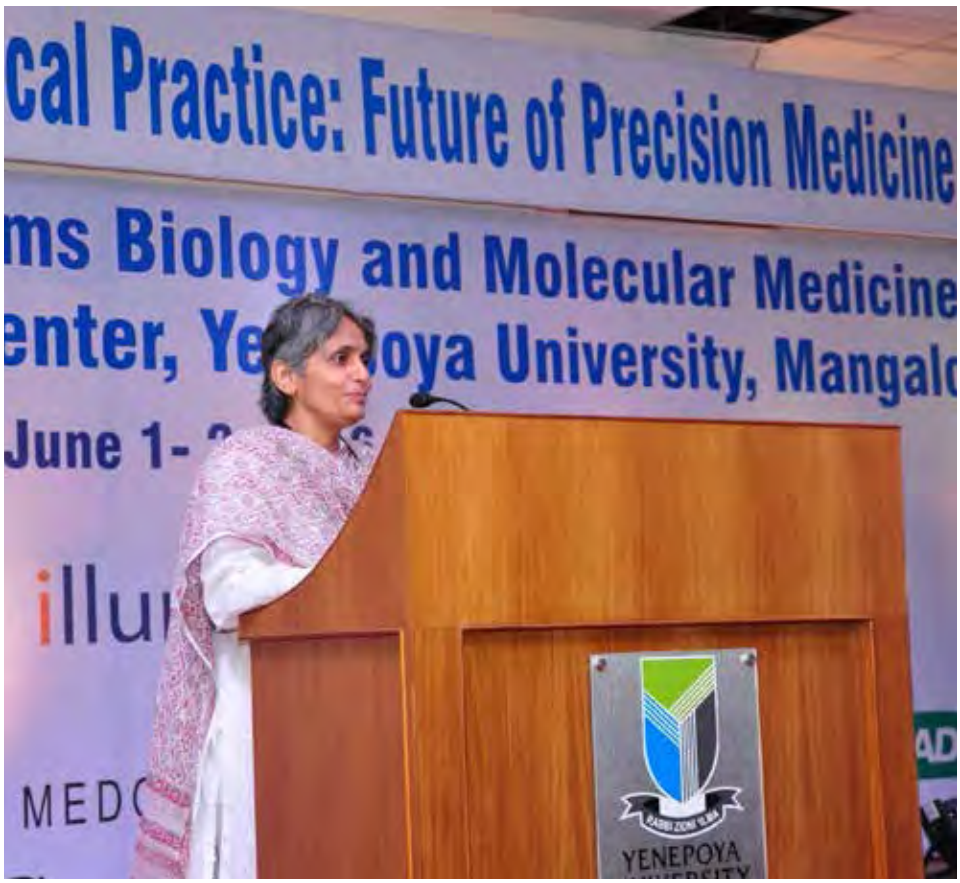
✳ Dr Thelma received the Fogarty International Research Career Award in 1997.
✳ Fellow, Indian National Science Academy
✳ Fellow, Indian Academy of Sciences, India
✳ Fellow, The National Academy of Sciences, India
✳ J.C.Bose fellow
✳ Ex-Member, Scientific Advisory Council to the Prime Minister
✳ Ex-Member, Science and Engineering Research Board (SERB)
✳ Ex-Member, Human Genetics Task Force, Dept. of Biotechnology;
✳ Subject expert, Indian Council of Medical Research
✳ Member, Guha Research Conference
✳ Trustee, XV International Genetics Congress Trust
✳ Ex-Vice President, Indian Society of Cell Biology
✳ Member - KVPY Management Committee

girls. Everyone was held to the highest standard. She began primary school at the age of 3. She got the best education which middle-class parents could afford and, her parents repeatedly reminded her and her two siblings that education was the only thing which would stand by them.

Opting Science

Since there was a close relative who was a doctor, Thelma always wanted to be a doctor but her father wanted her to do either a Master's in Maths or join the IAS. Somewhere at the back of her mind the notion of serving people was always there maybe because she saw the way her mother and her aunts tookcare of her grandparents. She was told that if she wanted to do medicine the best option was to get into biology. In Class X, she was the only one in her school to get first class in all four parts. Thelma did not do badly in her pre-university exams but she was only 14 years old and one had to be 16 to get into medical school so there was no option but to do a BSc. and Thelma was very disappointed. She went back to Mount Carmel College, Bangalore and took biology during her BSc.

Upon completing B. Sc., she decided to pursue a Master's in Zoology. While doing Master's, the head of the department gave her cytology as the special paper, instead of physiology – which she wanted. She could not come to terms with their decision and resisted dedicating too much time to the course. She constantly interacted with another mentor and her students who were pursuing Ph.D in Animal physiology. This stint motivated her to pursue a Ph.D in biomedical research.



Doing Ph.D

Due to poor preparation, she says, she did not get to do Ph.D at any of her first choice schools but she joined Ph.D. in the Zoology department, at Delhi University. Her obsession to do biomedical research led her to her Ph.D. mentor Prof. S.R.V. Rao. The first two or three years in the lab she recalls were a breeze, for in the 1970s the pressure of doing research in science was not as much as it is today and things were more relaxed. There were no computers or the internet. The students had to go through journals to read articles to be aware of current state of research on a subject. Thelma says that she cannot claim to have done great science at that time but what she did, she did well.. The lab had a very relaxed environment and the passion and commitment to a research question that she saw in her teacher made a lasting impression. Prof. Rao used to spend long hours at work, discussing not just the project at hand, but all other contemporary findings. He nurtured a passion for scientific research and emphasized the research process, rather than just the results. Thelma could not work on a direct biomedical project then but used a wild rat as her animal model to understand some basic concepts in cytogenetics. She had the opportunity to do a lot of tissue culture work.

During her PhD, the fellowship was just four hundred rupees. But it did not seem to matter. It covered her hostel costs, was enough for occasional outings and even small trips outside Delhi. It even allowed for small but precious gifts for her family when she visited them annually.

International Exposure

Once a person completes a Ph.D the obvious choice is to go for a Post-doc. Thelma now wanted to work in the area of genetic disease and engage in bio-medical research. She was fortunate enough to get a post-doctoral fellowship in 1984 at the Department of Research, University Hospital, Human Genetics Laboratory at Zentrum fur Lehre and Forschung (ZLF) at Basel, Switzerland. The renowned Dr Hans Jakob Muller took her on as a Post-doc student.

Because she was finally in a hospital setting, the experience was very satisfying for her. Thelma was supposed to work on the genetics of human male infertility. It interested her because she knew it would give her the opportunity to work in a clinical setting. Maybe it was an indirect way of looking for what she had missed by not being a doctor. But she felt that she was finally on the road to doing something she had always wanted to do. There she began work on assessing chromosome anomalies in male

Academic Achievements:

* Team Leader, Centre For Excellence In Genome Sciences And Predictive Medicine - Funded by Department of Biotechnology, Govt. of India
* Member, International consortia on Genetics of Celiac disease & Inflammatory bowel disorders
* Member, Task Force, Dept. Biotechnology & Indian Council of Medical Research
* Mentored several Ph.D. students, Published several research papers
* Recipient of several national and international research funding.
* Visiting scientist, Max Planck Institute for Molecular Genetics, Berlin, Germany
* Visiting Scientist, Dept. of Psychiatry, Hadassah Medical Centre, Jerusalem, Israel
* Visiting scientist, Dept. of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh, Pittsburgh, USA
* Fogarty International Research Career Award- Univ. Pittsburgh, USA
* Visiting Scientist- Dept. of Human Genetics, Memorial Sloan Kettering Cancer Centre, New York, USA
* Biotechnology Associateship- Institute of Human Genetics, Berlin, Max-Planck Institute, Munich, and Physical Chemistry Institute, Heidelberg, Germany
* Biotechnology Associateship- Centre for Cellular and Molecular Biology, Hyderabad

Member- Scientific and advisory committee
The Fragile X Society is based in Mumbai, India, and has successfully created a network all over the country with parents and eminent doctors. The society promotes public and professional awareness. We extend help to families with affected children in terms of literature (translated versions available on request), guidance and a deep understanding of how Fragile X Society can impact families.

Scientific Achievements:

Dr Thelma contributed significantly to the teaching of cytogenetics and developed a very strong teaching and research programme in human genetics. She pursued intensive research on the understanding of functional significance of repetitive sequences on the X and Y chromosomes using a rodent model.

Her later researches focused on: genetics of complex traits, particularly brain disorders including schizophrenia (SCZ), Parkinson's disease (PD), mental retardation (MR); and inflammatory diseases such as Rheumatoid arthritis and inflammatory bowel disorders.

Role of genes from the dopaminergic pathway in SCZ, PD and tardive dyskinesia are her major findings. Her studies on disease genomics of the genetically distinct Indian population provided major insights into the population specific genetic susceptibility patterns.

Pharmacogenetics, the science of inter-individual variation in drug response, is another area where her group made significant contributions. She has mentored 21 PhD students and has over 100 publications to her credit.

Other Research based Contributions:

Dr Thelma established the DNA-based diagnosis facilities for fragile X syndrome, the most common form of inherited mental retardation, with financial support from Department of Biotechnology. Her Lab is one of the few which offers this national level diagnostic service.

infertility and trained in in vitro fertilization method.

The Basel institution where she did Post-doc wanted her to stay on and offered her a job, but Thelma knew she had to come back to her country.

Returning to India

She returned to India and decided to become a teacher - scientist so that she could inspire others the way Prof. Rao did. When Thelma returned, Professor and Mrs Rao were not in the country. Thelma could return to her parent lab, but finding accommodation on the university campus for post-doctoral workers, especially women, was very difficult at that time.

She took over Professor Rao's teaching responsibilities to the students doing their Master's in Zoology for the six months when he was out of the country and also stayed with their three children. Meanwhile she applied for a Pool Officer's post and got the position. She joined as a Pool Officer, continued her research and fulfilled her assignment of teaching students doing their Master's. She was subsequently selected as a University Research Associate in the same department.

People often asked her why she did not opt for a permanent position as a college lecturer but Thelma enjoyed doing research in her parent lab and within there she nurtured the desire to have a university job where she could teach and also have a research lab of her own.

Thus she had several years of research experience, and knew her cytogenetics well. She worked with animal models but along the way she also had a chance to look at humans who wanted to get their chromosomes tested in the laboratory, so she also had experience working with human material. All this was in her bag while she waited for a job of her liking.

Getting a Job

She applied for the posts of lecturer and Reader in the Genetics Department in the South Delhi University Campus. When the interview letters came, she prepared very well. After performing well for the interview for the lecturer's post, she went in the afternoon for the interview for the Reader's post. The Vice-Chancellor of the University who was in both the interview panels jokingly remarked, 'Oh Thelma, you have returned like a bad coin'. Thelma said, 'No, I have returned as a prodigal daughter'.

