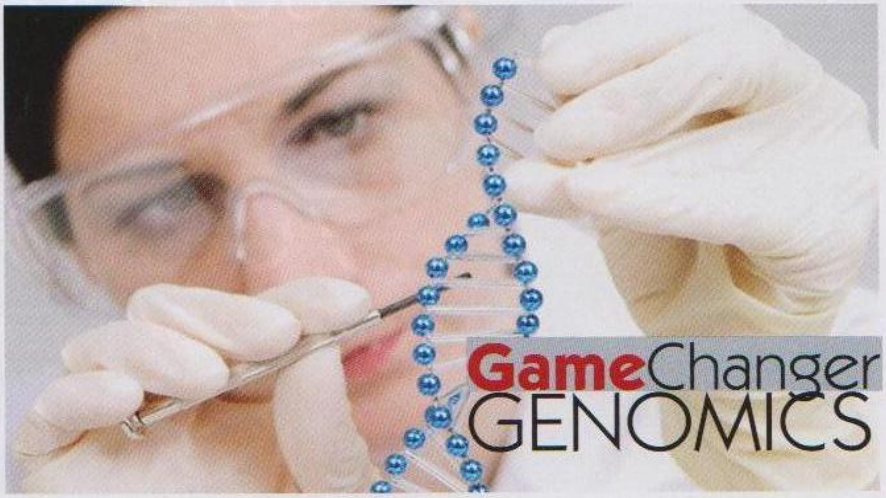
Genomics

Drives efficient, accurate, cost-effective healthcare

A paradigm shift

Ground-breaking technologies such as genomics, biosimilars, biofuels, gene therapy, proteomics and stem cells have changed the scope of science and effectiveness of healthcare delivery. In this issue *BioSpectrum* brings you a special series on these game-changing technologies. The first in this series throws light on the impact of genomics on drug discovery



"The genomics industry is driven by rapid advances in technology, particularly sequencing technology. There is a lot of activity happening in this sector. Asia is getting recognized as a rapidly growing place for genomics.

—**Dr Kirby Siemering**, business development manager, Australian Genome Research Facility, Australia

The cost of the first genome project was $2.7 billion. Today, we get these services for about $2,000; and it is believed that in 2011, the cost will slide to $1,000. In the next few years, the cost of specialized gene sequencing will probably reach about $100.

—**Dr Vijay Chandru**, chairman & CEO, Strand Life Sciences; president of Association of Biotechnology led Enterprises, India

Genomics enhances the possibilities of traditional science. When used wisely, it opens up new opportunities that usher in a new epoch of rational scientific exploration; and technical evolution within the life sciences sector."

—**Dr Stephen Rudd**, chief scientific officer, Malaysian Genomics Resource Center, Malaysia

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Genomics has taken the drug discovery world by storm. Eventually, it will have considerable impact on the prevention, screening, diagnosis and treatment of diseases; and will herald a new age of drug discovery.

Scientists are working towards new agents that will be used in the systematic treatment of diseases such as cancer. They are precisely targeting defined abnormalities found in individual patients. With these advancements, researchers hope that one day, cancer will become a chronic but controllable illness, like diabetes. The developments in immunoassay technology with ultra-sensitive detection, seem to hold potential in molecular diagnostics and drug development. This promises to assist drug developers, test for drug efficacy and drug safety; and also aid physicians to track disease progression.

The application of genomics within clinical trials, particularly within Asia, is largely an uncharted territory, and there is a mixture of both trepidation and excitement about the broader application of genomic knowledge for pharmaceutical indication and patient cohort stratification. Genotyping arrays, based on underlying genomic information, are commonly used in clinical trials to correlate adverse events, with key drug metabolism enzymes.

"Drug safety and efficacy are key reasons for the failure of strong drug candidates. With better characterization of genomic variation across populations and understanding of what this variation means within the terms of drug metabolism, absorption and off-target effects will undoubtedly be used with time, to better target drugs to the appropriate patients; and with a more genetically justified dosing regime. When these opportunities are realized, genomics will undoubtedly become a fundamental facet of clinical drug development," says Dr Stephen Rudd, chief scientific officer, Malaysian Genomics Resource Center, Malaysia.