Thelma was chosen for the lecturer's post. The Reader's post was not filled. This was 1987 and for the next eleven years, Thelma remained a lecturer and enjoyed teaching in the Genetics Department. But in the afternoon, she had to take an auto or board the Univer-

Summary of scientific contributions of Dr B K Thelma

Dr Thelma is well recognized for her consistent and original contributions in the field of medical genomics in the country. Working together with clinicians to utilize the valuable patient resource available in the ethnically distinct Indian population and using contemporary genome analysis technologies,her contributions to discovery genomics both in single gene and complex disorders have been consistent and seminal.

Some of the major findingsof global relevance in the last five years include:

- Discovery of
(a) ARL15, asusceptibility gene for rheumatoid arthritis (Negi et al., 2013) &
(b) seven non-HLA genes/loci for ulcerative colitis (Juyal et al., 2014) based on the first ever Genome-wide association studies in the country;
(c) several risk loci for celiac disease (Senapati et al., 2014) &

Based on next generation sequencing
(d) MID2 for X-linked intellectual disability (Geetha et al., 2014);
(e) PODXL for autosonal recessive juvenile parkinsonism (Sumedha et al., 2016a)&
(f) RIC3 for autosomal dominant Parkinson's disease (Sumedha et al., 2016b) &
(g) TAAR1 (John et al., 2017); TIMP2 (John et al., 2018) & a few more conferring susceptibility to schizophrenia

-Pharmacogenomics of methotrexate in rheumatoid arthritis (Senapati et al., 2014)&

Functional characterisationof pharmacologically relevant dopaminergic gene variants (Michealraj et al., 2014;Punchaichira et al., 2017)

- To address the biggest global challenge of phenotypic heterogeneity limiting the understanding of genetic basis of common complex disorders, her group is pursuing an innovative approach of combining the doctrines of Ayurveda for deep phenotyping of individuals with modern genome analysis tools (Ayurgenomics) which is breaking new ground for predictive and personalized medicine.

- Disease diagnostics: Besides high quality basic research, in an unparalleled contribution for translational medicine/science for society, her persistent efforts using a public-private partnership mode for screening ~200,000 newborns (NBS) in Delhi State for 46 inborn genetic diseases,has generated the first ever systematic epidemiological data and mutation spectrum. This undoubtedly is of immense value for facilitating national policy decision(s) onmakingNBS mandatory in India.

Taking discovery to lead molecule development under the Center of Excellence in Genome Sciences and Predictive Medicine is the current pursuit of her group.

B K THELMA AT HER PH.D. CONVOCATION IN 1983

sity bus and return to the North Campus to her parent lab because the science departments at the South Campus were rather new and did not have any research labs yet.

As a lecturer Thelma taught cytogenetics, a subject she thoroughly enjoyed teaching. Alongside, she started writing research grant proposals. Her projects were still on the animal model but all along she knew that she had to do human genetics. She kept telling herself that once she got sufficient lab space she would begin work in human genetics. And that was where the turning point lay.

The animal model they were working on had something called as a Fragile-X chromosome. Just around that time the gene responsible for the Fragile-X Syndrome, the biggest cause of inherited mental retardation in humans, was identified by scientists abroad. She started work on that gene and that marked the beginning of Thelma's human genetics work in her own lab. A series of lucky breaks had brought her to this point of research. She soon knew that she had got a much needed foothold to switch over to human genetics research 'to do what her heart was really longing for', to put it in her words.At that time human genetics research was being done in a small way and only in a few labs in the country and human molecular genetics was almost not there.

1995 was the time when the Department of Genetics was getting a facelift. A new science building Bachawat Block with reasonable lab space was allotted for the Genetics Department. It was also the time when Thelma got her first Human Genetics Project from the Department of Biotechnology, Government of India to work on the molecular diagnosis of Fragile-X Syndrome together with Professor Meena Gupta, a paediatric neurologist at G B Pant Hospital, as a clinical collaborator. Together with her, Thelma started screening mentally retarded kids from several special schools across Delhi to detect if they had the Fragile-X mutation. Since it is an inherited condition one has to not only screen the affected child but also the extended family. Identifying one mutation positive child could help the entire family as expectant mothers can then be offered a prenatal diagnostic test to identify if there is a mutation in the growing foetus and thus prevent the birth of yet another affected child in the family. It is indeed a piece of work of immense applied value and a service which Thelma's lab continues to offer even today to clinical collaborators seeking diagnosis for hundreds of their young patients and their anxious parents from all over the country.

Thelma has been the Head of the Department of Genetics in the University of Delhi South Campus. Thelma tends to dismiss her struggle to reach this stage of her career and says that science is all that matters.

Current Status

Dr Thelma currently is a Professor at the Department of Genetics and Team leader, Centre of Excellence for Genome Sciences and Predictive Medicine funded by the Dept of Biotechnology, Govt. of India. She is a Science Advocate who is involved with many governmental and non-governmental organizations. Backed by a large body of data from a SERB, Govt. of India funded novel feasibility study on newborn screening for inborn errors of metabolism, that she recently completed along with a large team of clinical collaborators from 20 hospitals across Delhi state, she is advocating for newborn screening program to be made mandatory in the country. It will reduce the burden of this preventablegroup of disorders in the country and is an excellent example of translational medicine and a technology for the masses.

Market Research

International Market of Genomics

by Kamal Pratap Singh

Genomics market expands from cell culture to Data analysis, which include products and services at every step of a Genomics experiment. So the whole gamut of organizations comes into picture and we are going to summarize few of them which are on the top of list and atleast gains attention of every Genomic person or organization.

The worldwide Genomics Market is systematically categorized on the basis of products, applications and technologies. Instruments, services, and consumables are the three key product segments, with a nearly 60% share, consumables dominated the industry in 2013. The Genomics market comprises following categories, each category is connected to other category in many instances like you need consumables and softwares both for PCR and Microarray:

Consumables & Reagents

Instruments Systems and their Software

Products and Services

Other technologies (genotyping, gene expression, gene editing etc.)

Statistical and Computational or Bioinformatics products and Services

Detailed Report of Products and services that are used in Genomics

A researcher uses few or all of the products and services that are describe below. Some of them cannot be avoided to get best results either in research or in production, but the best results depend on what we are going to buy and use in our experiment or production. Some companies sell all of them whereas some are specializes in one of the category. After discussing the products and services we will see which company is pioneer in the segment and serving the very best. The necessary requirements of a good genomics experiment

require the following:

Cell, cell Culture and Molecular Biology products

Cell Culture media and reagents, Transfection reagents, cloning kits, and enzymes, to western blotting technologies, Cellular, GeneArt Custom DNA Oligos and Gene Synthesis and detection service, etc.

Cell Analysis - Identification and Quantification

Labeling and detection technologies, antibodies and immunoassays, cell imaging systems (including microscopy), Automated Cell Counter, , Flow Cytometer etc.

Nucleic acid isolation, Analysis and Cloning kits

Enzymes like Reverse transcriptases, DNA Polymerases, Restriction and modifying enzymes etc.

Electrophoresis Instruments and reagents, etc.

Lab Plasticware and Supplies

like Pipettes Tips, Bottletop and Filter Units, Chamber Slides and Chambered Coverglass, Conical Tubes, Cryotubes, Laboratory Bottles PCR Tubes, Plates & Accessories, storage plates and plate sealers., Cell Culture Plastics etc.

Lab Equipment

Cold storage, ovens and furnaces, centrifuges, incubators and safety cabinets, water baths, and stirrers and shakers etc.

Purification and Filtration etc.

PCR Solutions

PCR Instruments, Enzymes & Master Mixes, Real-Time PCR Assays, etc.

Sequencing:

Instruments & Reagents for all type of sequencing i.e. from gold-standard Sanger sequencing technology and fragment analysis on the capillary electrophoresis (CE) platform to flexible and scalable next-generation sequencing (NGS) etc.

Microarray analysis

The complete solution comprises genotyping arrays, reagent kits, a fully automated workflow, and easy-to-use free data analysis tools, Instruments. etc.

Data Analysis

High-content screening (HCS), Lab Data Management & Analysis Software Software for Copy Number Analysis, Cytogenetics Analysis, Agrigenomics Solutions, miRNA Profiling, Transcriptome Profiling etc.

Software, and Services

for Enterprise Solutions, Instrument Services etc.

Hotspots of Sequencing requirements

Research Centers, Academic and Government Institutes

Hospitals and Clinics

Pharmaceutical and Biotechnology Companies

Other End Users (NGOs, and agri-genomics organizations among others)

Genomics Market, by application

Diagnostics - For instance, genome editing is used in target gene modification in plants and eradication of vector borne diseases such as yellow fever, dengue, Zika, West Nile, Schistomiasis, Leishmaniasis and Lymes disease which is the segment that is attracting major portion of investments in agricultural and healthcare sector.

Healthcare - Drug Discovery and Development and or Precision Medicine

Agri-genomics Research

Animal Research

Other applications (Marine Research, biofuels, and coal mines among others)

Size of Genomics Market

As pet the reports published by several Market research agencies Genomics market has been estimated at a current value of 17 Billion USD.

According to Goldstein Research analyst forecast the genomics market size is set to reach USD 24.5 billion by 2025, at a CAGR of 11.2%. Grand View Research, Inc. estimates the global genomics market size will reach USD 27.6 billion by 2025. MarketsandMarkets Research Private Ltd. valued global Genomics market at USD 13.45 Billion in 2016 and is expected to grow at a CAGR of 10.2% to reach to USD 23.88 Billion by 2022. Research and Markets' report The global Genomics market is expected to reach USD 23.88 Billion by 2022 from USD 14.71 Billion in 2017, at a CAGR of 10.2%.

According to Goldstein Research Based on geography, Europe accounted for the largest share of the overall genomics market in 2017 at over 37.25%. While APAC is expected to witness the most significant development owing to strengthening economies of developing countries such as India and China and the increased focus of the respective governments on encouraging research in the field of genomics, in addition, China hosts the world's largest genomic research institute, the Beijing Genomics Institute in order to sustain the growth of genomics market. North America genomics market will grow at the substantial rate due to the ample amount of funds and presence of companies undertaking research in the field of genomics.

Profile of Top Genomics services provider worldwide

Because of our inability to include every organization we will talk about only those here which shares more than 60% global market share in their respective segments. Some of them are specialized and into only one domain but some have captured the whole supply chain. We will discuss those first which provides one stop solutions for all the needs of research and industry of Genomics.

One stop Source

It is very difficult to find a one stop source for all your needs in Genomics or any other Biotechnology segment but in Genomics our research says that **Thermo Fisher Scientifc** can be considered for all needs when you do Genomics. It includes all the categories we discussed and their sub categories like for

Consumables & Reagents

Instruments Systems and their Software

Products and Services

Other technologies (genotyping, gene expression, gene editing etc.)

Statistical and Computational or Bioinformatics products and Services

Top manufacturers of Genome sequencers

Sequencers gain special attention because the instrument is sophisticated and costly and only few companies in world have dared to develop DNA Sequencers. These companies in alphabetic order are:

Illumina Illumina, Inc. is an American company incorporated in April 1998 that develops, manufactures and markets integrated systems for the analysis of genetic variation and biological function. The company provides a line of products and services that serve the sequencing, genotyping and gene expression and proteomics markets. Its headquarters are located in San Diego, California. Illumina's technology had purportedly by 2013 reduced the cost of sequencing a human genome to US$4,000, down from a price of US$1 million in 2007.[2] Customers include genomic research centers, pharmaceutical companies, academic institutions, clinical research organizations and biotechnology companies.

LI-COR LI-COR biotechnology instruments and reagents, which are based on near-infrared fluorescent and chemiluminescent detection, are used in a large variety of assays, such as western blot assays and cell-based assays, as well as in vivo imaging and DNA analysis. Primary applications include cancer re-

search, drug discovery, genomics research, neuroscience, cell biology, and education. LI-COR automated DNA sequencers were the primary systems used by Genoscope, the French National Sequencing Center to sequence chromosome 14 of the Human Genome Project.

Oxford Nanopore Technologies

Oxford Nanopore Technologies Limited is a U.K.-based company which is developing and selling nanopore sequencing products (including the portable DNA sequencer, MinION) for the direct, electronic analysis of single molecules. In July 2016, a MiniON nanopore sequencer was included on the ninth NASA/SpaceX commercial cargo resupply services mission to the International Space Station

Pacific Biosciences Pacific Biosciences of California, Inc. is a biotechnology company founded in 2004 that develops and manufactures systems for gene sequencing and some novel real time biological observation. In 2010, The Scientist named the company and their first product the top life science innovation of the year, and the company received the 2010 Advanced Sequencing Technology Award from the National Human Genome Research Institute. Technology Review magazine included them in their list of the top 50 most innovative companies for both 2010 and 2011. Founder and Chief Technical Officer Dr. Stephen Turner was awarded the 2010 Ewing Marion Kauffman Foundation Outstanding Postdoctoral Entrepreneur award for his work at the company.

Roche Diagnostics is a diagnostic division of Hoffmann-La Roche which manufactures equipment and reagents for research and medical diagnostic applications. Internally, it is organized into five major business areas: Roche Applied Science, Roche Professional Diagnostics, Roche Diabetes Care, Roche Molecular Diagnostics and Roche Tissue Diagnostics (Ventana).

Thermo Fisher Scientific Thermo Fisher Scientific is the world leader in serving science, with revenues of more than $20 billion and approximately 70,000 employees globally. Our mission is to enable our customers to make the world healthier, cleaner and safer. We help our customers accelerate life sciences research, solve complex analytical challenges, improve patient diagnostics, deliver medicines to market and increase laboratory productivity. Through our premier brands – Thermo Scientific, Applied Biosystems, Invitrogen, Fisher Scientific and Unity Lab Services – we offer an unmatched combination of innovative technologies, purchasing convenience and comprehensive services. From whole genome sequencing to targeted sequencing of specific genomic regions, sequencing portfolio supports a wide range of throughput and research application needs for DNA sequencing.

Multiple products and services providers:

The following companies provides other instruments and accesories required for Genomics research:

Agilent Technologies
Bio-Rad Laboratories
Danaher
Eurofins Scientific
Merck
PerkinElmer Inc
Qiagen
Thermo Fisher Scientific
Waters

Some others known in category:

Cepheid
23andMe
Bayer
Affymetrix (Thermo Fisher)
Myriad Genetics
Shimadzu Analyticals
Corning India
Sartorius AG
BD Biosciences
Eppendorf
GE Healthcare

Some of the best International Genomics Research Centers

The National Institute of Biomedical Genomics (NIBMG)

NIBMG has been established as an autonomous institution by the Government of India, under the aegis of the Department of Biotechnology. This is the first institution in India explicitly devoted to research, training, translation & service and capacity-building in biomedical genomics. The Institute operates from its huge 30-acre campus with academic blocks, student and faculty housing, guest houses, conference centre and other facilities. The Institute started to function in the year 1998 with the mandate to undertake, promote and co-ordinate research, train workers and to serve as information resource in identified aspects of plant genomics to build a frontline institution. NIPGR is poised to contribute towards frontier areas of Plant Biology such as, Computational Biology, Genome Analysis and Molecular Mapping, Molecular Mechanism of Abiotic Stress Responses, Nutritional Genomics, Plant Development and Architecture, Plant Immunity, Molecular Breeding, Transgenics for crop improvement and other emerging areas based on plant genomics.

The National Human Genome Research Institute (NHGRI)

NHGRI began as the National Center for Human Genome Research (NCHGR), which was established in 1989 to carry out the role of the National Institutes of Health (NIH) in the International Human Genome Project (HGP). The HGP was developed in collaboration with the United States Department of Energy and begun in 1990 to map the human genome. .In 1997 the United States Department of Health and Human Services renamed NCHGR the National Human Genome Research Institute (NHGRI), officially elevating it to the status of research institute - one of 27 institutes and centers that make up the NIH. With the human genome sequence complete since April 2003, scientists around the world have access to a database that greatly facilitates and accelerates the pace of biomedical research.

Sanger Institute

The Wellcome Sanger Institute is one of the premier centres of genomic discovery and understanding in the world. It leads ambitious collaborations across the globe to provide the foundations for further research and transformative healthcare innovations. Its success is founded on the expertise and knowledge of its people and the Institute seeks to share its discoveries and techniques with the next generation of genomics scientists and researchers worldwide.

Broad Genomics

has a 25-year track record of delivering on transformative projects in the field of genomics. From the Human Genome Project onward, the group has led the execution of major resource projects including the HapMap, the 1000 Genomes Project, The Cancer Genome Atlas, Comparative Reference Genomes, the ENCODE Project, NIH Roadmap Epigenomics Mapping Consortium, the Genotype-tissue Expression Project, and the Human Microbiome Project.

Beijing Institute of Genomics (BIG)

Founded in 2003, Beijing Institute of Genomics, Chinese Academy of Sciences (CAS) is located in the Olympic Science and Technology Park since 2013. Since its establishment, BIG has accomplished several major research projects with remarkable success, especially the Chinese Superhybrid Rice Genome Project. The institute also actively participated in the Human Genome Project (HGP) and HapMap Project. BIG has established "CAS Key Laboratory of Genome Sciences & Information", "CAS Key Laboratory of Genomic and Precision Medicine", and "Big Data Center" (BIGD), as well as a state-of-the-art Core Genomic Facility, together with public safety

CSIR-Institute of Genomics & Integrative Biology (IGIB)

IGIB is a premier Institute of Council of Scientific and Industrial Research (CSIR), engaged in research of national importance in the areas of genomics, molecular medicine, bioinformatics and proteomics.

The Genomics Institute of the Novartis Research Foundation (GNF)

GNF serves as a bridge between basic science and preclinical drug discovery for Novartis' global research organization, the Novartis Institutes for BioMedical Research (NIBR). GNF's nearly 600 scientists and engineers are committed to pushing the boundaries of science in pursuit of new medicines. Multi-disciplinary teams are focused on making advances in the areas of oncology, autoimmunity, cardiovascular disease, diabetes, musculoskeletal disorders, and infectious disease.

The Innovative Genomics

The IGI began in 2014 through the Li Ka Shing Center for Genetic Engineering, which was created thanks to a generous donation from the Li Ka Shing Foundation. The Innovative Genomics Initiative formed as a partnership between the University of California, Berkeley and the University of California, San Francisco. Combining the fundamental research expertise and the biomedical talent at UCB and UCSF, the Innovative Genomics Initiative focused on unraveling the mechanisms underlying CRISPR-based genome editing and applying this technology to improve human health.

The Arizona Genomics Institute (AGI)

AGI was formed in 2002 when Dr. Rod A. Wing joined the School of Plant Sciences at the University of Arizona in Tucson. The primary focus of AGI is in the area of structural, evolutionary and functional genomics of crop plants where it has played significant roles in over 30 plant and animal genome projects.

Table: List of Genomics companies in India

1.	3B BlackBio Biotech	24.	Dr. Surapaneni's Genomic	47.	Jenome Technologies
2.	ABC Genomics	25.	EasyDNA	48.	Kyvor Genomics
3.	Acme Progen Biotech	26.	Eminent Biosciences	49.	LeucineRichBio
4.	Advanced Healthcare	27.	Excel Biosolution	50.	Life code technologies
5.	Agile Lab assure	28.	Ganit Labs	51.	Mapmygenome
6.	AgriGenome	29.	Genavali	52.	Medgenome
7.	ArrayGen Technologies	30.	GeneOmbio	53.	Nucleome Informatics
8.	Artivatic Data Labs	31.	Genes N Life Health Care	54.	Nutritional Genomix
9.	Bengaluru Genomics	32.	Genetech	55.	Oncogenomics Lifesciences
10.	Bio Discovery Group	33.	Genetic Healing	56.	Positive Bioscience
11.	Bio Globus	34.	GeneXpert	57.	Pramukh Health
12.	BioAxis DNA	35.	Genome Diagnostics	58.	Premas Life Sciences
13.	BioBeams	36.	Genome Life Sciences	59.	Redcliffe Life sciences
14.	BioInnovations	37.	Genomics Central	60.	Rishi Biotech
15.	Bionivid Technology	38.	Genotypic Technology	61.	Saibiosystems
16.	Bioserve Biotechnologies	39.	Global Genecorp	62.	Sciegenom Labs
17.	Cancer Genetics	40.	Helix Genomics	63.	Scientific Bio-Minds
18.	Clevergene	41.	Hemogenomics	64.	Shodhaka Life Sciences
19.	Dhiti Omics	42.	iGenetic	65.	Strand Life Sciences
20.	DNA Diagnostics Centre	43.	Igenomix	66.	Synteny Life Sciences
21.	DNA Forensics Laboratory	44.	Indian Biosciences	67.	Xcelris Genomics
22.	DNA labs India	45.	inDNA Research Labs	68.	Xcode Life
23.	Dr. Shruti Bajaj	46.	InterpretOmics	69.	Yaazh Xenomics

Top Company - Global

Oxford Nanopore - Game Changer in Genomics

by Kamal Pratap Singh

As said "an ace in the hole for DNA sequencing" by world's most reputed Science journal i.e. Nature, it is true that Oxford is going to change what people think of Genomics. It is also evident that Gordon Sanghera and his team have developed a revolutionary device that will change the course of what people know and do with DNA Sequencing. So this special article will show you that why OXFORD has been selected for special coverage despite the presence of other major players in the market.

Nanopore company is a spinout company of Oxford University. Naopre is a another technology that has made an impact in the market and gaining confidence each day passing by. It provide latest technology in DNA sequencing technology at lowest or no cost*. It has produced smallest DNA sequencing device at a cost of 1000$ only when others are offering sequencing for upto 600,000$.