Benchmarking of sequencing machines by generation

Parameters	Sequencing machines		
	First generation	Next generation machines	
		Second generation	Third generation
Year	1970 – 2000	2006-2010	2011
Type of sequencer	Sanger	454, Illumina, Helicos, Solid	PacBio
Read length (bases)	800	100-700 (454), 36-101(Illumina)	NA
Maximum yield per day	1 megabase	200 megabase (454), 20 gigabase (Illumina)	NA

Source: Frost & Sullivan

Tech upgrade for genomics

Custom-made cells lines

With the help of zinc-finger technology, custom-made cell lines have become a reality. "It's all about cells and cell biology," says Mr Dave Smoller, president, (Research Biotech Business Unit), Sigma-aldrich.

Scepter hand-held cell counter

Cell counting is now portable, using the new Scepter Handheld Automated Cell Counter from EMD Millipore. The Scepter has a screen that displays instructions to guide the user throughout the process.

Diffinity RapidTip

The Diffinity RapidTip is a one-step pipette tip for use in DNA purification. Following a polymerase chain reaction (PCR), samples contain more than just the DNA of interest. They also contain nucleotides, primers and other impurities that must be removed. Traditional techniques for purifying DNA involve several steps of washing, buffering and rinsing; that can take up to 30 minutes or longer. With the Diffinity RapidTip, all those steps are combined into a single, normal-looking pipette tip.

Gel Doc EZ, gel imaging system

With Gel Doc EZ, the newest gel imaging system from Bio-Rad Laboratories, researchers can load a gel and get print-quality images of up to 1200 dpi in seconds, at just a single push of a button.

Illumina HiSeq 2000

Ambry Genetics, a global leader in genomic services to the healthcare and life sciences industries, officially launched their Illumina HiSeq 2000 Next Generation Sequencing Services in December 2010. "We have continued to invest and develop our sequencing operations to become Illumina experts. All of our customers are excited about the Illumina HiSeq, because it expands our whole genome and exome sequencing services to the next level; and gives them the opportunity to reduce costs; while providing more data," says Mr Ardy Arianpour, VP (Business Development), Ambry Genetics.

Third-generation sequencer

Like other single-molecule sequencing machines, the PacBio RS reads a burst of fluorescent color, as a tagged nucleotide is incorporated into a single molecule of DNA. However, what differentiates this technology from others is the anchored DNA polymerase processes nucleotide binding in real time.

Scientific intelligence redefines healthcare

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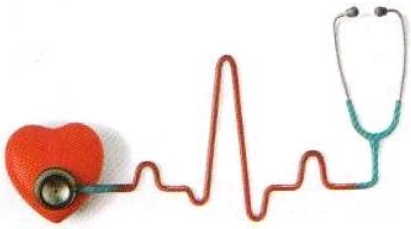
Science is continuously evolving, and at every stage of its development, innovations have brought about technological revolutions. We are now in an era of data-intensive science. It is part of the current age which has been called the 'fourth paradigm' — that goes beyond experimental and theoretical research, and computer simulations of natural phenomena. We require new tools, techniques and working mechanisms to move ahead and embrace the changes to come.



Pacific BioSciences claims that it can map a genome in 15 minutes for less than $1000, by 2013

"A genome sequence is not an answer, and the human genome sequence is not a cure; but it is a foundation upon which complex experiments to understand the fundamentals of disease and development of therapeutics may be built"

—**Dr Stephen Rudd,** chief scientific officer, Malaysian Genomics Resource Center, Malaysia

Currently, we are witnessing the genomics revolution, that started with the sequencing of the human genome, a decade ago. Today, we have sequenced the genomes of several organisms, and are able to better understand their occurrence and mechanisms. Understanding the link between genes and diseases enhances approach to healthcare.

"Genomics, depending on its definition, is the core of the life sciences industry. From the earliest experiments, when genes were first cloned into bacterial plasmid vectors, scientists were aware of the need to read and understand the DNA sequences of the plasmid and the cloned gene. The genome provides an amazing starting point from which researchers and scientists can, using advanced bioinformatics tools, build new testable hypotheses," says Dr Rudd of Malaysian Genomics Resource Center.

According to global business analyst firm Frost & Sullivan, the number of completely sequenced genomes has grown nearly 25 times in the last 10 years — from about 45 in 1999 to 1,100 in 2009. Similarly, the number of on-going genome sequencing projects, or incomplete genome sequences, has risen from about 100 to 4,500 in the same period. "A genome sequence is not an answer; the human genome sequence is not a cure; but it is a foundation upon which complex experiments to understand the fundamentals of disease and development of therapeutics, may be built," adds Dr Rudd.