Company history

Oxford Nanopore Technologies was spun out from the University of Oxford in 2005. Until May 2008, the company was named Oxford NanoLabs Ltd. Oxford Nanopore employs a team of more than 300 people including scientists, engineers, informaticians, manufacturing and commercial specialists.

The company was founded by Dr Gordon Sanghera, Dr Spike Willcocks and Professor Hagan Bayley, who is currently Professor of Chemical Biology at the University of Oxford, with seed funding from IP Group plc. Gordon Sanghera has been CEO since the Company's foundation (Read his interview in next article of this issue.)

Since 2008 the Company has also been working with collaborators at Harvard, Boston University and the University of California Santa Cruz. In 2008, Dr John Milton and Clive G. Brown joined the executive management team, bringing

Image: Earliest Model of MinION

Image Source: NASA. MinION is first DNA sequencer to reach outer space and produced real time data.

previous experience of having developed DNA sequencing technology at Solexa, which was acquired and commercialised by Illumina.

In July 2009, the Company relocated to the Oxford Science Park. Our premises at Edmund Cartwright House were inaugurated by the UK Science and Innovation Minister, Lord Drayson. In 2011, an additional 7,000 square feet on the Oxford Science Park was opened and a new Cambridge office was also opened.

In February 2012 at the AGBT conference, Oxford Nanopore presented a variety of nanopore DNA 'strand sequencing' and protein-analysis data, and an overview of the hardware and software behind the GridION and MinION systems. These data included small genomes that had been sequenced using the Company's technology over the sense and antisense strands, showing tens of kilobases in single reads. This was the first nanopore sequence data to be shown worldwide since the technique was first theoretically proposed in 1996.
In spring 2014, the MinION Access Programme (MAP) was commenced; early access users were invited to contribute a refundable $1,000 deposit to use the MinION in its earliest stages of release. Over the subsequent months, performance and processes were improved and publications on the technology started to emerge.
In October 2014, at the ASHG conference, the PromethION was presented for the first time. PromethION is a tablet-sized benchtop instrument giving users the choice of the number of samples and the number of nanopores being used for a particular experiment, ranging from individual samples at a time to multiple samples in parallel.

In May 2015, the first nanopore sensing conference was convened (London Calling) where users of MinION technology gathered to hear from 20 speakers and additional abstracts from numerous other MAP participants across a range of applications. MinION became commercially available at this time.

In July 2015, the PromethION Access Programme was opened for registration.

In May 2016, the second London Calling conference was convened. A series of announcements were made including the full availability of the new R9 nanopore with improved performance. The mobile phone compatible, pipeline product SmidgION was announced.

In October 2016, registration for the VolTRAX Introduction Programme was announced.

In December 2016, the second Nanopore Community Meeting was held. During this meeting, three groups presented or released the first human genomes to be sequenced on the handheld MinION.In February 2017, the GridION X5 was announced; a desktop system integrating five MinION Flow Cells with integrated compute function, that can be used to offer nanopore sequencing as a service. In May 2017, the GridION X5 started shipping and the company introduced 1D squared, a new method of sequencing that gives a boost in accuracy while keeping simple library prep processes.

In June 2017, Oxford Nanopore launched its RNA sequencing solutions. This provides the only direct, real time RNA sequencing technology and additional cDNA analysis.

In October 2018, Oxford Nanopore announced its entry into the Chinese market, having appointed a distributor and established its first sales to customers.

In Jan 2018 Nature Biotechnology reported that Oxford Nanopore's sequencer has generated a whole human genome which is having size over 91.2 Gb of sequence data, or 30x coverage of the genome. They achieved single reads of up to 882 kb, with over half the reads coming in at more than 100 kb. The technology also closed 12 remaining gaps in the reference genome, in highly repetitive sequences where shorter reads won't do the trick.

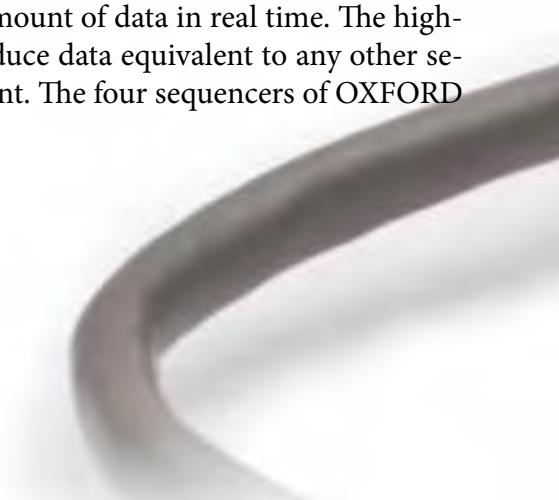
Products

We will see now how Oxford is ready to disrupt the sequencing research and market through their instruments. The Hallmark product of OXFORD NANOPORE i.e. the Minion is available in the market for a minimum price of 1000USD only. Minipore is the only product in market which can process a sample at lowest cost where you need not to run PCRs. gel documentation etc., it prepares a sample and gives sequencing result in real time which you can get even in a village or a remote environment where cost and feasibility of availability is highly required.

All other sequencers are just an upgrades of MinION to produce large amount of data in real time. The highest version is PromethION which has 48 units of MinION and can produce data equivalent to any other sequencers like of ILLUMINA's NextSeq 550 and NextSeq 550Dx Instrument. The four sequencers of OXFORD NANOPORE are:

MINIION
PromethION
GridION

and the company also has a range of accessories like
SmidgION
VolTRAX
MinIT



The MinION

The MinION is being used for a number of biological analysis techniques including de novo sequencing, targeted sequencing, metagenomics, epigenetics and more.

Each consumable flow cell can now generate 10–20 Gb of DNA sequence data. Ultra-long read lengths are possible (hundreds of kb) as you can choose your fragment length. The MinION streams data in real time so that analysis can be performed during the experiment and workflows are fully versatile.

The MinION weighs under 100 g and plugs into a PC or laptop using a high-speed USB 3.0 cable. No additional computing infrastructure is required. Not constrained to a laboratory environment, it has been used up a mountain, in a jungle, in the arctic and on the International Space Station.

The MinION is commercially available, simply by paying a starter-pack fee of $1,000. The MinION starter pack includes materials you need to run initial sequencing experiments, including a MinION device, flow cells and kits, as well as membership of the Nanopore Community.

GridION X5 is a compact benchtop system designed to run and analyse up to five MinION Flow Cells. It is ideal for labs with multiple projects that need the advantages of nanopore sequencing: simple library preparation, real-time analysis and new biological insights from long reads. The GridION X5 also allows users to offer nanopore sequencing as a service.

The GridION X5 allows up to five experiments to be run concurrently or individually; users may choose to use as much or as little of this total resource as they need at any one time. The current chemistry and software release enables generation of up to 150 Gb of data during a GridION X5 run and the compute module is able to analyse that data in real time. Using the same core technology as the MinION and PromethION, the GridION X5 offers real-time, long-read, high-fidelity DNA and RNA sequencing.

PromethION is a standalone benchtop system designed to run up to 48 flow cells at any time. The system allows on-demand sequencing. Users can start and stop running individual experiments as required, or deploy multiple flow cells onto single experiments for greater speed or throughput.

Each of the 48 Flow Cells allows up to 3,000 nanopores to be sequencing simultaneously, with a potential to yield up to 15 Tb in 48 hours for the whole device. Flow Cells can be run individually or concurrently. (This compares to up to 512 nanopores for a single MinION Flow Cell.)

PromethION offers the same real-time, long-read, direct DNA and RNA sequencing technology as MinION and GridION, at much larger scale.

Oxford Nanopore offers a range of options for converting your original biological sample to a form ready for application into a nanopore sensing device.

Oxford Nanopore has developed **VolTRAX** – a small device designed to perform library preparation automatically, so that a user can get a biological sample ready for analysis, hands-free. VolTRAX is designed as an alternative to a range of lab equipment, to allow consistent and varied, automated library prep options.

VolTRAX v1 has been available in an early access programme, and VolTRAX V2 will be released soon.

MinIT is a companion to the MinION personal DNA/RNA sequencer. It is pre-configured with the software that controls the MinION (MinKNOW), carries out data acquisition and performs basecalling.

As a self-contained unit, MinIT can be purchased at the same time as the starter pack, eliminating the need for a dedicated laptop or as a standalone unit to replace the current laptop if an upgrade is needed. Whether working in remote locations or in laboratories, this is a small footprint and easy to implement solution.

Flongle is an adapter (flow cell dongle) for MinION or GridION that enables direct, real-time DNA or RNA sequencing on smaller, single-use flow cells.

Providing access to sequence data as soon your experiment starts, Flongle is designed to be the quickest, most accessible and cost-efficient sequencing system for smaller tests and experiments.

MinKNOW, the operating software for nanopore technology, carries out several core tasks including: data acquisition; real-time analysis and feedback; data streaming whilst providing device control including selecting the run parameters; sample identification and tracking and ensuring that the platform chemistry is performing correctly to run the samples and local basecalling. Local basecalling offers the user experimental setups for sequencing without any local infrastructure or where a stable internet connection is not available. Other compute setups using local infrastructure and basecallers are available, if required, and are detailed here.

MinKNOW produces FAST5 (HDF5) files, and/or FASTQ files, according to your preference. FAST5 contains raw data and basecalling information.

Top Company - Indian

Genotypic - Forerunners in Indian Genomics

by Kamal Pratap Singh

In the bunch of Genomic companies it is not very much sad that India does have Genotypic Technology (GT) as the premiere Genomics organization. This company require attention because of many reasons. Studying as an example of this company we will see that how Genomics evolved and runs in the country.

The reason why GT came 1st in our survey is because no other company is providing these many Genomics services to clientele from a such long time, Unlike others 'GT' company is both into R&D and sales of Genomics Services and products.

GT was started way back in 1998 when Genomics era was in its adolescence. Set up in 1998 but Genotypic commenced its business operations in 2000 as a Genomics services provider. It took 7-8 years to get recognition in the market but persistency in work gave fruits and recognition came with the Agilent (Life science instruments and distributor company). GT became World's first company to be Agilent technologies Certified Service Provider for three major microarray applications-– Gene Expression, ChIP on chip and miRNA profiling and India's first Certified Service Provider for Ion Torrent PGM.

Today it has become become sole distributor of Oxford Nanosequencers (Latest DNA sequencing technology) in India. The company has also working with ion torrent (Thermo Fischer) and illumina.

About Genotypic Technology Pvt Ltd

GT's story was started as the first Genomics service provider in India providing Microarray solutions. Even after the discovery in 1980s Microarray was a new concept in India at the time and this helped GT a lot to tap the potential of the Genomics market. After Microarray, company started providing Next Generation Sequencing (NGS) and Bioinformatics services and solutions to domestic / international pharma, biotech companies and academia and research institutes.

The company always sticked to maintain standard and thus soon afterwards it became the first Genomics Company to run its business processes on SAP ByD and acquired An ISO 9001: 2008 certification for 11,000 square feet genomics facility in Bangalore, India.

From the starting, Genotypic has a rich history of clientele both in industry and in academia which takes services of GT for a range of services like protocol optimization, probe designing, array layouts, project designing, and nucleic acid analysis, in-depth analysis etc.

Brief background of Dr Mugasimangalam C Raja, President, Founder and CEO and Dr Sudha Narayana Rao

Dr Mugasimangalam C Raja, holds a Masters & Ph.D in Biotechnology from Madurai Kamaraj University, Madurai, Tamil Nadu. His research career post-Ph.D, involved developing techniques for DNA sequencing (Weizmann Institute, Israel) and mutating specificity of restriction enzymes (Sidney Kimmel Cancer Center, San Diego, USA).

Dr Raja worked as a Human Genome Project Scientist at the US Government's Argonne National Lab Argonne II, USA. He has developed two novel methods for constructing cDNA microarrays during his stint at QBI Enterprises Ltd., Israel. His accomplishments include several peer reviewed research articles, inventions reports, and several US patents.

Dr Sudha Narayana Rao holds a Ph.D. in Biotechnology from Madurai Kamaraj University, Madurai. She has completed her Post-doctoral research in Neurobiology at the Medical Center in Cornell University, New York and subsequently worked as consultant Neurobiologist for QBI Enterprises, Israel. She has to her credit several publications in peer-reviewed journals.

Major Achievements of Genotypic

Genotypic has been acknowledged and cited in over 350 major publications. They have In-house R&D facility certified by Department of Scientific and Industrial Research (DSIR), Government of India.

GT has bagged many research grants from prestigious institutions in India and abroad.

GT has Received SAP ACE 2010 award for Best Run companies for implementing SAP ByD on demand- First in Life sciences worldwide.

GT has Completed over 500 Next Generation Sequencing projects and over 2000 Microarray projects

Dr Mugasimangalam C Raja

Dr Sudha Narayana Rao

Co Founder and Executive Director

Strengths of company

Today GT has Dynamic team of Doctorates and Post graduates people who have expertise in Molecular biology and are working on nucleic acid extractions, PCR, QPCR and Quality Control, Microarray and Microarray Data Analysis, Next Generation Sequencing and NGS Data Analysis, Array Design Informatics.

GT provide Genomics, Bioinformatics/ Data Analysis and data Interpretation services- all under one roof.

For clients GT give assurance of Strict confidentiality of data and secure data transfer through our high end server.

Over the years, Genotypic has established a rapport providing advanced and high value services to academia, pharma and biotech companies across the globe. For academia, Genotypic is the trusted collaborator-from 'conceptualization' to 'publications'. Among technology partners, Genotypic has been the trusted partner, from project planning to meticulous execution, meeting the global industry standards.

Genotypic's proven track record of client satisfaction in providing high quality genomics and bioinformatics services and solutions has made it the first choice genomics service provider in India and also with long standing clients abroad. Genotypic has forged strategic alliance partnerships with world renowned companies in South Africa, Singapore, Malaysia, Thailand and Israel to support and complement Genotypic's presence in these regions.

Feedback of clients/customers.

From the very starting we handle all client's request with great care and try to solve every problem as soon as possible. After delivery of service as per our company policy we take feedback of clients. In these many years we have received so many great compliments for our products and services from clients all around the world. Some of them which I never forget are:

"Biointerpreter is very useful to us in finding various transcriptional factors. It is an efficient tool to interpret gene expression data."

from Dr.Neeru Dhamija and Dr Debasis mitra, , NCCS, Pune

"We find the software useful for a crude analysis, that is, if we want to get an overview of what is happening in our system."

from Ms Sakshi and Dr Jaya Tyagi, , AIIMS, Delhi.

"Biointerpreter allowed me to see clear functional difference of 3 categories of ovarian tumors. I got a better view of the Biology behind the differential expression."

from James Cherry, SAIC-Frederick, NCI at Frederick, Gene Expression Laboratory, MD, USA.

"The software is very useful in Microarray data interpretation and in predicting mechanism of action."

from Dr. Abhijit Chatterjee, , Zydus Research Centre, India.

"Our initial experience with Genotypic Technology for our gene expression analysis using Microarrays was positive. We were pleased with the level of professionalism and the diligence with which Genotypic Technology carried the analysis. Their experts are very knowledgeable to give us generous consults on study design and are very cooperative with our requests. The final reports were generated with user-friendly format and were delivered on time. We will plan to use Genotypic Technology in the future for more Microarray studies."

from Dr.Zuomei Li, , Methylgene Inc., Canada.

"We are using Genotypic's Microarray services for the past 3 years. It is Great!"

from Prof. Arunkumar, MRDG, Indian Institute of Science, Bangalore.

"We worked with Genotypic for gene expression profiling of three of our enzyme healthcare formulations. From the results provided by Genotypic we could quickly understand the mechanism of action of the formulations. The results were of high standard and acceptable to the medical community. The Microarray studies for the fourth and fifth

formulations are currently underway."

from Shilpa S., Manager, Product development, Advanced Enzyme Technologies Ltd., (Speciality enzymes and Biochemicals, Inc).

"Genotypic offers quick service, swift analysis and crisp interpretation. Their technical expertise in different areas of Microarray technology has been of great value to us."

from Microarray team of Astra Zeneca (India).

Some big grants from Govt and/or industry

NIH Grant on Transcriptional analysis of the Guinea pig model of Tuberculosis and DBT Grant (in year?)on Biomarker Discovery and Validation of Blood Immune Response following HIV -TB Co-infection.

Ongoing and completed projects in GT

These are Development of chickpea gene expression microarray, Next generation sequencing and de novo transcriptome analysis of Costus pictus D. Don, a non-model plant with potent anti-diabetic properties, de novo Transcriptome Assembly (NGS) of Curcuma longa L. Rhizome Reveals Novel Transcripts Related to Anticancer and Antimalarial Terpenoids.

We are working on some major projects like Cancer profiling for clinical intervention and biomarker discovery, Genomics approach to identify diseases related to chromosomal aberrations in humans, Development of gene panel for mitochondrial genome, Development of SNP markers in plants

Some Collaborating partners

There are so many but to name a few we have worked in collaboraition with National Institute of Plant Genome Research (NIPGR), Central Sericultural Research & Training Institute (CSRTI), Centre for Cellular and Molecular Biology (CCMB), HCG ? , Vellore Institute of Technology, Sri Devaraj Urs Academy of Higher Education and Research (SDUAHER), M S Ramaiah University of Applied Sciences Narayana Nethralaya, Colorado state university (USA) any many more.

Best publications from Genotypic

De Novo Transcriptome Assembly (NGS) of Curcuma longa L. Rhizome Reveals Novel Transcripts Related to Anticancer and Antimalarial Terpenoids, Ramasamy S. Annadurai et al., PLOS One, 2013, Published online 28th February 2013

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Future Projections of GT

Genotypic is constantly striving to enhance its technology platforms and capacity to enable researchers to maximize their use in life sciences research. Genotypic as technology partner for biological researchers has also collaborated with academia and industries to run pilot projects, procedure standardization and platform standardizations. Genotypic is vbest known for simplifying complex genomics and to bridge the gap between the biology and technologies.

Genotypic envisions becoming a global leader providing affordable high-end Genomics and Bioinformatics services and solutions to customers through continuous innovation, diligence, commitment and ingenious approaches.

Strive to develop and provide novel Microarray and Next Generation Sequencing applications to integrate with genomic technologies in turn widen the gamut of tools in systems biology research.

Continuous development of methodologies for integration and analysis of disparate biological data such as nucleic acid sequencing, gene expression, biomedical data and literature to generate coherent understanding of biological systems.

As knowledge partners, to initiate joint projects with Industry and Academia, to explore new avenues and challenging problems in biological research by providing high-end biotechnology research services.

Impart knowledge on cutting-edge technologies to researchers from industries and academia via direct interactions, websites, workshops, symposia, presentations and training courses.

Achieve highest level of customer satisfaction by providing right solutions at a right price with extended support from professionals

Source: http://www.genotypic.co.in/

PRESS RELEASE

A report on BRSI-CEES workshop on Agripreneurship Development among Aspiring Farmers, Lucknow

The Centre for Energy and Environmental Sustainability (CEES), Lucknow and Biotech Research Society, India (BRSI) organized a three-day workshop on Agripreneurship Development Among Aspiring Farmers during September 15-17, 2018.

The aim of this workshop was to educate, train and motivate the young farmers to develop the qualities of entrepreneurship among them. The workshop was inaugurated by Prof Ashok Pandey, Distinguished Scientist, Centre for Innovation and Translational Research, CSIR – Indian Institute of Toxicology Research, Lucknow. Ms. Nishi Morya CEO, Adhita Biosciences Pvt Ltd., a fast growing agri-based Biotech start-up and Ms. AparjitaMehra, Prasar Bharti were guest of honor in the session. Dr VivekMorya welcome the participants and invitees and briefed the aim and scope of the workshop. Then all the young farmers introduced themselves. This was followed by the inaugural address by Prof Pandey who discussed the need to adopt new thought-process in agri-production, linking it with agr-business. In this context. Prof Pandey highlighted the role and initiatives of BRSI in skill development and entrepreneurship programs and workshop being organized by it. He also mentioned about the activities of CEES and appreciated the networking initiatives of Aditha Biotech with CEES for the organization of the workshop. Ms Nishi Morya and Ms AparajitaMehra also addressed the participants.

There were 26 participants from nine districts from UP, MP and Bihar and a total of 18 invitees/speakers who addressed the participants. Post-lunch session was devoted on technical talks. Professor SP Singh, NDATU and Prof. Venkatesh Dutta, BBAU talked on Farm Management and Crop Selection. Prof Singh gifted the participants hybrid seeds of bottle guard (developed in his own lab at Narendra Dev Agriculture University). He also invited the participants to visit the ND university for seeing vertical farming of the gourds crop. Professor Venkatesh Dutta, who has been working on the management of resources for sustainable use to achieve an inclusive growth, discussed about the agro-climatic zone of Uttar Pradesh, Bihar, and Madhya Pradesh. He elaborated the specific crops for different agro-climatic zones to ensure the maximal productivity. Prof. Dutta offered a a free consultancy to the participant, while selecting any kind of crop for cultivation.

The second day of the workshop started with lecture of the Sri P.S. Ojha, State Coordinator / Member Coordinator, Uttar Pradesh Bio-Energy Development Board. Sri Ojha provided detailed information about the various schemes of the Uttar Pradesh government for the agri- entrepreneurship development. He explained how the young farmers can create a cluster and may avail support up to one crore form the government to initiate the agriculture-based business. He offered help and support to the participants for their any specific question or need in this regard from UP Govt.

Photo: Prof Ashok Pandey (sitting second from left) Prof TP Singh (sitting third from left)

A report on the BRSI International Workshop-cum-Training Course on " Techno-economic Analysis and Life-cycle Assessment"; July 9-13, 2018; CSIR-NIIST, Trivandrum and August 6-10, 2018 at CSIR-IITR, Lucknow

Under the Skill Development program, BRSI organized a workshop-cum-Course on "Technoeconomic and Life-Cycle Assessment as Tools for Sustainability Analysis", which aimed to provide a high level knowledge with lectures and hand-on trainings to the young researchers working in the areas of Biotechnology/Biochemical/ Engineering/Environmental Bioengineering/ Microbiology.The workshop was organized at CSIR-National Institute for Interdisciplinary Science and Technology (NIIST), Trivandrum during July 9-13, 2017 in association with NIIST and at CSIR-Indian Institute of Toxicology Research (IITR), Lucknow during August 6-10, 2018 in association with IITR.

Prof GS Murthy, Oregon State University, USA was workshop Director.

Organization of the Course

The course consisted of lectures, mandatory class readings and class discussions. The participants were required to choose a project that involved assessing a particular technology/ process/practice for technical feasibility, economic viability, environmental impacts and resource sustainability analysis before coming to the workshop. Assessing such complex problems is challenging, involves a lot of peer-peer discussions and evaluation of technical results using multiple approaches. A significant part of the course consisted of in-class discussion in an informal setting. Participants analyzed two case studies in class to understand the examples of the analyses and were demonstrated the application of concepts discussed in lectures.

Learning Outcomes

By the end of this course, participants were expected to be able to:

- Describe different aspects of sustainability.
- Evaluate technical feasibility of a given system.
- Assess economic viability of a given system.
- Evaluate environmental impacts of a given product/process using life cycle impact assessment methods.

The workshop at Trivandrum was opened on 9th July 2018 with a welcome address by Dr P Binod, who on behalf of BRSI and CSIR-NIIST welcomed Prof GS Murthy, Prof Ashok Pandey and participants of the workshop. Dr Binod mentioned the goals of the workshop and also briefly informed the selection process. Prof Pandey discussed BRSI programs about Skill developments and knowledge portfolios. He emphasized that BRSI would continue to provide an excellent and active platform to its members for networking and collaboration. He thanked Prof Murthy for him time and immense support for the workshop at Trivandrum and Lucknow.

The closing session of the workshop was held on 13th July 2018, which was chaired by Prof TP Singh, President BRSI. Prof Singh in his address mentioned the new initiatives taken by BRSI and added that the workshop is the first one in several others such programs from BRSI to come in future. He thanked Dr Binod and Dr Nampoothiri for their time and efforts in up-keeping the Central Office of BRSI. Dr Bhaskar thanked Prof Singh for his leadership initiatives. He thanked Prof Pandey but for whose efforts this workshop would not have been possible. He also thanked Prof Murthy for his endeavor to conduct the workshop and hoped that the participants will be hugely benefitted by the workshop.

Dr P Binod, Central Office Executive was coordinator of the workshops at Trivandrum and Lucknow. All the participants successfully completed the course and were given the certificate by Prof TP Singh and Prof GS Murthy.

The workshop at Lucknow was opened on 9th July 2018 with a welcome address by Prof Ashok Pandey, who on behalf of BRSI welcomed Prof GS Murthy and Prof Alok Dhawan, Director, CSIR-IITR who chaired the opened session. Prof Pandey mentioned the goals of the workshop and also briefly informed the selection process. He also discussed BRSI programs about Skill developments and knowledge portfolios. He emphasized that BRSI would continue to provide an excellent and active platform to its members for networking and collaboration. He thanked Prof Murthy for him time and immense support for the workshops and Prof Dhawan for his strong support for the workshop by holding it IITR. Prof Dhawan welcomed Prof Murthy and participants and briefly gave details about IITR. He appreciated the initiatives of BRSI for coming forward to conduct such important courses/workshops.

NEWS: Govt & Industry

CSIR Technology Awards 2018

CSIR Technology Awards 2018 under category of: Life Sciences, Physical Sciences including Engineering, Innovation, and Business Development and Technology Marketing were awarded on the occasion of CSIR Foundation Day, 26th September 2018. The awards were given away by Dr. Harsh Vardhan, Hon'ble Minister, Ministry of S&T, ES & EFCC and Vice President, CSIR to the winners during the Foundation Day of the CSIR.

CSIR had instituted 'Technology Awards' in 1990 to foster and encourage multi-disciplinary in-house team efforts and external interaction for technology development, transfer and commercialization.

This year the winners are: CSIR-Institute of Microbial Technology, Chandigarh; CSIR-Central Glass & Ceramic Research Institute, Kolkata; CSIR-Indian Institute of Chemical Technology, Hyderabad; CSIR-Central Institute of Mining and Fuel Research, Dhanbad and CSIR-Indian Institute of Petroleum, Dehradun

CSIR-Institute of Microbial Technology (CSIR-IMTECH) has won the award for 'Clot Busters for Thrombolytic Therapy'

Coronary Artery Diseases (CADs) are increasing at an alarming rate; the World Health Organization (WHO) estimates that 60 per cent of the world's cardiac patients will be Indians.

CSIR-IMTECH previously, had developed innovative processes for the natural and recombinant Streptokinase, vital, life-saver injectable protein drugs that saves up to 40% of human lives after heart attacks if given within a few hours of the onset of chest pain. The products are in the market.

Advancing further, the CSIR-IMTECH team has designed and developed a state-of-the-art new-generation clot buster drug. The Clot Specific Streptokinase (CSSK), a novel patented thrombolytic biopharmaceutical therapeutic protein drug is unique in its functions such as fibrin specificity and molecular switch, where the engineered clot buster circulates in an inactive state without significantly activating the blood plasminogen.

Once it encounters and binds to the pathological blood clot, it is activated and thereby generates plasmin in and around the vicinity of the clot. This in turn cleaves the fibrin clots without the occurrence of generalized proteolysis, as often happens during streptokinase mediated and other thrombolytic based therapies. The clot-buster drug (CSSK) thus has higher stability and minimal side effects compared to several currently employed thrombolytic drugs.

CSSK has been patented in India, Europe and USA. The technology package of the clot buster has been transferred to Nostrum Pharmaceuticals, a US based company. The Phase II Clinical trial of this clot buster is in progress.

'Innovative, Low Cost Membrane Systems as Import Substitutes for Production of Medical Grade Water and Resource Recovery' of CSIR-Indian Institute of Chemical Technology has won the "Certificate of Merit" under the CSIR Technology Awards 2018

The CSIR-IICT team has designed a fully automated, cascaded reverse osmosis system with post treatment, as an inexpensive substitute for production of ultrapure water for medical, laboratory and biochemistry applications. The systems are highly compact and available with 25–40 Lit/hr and 250–500 Lit/hr capacities, with minimal installation costs.

The system can produce both Type-2 water of resistivity up to 5 MegOhm.cm and Type-3 water with total dissolved solids in the range 1–3 ppm (Conductivity < 5 µS/cm) at an operating cost of just 5 paise per Lit. It is used in preparation of dialyzing fluid in haemodialysis centers of hospitals, microbial cultures in biotech industry, boiler feed in caustic soda and power plants, input water for radiators and batteries of automobiles, etc.

The technology has been transferred to two private firms namely Plantris Ventures Ltd., New Delhi and Althion Healthcare Equipment & Devices, Hyderabad where the device is being produced. The device is deployed at numerous places including CSIR-IICT, CSIR-CCMB, Care hospitals, Huwel Life Sciences, JNTU Kakinada, University of Hyderabad, Osmania University and JNTU Hyderabad.

The 2018 Nobel Prize in Physiology or Medicine

The Nobel Assembly at Karolinska Institutet has awarded the 2018 Nobel Prize in Physiology or Medicine jointly to James P. Allison and Tasuku Honjo for their discovery of cancer therapy by inhibition of negative immune regulation.

James P. Allison studied a known protein that functions as a brake on the immune system. He realized the potential of releasing the brake and thereby unleashing our immune cells to attack tumors. He then developed this concept into a brand new approach for treating patients.

In parallel, Tasuku Honjo discovered a protein on immune cells and, after careful exploration of its function, eventually revealed that it also operates as a brake, but with a different mechanism of action. Therapies based on his discovery proved to be strikingly effective in the fight against cancer.

Allison and Honjo showed how different strategies for inhibiting the brakes on the immune system can be used in the treatment of cancer. The seminal discoveries by the two Laureates constitute a landmark in our fight against cancer.

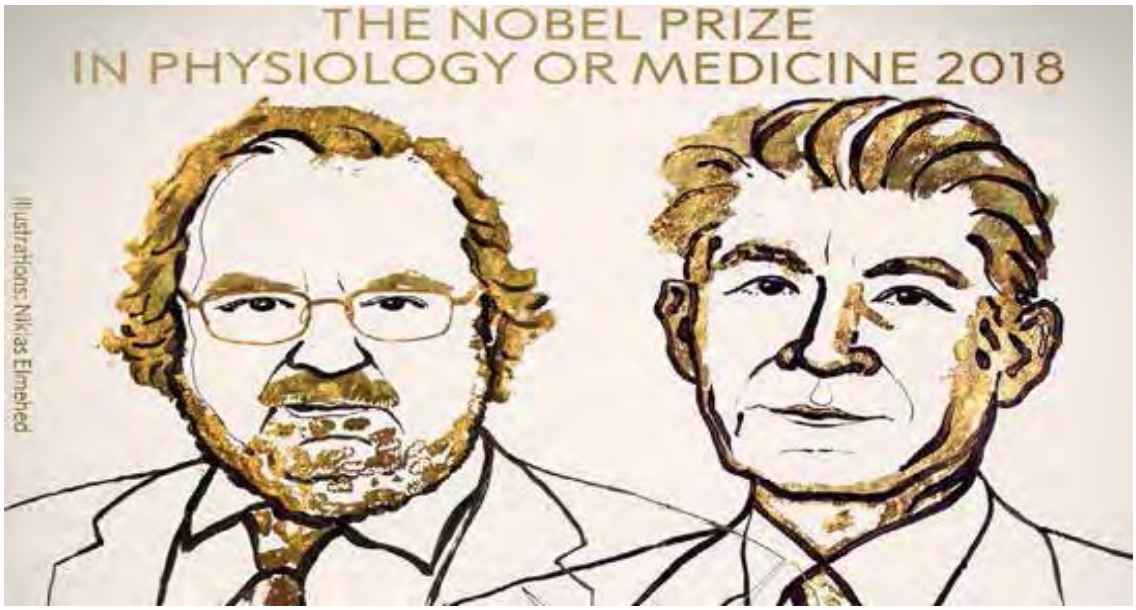

Photo: James P. Allison(Left) and Tasuku Honjo (Right)

The India International Science Festival (IISF) concluded in Lucknow on 8TH October 2018

The four-day long mega science expo, India International Science Festival (IISF) concluded in Lucknow on 8TH October 2018. IISF-2018 witnessed a vast gathering of more than 10 lakh people and more than 22 thousand registrations, the highest in its four-year history making it the largest festival of its kind in Asia.

IISF which was inaugurated by the President of India Shri Ram Nath Kovind saw a confluence of Scientists, researchers, students, farmers and people from a wide spectrum discussing, debating, and witnessing how science and technology are shaping New India. Congratulating all the stakeholders, the Union Minister informed the gathering that the four-day long festival saw a presentation of more than twelve hundred research papers, the participation of nearly twenty thousand experts and delegates participating in the event.

Speaking at the valedictory function Dr. Harsh Vardhan Union Cabinet Minister at Ministry of Science & Technology, Ministry of Environment, Forest and Climate Change and Ministry of Earth Sciences said that after witnessing the huge participation in this four-day-long science festival, it will not be wrong to add Jai Anusandhan to the quote "Jai Jawan, Jai Kisan, Jai Vigyan" given by former Prime Ministers of India. "More than 1200 research papers were presented, participation of more than 1500 farmers was witnessed apart from a sea of young enthusiasts of science making this festival unique of its kind in the world" said Dr. Vardhan congratulating all the stakeholders and further adding that such science festivals should now be a regular feature of not only Central but state government as well.

Union Minister Shri Nitin Gadkari who was the chief guest at the valedictory function launched a website dedicated exclusively to science in India (http://scienceindia.in/). Highlighting the pervasive role of Science & Technology across all the major schemes of Government of India Shri Gadkari said that today is the time to make India a super economic power. "Innovation, Entrepreneurship, Technology, Research and Science; we name it as knowledge and conversion of knowledge into wealth is the future of our country", said the Union Minister. Sh. Gadkari also elucidated how research and technology in alternative fuel (esp. biofuel) is swiftly changing the transport industry.

IISF 2018 also saw two major Guinness World Records being made one of which was a World Record successful attempt to "isolate DNA" by 550 students from class 8th to 10th standard.

IISF-2018 with its focal theme "Science for Transformation" had more than 23 special events in its 4th edition. The fifth edition of the science festival will be held in eastern India.

Source: PIB, India

Chief scientific officer of a high-flying cannabis product company faked data at the NIH

The chief scientific officer of a cannabis product company whose stock price has been hotter than a flaming joint (sorry) was known more than 18 months ago to have committed research misconduct while at the U.S. National Institutes of Health — casting a cloud of suspicion over the firm's operations.

Marketwatch reported yesterday that the company, India Globalization Capital, which trades on the New York Stock Exchange as IGC, has at least nine other "red flags" for investors, from questions about its ability to manufacture cannabinoids to a history of trouble with the U.S. Securities and Exchange Commission.

Until August, the company's stock had been trading below 50 cents per share. It began a dramatic rise, eventually reaching $13 per share.

Following publication of the MarketWatch story, the stock began to tumble, and today's trading has it mostly between $4 and $5.

Source: Retraction Watch

Former director of U.S. research watchdog agency moves to NIH

Kathy Partin, who served as director of the U.S. Office of Research Integrity (ORI) for just under two years until being removed from the post late in 2017, has a new position at the U.S. National Institutes of Health (NIH), Retraction Watch has learned.

As of Sept. 30, Partin is intramural research integrity officer at the NIH. She replaces Melissa Colbert, who will be retiring. Partin, who spent more than 20 years at Colorado State University as a researcher and then as director of the office of research integrity and compliance review, was appointed ORI director in December 2015. Within months, Science reported that Partin was facing a "staff revolt" because of "profound concern about the tone and direction" of her management. In 2016, the agency only made seven findings of misconduct, compared to 14 in 2015 and 11 the year before. In 2017, the agency issued seven findings, and it has issued nine to this year to date.

In November 2017, Partin left the ORI, officially as a temporary reassignment to the Office of the Vice President for Research at the Uniformed Services University of the Health Sciences. Since that time, Wanda Jones has been interim director.

Cancer researcher is up to 40 retracted papers

Fazul Sarkar, the cancer researcher formerly of Wayne State University who once tried to sue critics on PubPeer, has had another seven papers retracted. That makes a total of 40, and places him in the Top 10 of our leaderboard of authors with the most retractions. Three of the retractions appear in Molecular Cancer Therapeutics and four are from PLOS ONE. All involve falsification of data; one article had been corrected earlier, in 2014.

Source: Retraction Watch

RESEARCH NEWS

From other High Impact Journals

Universal vaccine platform that's cheaper and shelf stable

Researchers at The University of Texas Medical Branch at Galveston have developed less expensive way to produce vaccines that cuts the costs of vaccine production and storage by up to 80 percent without decreasing safety or effectiveness. The findings are currently available in EBioMedicine.

Vaccines are the most effective way to prevent and eradicate infectious diseases. Currently, many vaccines have to be manufactured in cell culture or eggs, which is expensive and carries the risk of contaminations. In addition, most vaccines must be kept refrigerated during the transportation from manufacturers to health care clinics. In tropical and subtropical regions, such cold storage requirements could contribute to more than 80 percent of the vaccine cost.

"The ability to eliminate cell culture or eggs and cold storage will change the process of vaccine development," said UTMB's Pei-Yong Shi, professor in the department of biochemistry and molecular biology. "Importantly, this vaccine technology could potentially serve as a universal platform for development of live-attenuated vaccines for many viral pathogens."

To achieve these goals, the UTMB team engineered a live-attenuated Zika vaccine in the DNA form. Once the DNA is delivered into our body, it launches the vaccine in our cells, leading to antibody production and other protective immunity.

With this production method, there is no need to manufacture the vaccine in cell culture or eggs at factories. Because DNA molecules are shelf stable, the vaccine will not expire at warm temperatures and could be stockpiled at room temperature for years.

Using UTMB's Zika vaccine as a model, the research group showed that the DNA platform worked very efficiently in mice. After a single low dose, the DNA vaccine protected mice from Zika virus infection, mother-to-fetus transmission during pregnancy and male reproductive tract infection and damage.

"This is the first study to demonstrate that, after a single low dose, a DNA vaccine could induce saturated protective immunity," Shi said. "We will continue testing this promising Zika vaccine platform and then apply the platform to other viruses."

Other authors include UTMB's Jing Zou, Xuping Xie, Huanle Luo, Chao Shan, Antonio Muruato, Scott Weaver and Tian Wang.

Journal Reference:

Jing Zou, Xuping Xie, Huanle Luo, Chao Shan, Antonio E. Muruato, Scott C. Weaver, Tian Wang, Pei-Yong Shi. A single-dose plasmid-launched live-attenuated Zika vaccine induces protective immunity. EBioMedicine, 2018; DOI: 10.1016/j.ebiom.2018.08.056

Scientists create flies with ancient genes to study evolution

The work, published in the journal eLife, found that two mutations that arose 140 million years ago changed the function of a critical developmental gene, which now regulates development of the head and other structures in virtually all species of present-day flies.

"By introducing individual mutations that happened in the deep past into the ancient genes, we were able to show precisely how each one affected development many millions of years ago," explains Stephen Small, an NYU biologist and one of the paper's senior authors.

"We found that just two chance mutations were the major causes of a profound change in the animal's developmental processes -- a change that became indispensable in all of its present-day descendants," says Joseph Thornton, the paper's other senior author and professor of Ecology and Evolution and Human Genetics at the University of Chicago.

The study is the first to use ancestral reconstruction in the field of the evolution of development, or evo-devo.

The researchers focused on the evolution of a gene called bicoid. Bicoid triggers the formation of structures at the head (anterior) end of embryos in the fruit fly, an important model organism because many aspects of its genetics and development are shared with humans and other animals. Bicoid serves as the "master regulator" of anterior development by turning on expression of a set genes that carry out head development and suppress tail development, and doing so only at the anterior end.

Bicoid has long presented an evolutionary puzzle. Fly embryos lacking active Bcd protein die very early because instead of forming a head they form tail structures at both ends. But the bicoid gene does not even exist in other insects or more distantly related animals, which use other genes to control anterior development. Bicoid shows that even the most fundamental aspects of development can change drastically during evolution, but how that process occurs is unknown.

The Small and Thornton laboratories sought to understand how bicoid evolved its new developmental function through several means: recreating the precursor gene from which it evolved, characterizing its biochemical functions, introducing it into modern-day fruit flies whose own bicoid gene had been removed, studying its effects on the formation of head structures and expression of the specific genes that drive head development, and introducing historical mutations into the ancestral gene to determine their effects.

Their initial results showed that flies carrying the precursor gene fail to develop a head, with tails at both ends and none of the key genes involved in head development properly expressed. The group then introduced into the precursor gene every mutation that happened during the ancient interval during which bicoid evolved its new role.

Most of the changes had little or no effect on bicoid's functions, but two of them together allowed bicoid to activate a completely new set of target genes. When introduced into fly embryos, this evolutionary mutant version of bicoid activated most of the genes involved in head development in their proper places, and the embryos formed recognizable, albeit incomplete, head structures instead of tail structures at the anterior end.

The group concluded that these two mutations, when combined, were the predominant causes of bicoid's functional evolution, with additional mutations during the same ancient period fine-tuning the gene's new function.

"By combining the most advanced techniques from developmental biology and evolutionary genetics, we were able to dissect how molecular changes in an ancient gene fundamentally changed one of the most important -- and otherwise conserved -- processes in animal development," Small notes.

Journal Reference:

Qinwen Liu, Pinar Onal, Rhea R Datta, Julia M Rogers, Urs Schmidt-Ott, Martha L Bulyk, Stephen Small, Joseph W Thornton. Ancient mechanisms for the evolution of the bicoid homeodomain's function in fly development. eLife, 2018; 7 DOI: 10.7554/eLife.34594

Probiotic bacillus eliminates staphylococcus bacteria

A new study from National Institutes of Health scientists and their Thai colleagues shows that a "good" bacterium commonly found in probiotic digestive supplements helps eliminate Staphylococcus aureus, a type of bacteria that can cause serious antibiotic-resistant infections. The researchers, led by scientists at NIH's National Institute of Allergy and Infectious Diseases (NIAID), unexpectedly found that Bacillus bacteria prevented S. aureus bacteria from growing in the gut and nose of healthy individuals. Then, using a mouse study model, they identified exactly how that happens.

The scientists recruited 200 volunteers in rural Thailand for the study. This population, they speculated, would not be as affected by food sterilization or antibiotics as people in highly developed urban areas. The scientists first analyzed fecal samples from each of the study participants for bacteria correlated with the absence of S. aureus. They found 101 samples positive for Bacillus, primarily B. subtilis -- the

type found mixed with other bacteria in many probiotic products. Bacillus bacteria form spores that can survive harsh environments and commonly are ingested naturally with vegetables, allowing them to temporarily grow in the intestine. The scientists then sampled the same 200 people for S. aureus in the gut (25 positive) and nose (26 positive). Strikingly, they found no S. aureus in any of the samples where Bacillus were present.

In mouse studies, the scientists discovered an S. aureus sensing system that must function for the bacteria to grow in the gut. Intriguingly, all of the more than 100 Bacillus isolates they had recovered from the human feces efficiently inhibited that system.

Using chromatography and mass spectrometry techniques, the scientists identified fengycins, a specific class of lipopeptides -- molecules that are part peptide and part lipid -- as the specific Bacillus substance that inhibited the S. aureus sensing system. Additional tests showed that fengycins had the same effect on several different strains of S. aureus -- including high-risk USA300 MRSA which causes most community-associated MRSA infections in the United States and is an increasingly common cause of healthcare-associated MRSA infections.

To further validate their findings, the scientists colonized the gut of mice with S. aureus and fed them B. subtilis spores to mimic probiotic intake. Probiotic Bacillus given every two days eliminated S. aureus in the guts of the mice. The same test using Bacillus where fengycin production had been removed had no effect, and S. aureus grew as expected.

The NIAID and Thai scientists next plan to test whether a probiotic product that contains only B. subtilis can eliminate S. aureus in people. They plan to enroll more Thai volunteers for the project. Michael Otto, Ph.D., the NIAID lead investigator, says, "Ultimately, we hope to determine if a simple probiotic regimen can be used to reduce MRSA infection rates in hospitals."

Journal Reference:

Pipat Piewngam, Yue Zheng, Thuan H. Nguyen, Seth W. Dickey, Hwang-Soo Joo, Amer E. Villaruz, Kyle A. Glose, Emilie L. Fisher, Rachelle L. Hunt, Barry Li, Janice Chiou, Sujiraphong Pharkjaksu, Sunisa Khongthong, Gordon Y. C. Cheung, Pattarachai Kiratisin, Michael Otto. Pathogen elimination by probiotic Bacillus via signalling interference. Nature, 2018; DOI: 10.1038/s41586-018-0616-y

Largest ever genetic study of blood pressure

The largest ever genetic analysis of over one million people has identified 535 new genes associated with high blood pressure.

The researchers concluded : "The combined effect of all associated variants shows a large aggregated risk, warranting further investigation of a potential precision medicine strategy to prevent future cardiovascular disease amongst patients at high genetic risk."

High blood pressure is a highly heritable and modifiable risk factor for cardiovascular disease.

All the genetic variants identified so far only explain between 3% and 4% of the difference between two people with different blood pressures.

But this newest study has identified three times more genetic traits which influence blood pressure.

The findings, published in Nature Genetics, have identified new biological pathways for blood pressure regulation with the potential for improved cardiovascular disease prevention in the future.

Scientists examined around 7 million common genetic variants for an association with systolic and diastolic blood pressure as well as pulse pressure.

They identified a total of 535 new genes influencing blood pressure in an individual, bringing the total number of genes identified to 901.

Researchers said: "The combination of

Blood Pressure Categories

American Heart Association | American Stroke Association

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

all blood pressure variants is associated with?>?10mmHg higher systolic blood pressure and odds of 2.59 and 1.45 for increased risk of hypertension and cardiovascular outcomes, respectively."

There is also a genetic overlap between hypertension and lifestyle exposures, with many blood pressure genes also associated with, for example, an individual's intake of fruit, water, tea, caffeine, alcohol and salt.

Journal Reference:

Evangelos Evangelou et al. Genetic analysis of over 1 million people identifies 535 new loci associated with blood pressure traits. Nature Genetics, 2018; 50 (10): 1412 DOI: 10.1038/s41588-018-0205-x

Cancer stem cells use normal genes in abnormal ways

CDK1 is a "normal" protein -- its presence drives cells through the cycle of replication. And MHC Class I molecules are "normal" as well -- they present bits of proteins on the surfaces of cells for examination by the immune system. But a University of Colorado Cancer Center study published in the journal Cancer Research shows that a population of cancer cells marked by MHC Class I molecules and high CDK1 is anything but normal. In fact, these MHC Class I-high, CDK1 high molecules may be at the heart of conditions including melanoma, pancreatic and colon cancers. These cells may, in fact, be the long-sought cancer stem cells that often resist treatments like chemotherapy to reseed these cancers once treatment ends.

From the outset, the goal of this study was different than most. Often, cancer researchers will grow tumors and then ask what kinds of drugs or genetic changes make tumors grow or shrink. However, the current study wondered not what makes tumors change size, but what factors in these cells initiate tumor growth in the first place. To answer this question, the study used patient samples, mouse models and publicly available genetic data to search for the genetic/genomic commonalities in cells capable of initiating melanoma, pancreatic and colon cancers.

The findings start with a molecule called MHC Class I, a common molecule that coats the outside of human cells and functions a bit like a hand waving a flag. When MHC Class I molecules wave "flags" (actually bits of proteins), that are not from host tissue, the immune system recognizes the cell as foreign and attacks it. For this reason, most cancer cells downregulate MHC as a way of evading the immune system.

But the current study shows that the population of cancer cells able to initiate the formation of new tumors does not downregulate MHC Class I molecules. In fact, if anything this special population of cancer cells upregulates MHC Class I molecules.

"Probably, these cells have another way to evade the immune system," says Mayumi Fujita, MD, PhD, investigator at CU Cancer Center and professor in the CU School of Medicine Departments of Dermatology and Immunology/Microbiology.

Oddly, this population of cancer cells that retains MHC Class I molecules also retains another feature of healthy cells, namely the presence of a protein called CDK1. CDK1 is a master regulator of the cell cycle -- with CDK1, cells progress through the cycle of replication; without CDK1, they do not. In this case, the more CDK1, the more able melanoma cells were to initiate new tumors.

"Our next question was why," Fujita says. "Why would CDK1 control not just the cell cycle, but also stem-ness?"

Finally, the answer includes something that is not "normal." Sox2 is a transcription factor that helps embryonic and neural stem cells keep their stem-ness. It is also a known marker of cancer stem cells, implicated in the development of more than 25 forms of the disease. Despite its identification as a driver of cancer, Sox2 remains a difficult target.

"It's very difficult to control a transcription factor like Sox2. We can show Sox2 is very important for tumorigenesis, but it's difficult to have a Sox2 inhibitor," Fujita says.

However, the current study found that CDK1 directly interacted with Sox2 to keep these cancer cells "stemmy." And here is the important part: "If CDK1 controls Sox2 function through this interaction, probably we can someday inhibit it, maybe through some way of targeting CDK1 or perhaps some way to interfere with the interaction of CDK1 with Sox2," Fujita says.

Importantly, this signature of MHC Class 1, CDK1 and Sox2 was common across melanoma, colon and pancreatic cancers, implying that cancer stem cells across cancer types may share common features.

"We can't say that all tumor types have this signature, but it's prevalent. We think probably this phenotype is very common in melanoma, pancreatic and colon cancer," Fujita says.

Moving forward, the Fujita group hopes to further define the mechanism of Sox2 regulation via CDK1 in

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Domestic industry development strategy

Small scale industry development strategy

Laboratory setup

Contract research services

Method development & validation

Visit: http://shreejibiotech.com/

hopes of finding essential links that might be targets for new drugs aimed, eventually, at stopping the action of Sox2.

Journal Reference:

Dinoop Ravindran Menon, Yuchun Luo, John J. Arcaroli, Sucai Liu, Lekha Nair KrishnanKutty, Douglas G Osborne, Yang Li, Jenny Mae Samson, Stacey Bagby, Aik-Choon Tan, William A Robinson, Wells A Messersmith, Mayumi Fujita. CDK1 interacts with Sox2 and promotes tumor initiation in human melanoma. Cancer Research, 2018; canres.0330.2018 DOI: 10.1158/0008-5472.CAN-18-0330

15 emerging technologies that could reduce global catastrophic biological risks

Through an extensive literature review and interviews with more than 50 experts, the Center project team identified 15 example technologies and grouped them into 5 broad categories that are significantly relevant to public health preparedness and response:

Disease Detection, Surveillance, and Situational Awareness: Ubiquitous Genomic Sequencing and Sensing, Drone Networks for Environmental Detection, Remote Sensing for Agricultural Pathogens

Infectious Disease Diagnostics: Microfluidic Devices, Handheld Mass Spectrometry, Cell-Free Diagnostics

Distributed Medical Countermeasure Manufacturing: 3D Printing of Chemicals and Biologics, Synthetic Biology for Manufacturing MCMs

Medical Countermeasure Distribution, Dispensing, and Administration: Microarray Patches for Vaccine Administration, Self-Spreading Vaccines, Ingestible Bacteria for Vaccination, Self-Amplifying mRNA Vaccines, Drone Delivery to Remote Locations

Medical Care and Surge Capacity: Robotics and Telehealth, Portable Easy-to-Use Ventilator

The project team noted their list is not exhaustive or an endorsement of specific companies. The team used a modified version of DARPA's Heilmeier Catechism to standardize the process of evaluating each technology and formulating guidance for funding decisions. That process informed the team's high-level assessment of the readiness of each technology (from early development to being field-ready), the potential impact of the technology on GCBR reduction (from low to high), and the amount of financial investment that would be needed to meaningfully deploy the technology (from low to high). Details on these findings are included in the report.

Source: Johns Hopkins Center for Health Security.

Artificial enzymes convert solar energy into hydrogen gas

In a new scientific article, researchers at Uppsala University describe how, using a completely new method, they have synthesised an artificial enzyme that functions in the metabolism of living cells. These enzymes can utilize the cell's own energy, and thereby enable hydrogen gas to be produced from solar energy.

In the new article, published in the journal Energy and Environmental Science, an interdisciplinary European research group led by Uppsala University scientists describe how artificial enzymes convert solar energy into hydrogen gas. This entirely new method has been developed at the University in the past few years. The technique is based on photosynthetic microorganisms with genetically inserted enzymes that are combined with synthetic compounds produced in the laboratory. Synthetic biology has been combined with synthetic chemistry to design and create custom artificial enzymes inside living organisms.

"We've now been able to use the method we developed to produce enzymes that use the cell's own energy to produce hydrogen gas," says Adam Wegelius, a PhD student at the Department of Chemistry -- Ångström Laboratory, Uppsala University.

Journal Reference:

Adam Wegelius, Namita Khanna, Charlène Esmieu, Giovanni Davide Barone, Filipe Pinto, Paula Tamagnini, Gustav Berggren, Peter Lindblad. Generation of a functional, semisynthetic [FeFe]-hydrogenase in a photosynthetic microorganism. Energy & Environmental Science, 2018; DOI: 10.1039/C8EE01975D

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