"The breakthrough in genomics can be seen as an urge to understand biology and hence disease. If you are working in healthcare or agribiotechnology, it could be associated with disease and development. Genomics is going one step further in completing the causality chain. Another significant impact is the ability to read the genetic signatures, in an efficient and high-throughput manner. There have been great advances in technology since the completion of Human Genome Project in 2003, currently we are seeing what is known as next generation sequencing (NGS). This is bringing about a Moore's Law in biology, where the cost is halving; and the speed is doubling at an exponential rate. We are seeing a six-month cycle of doubling," comments Dr Vijay Chandru, chairman & CEO, Strand Life Sciences. Dr Chandru is also the president of Association of Biotechnology led Enterprises (ABLE), India.

The pharmaceutical, biotechnology and medical technology industries have been drastically changed since the emergence of genomes. Vaccines, diagnostics, antibiotics have been given a much awaited push to make them more efficient, accurate and cost-effective.

Genetic analysis THE IMPACT

Genomics has been creating waves in the life sciences industry. There are so many areas that have been given a new lease of life. Four major areas have seen profound impact: agriculture, healthcare, environmental and industry. There have been applications in non-food crops and other products (like biodegradable plastics, vegetable oil and biofuels).

Once a genome has been sequenced and analyzed, specific functions of the gene can be identified and studied in detail to assess ways in which the functions can be improved. From this information, it becomes easier to develop better and more effective treatments or solutions.

Agriculture

Once the genes of crops are analyzed and studied, there are endless possibilities for improvement. One of the main areas of interest is crop yield. Scientists have been studying the genes which control yield; and are finding ways to enhance them. Bioinformatics analysis is being used to compute the effect of different types of genes on yield, by determining the effect of the interaction between genes.

Another prominent area in agriculture is plants' resistance to abiotic and biotic stress factors like temperature, pH levels in the soil, pests. Genes control how plants react to all these factors, and once we know how to eliminate them, the crop yield goes up. One such example of genomics application is the technology incorporated by Indian seed company, Bangalore-based Metahelix Life Sciences, using *Bacillus thuringiensis* (Bt) gene called cry1c, into cotton plants, that offer resistance to two pests — *Spodoptera* and bollworms.

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Healthcare

Disease prevention

The genetic make-up of human beings are largely identical, but there are certain variations that create a huge impact. Many diseases are a direct or indirect result of genetic disorders, due to these variations. Some of these variations include mutations such as insertions, deletions, translocations, copy number variations (CNV) and changes in the shape/size/number of chromosomes.

Diagnostic companies have taken a keen interest in biomarker research, where genetic biomarkers help to identify disease and its prevention. One of the most important ways in which biomarkers can impact clinical diagnostics is by generating economical, accurate and rapid testing solutions, driven by analysis of sequenced genome data, to assist the physician and patient community.

"For a long time now, genomics has been playing a vital role in target development and biomaker discovery. In clinical trials, biomarkers are used for drug safety and efficacy. This helps to develop personalized medicine based on individual's genes. Based on a person's genetic make-up they can be prone to different diseases, and react differently to various drugs. Genomics identifies these genes," says Dr Kirby Siemering, business development manager, Australian Genome Research Facility, Australia.

Personalized healthcare

Apart from genetic variations, people vary due to difference in their exposure to environmental factors. Personalized medicine is a new field of science that helps to improve disease management or predisposition towards a disease. It optimizes medical outcomes by helping physicians choose the disease management approaches that would best suit a patient's unique genetic and environmental profile. Some of these approaches include genetic screenings to diagnose diseases, and their subtypes more precisely, and in selecting medication for a particular patient group.

One of the first examples of personalized medicine is the development of Herceptin, manufactured by Genentech for the treatment of breast cancer. Around 25 percent of breast cancers are Herceptin receptor positive, therefore, it can be prescribed to this sub-population, to maximize the effectiveness of the treatment.

Personalized medication strives to apply genomic information to pharmacology, to check if a specific drug will work in a specific patient, with a specific genetic build. It involves segregation of the patient population with a particular disease, into narrow groups; based on their genetic make-up; and determines its effect on drugs that are targeted to the disease. Pharmaceutical companies are discovering that this sort of niche marketing can have significant benefits like improved health outcomes and cost-effective healthcare.

GLOBAL PERSONALIZED MEDICINE MARKET TO TOUCH $452 BN BY 2015

Shift to managed healthcare

"Genomics, with its amazing capabilities using next generation sequencing technologies, brings in unimaginable change in the life sciences, healthcare and research sectors. Hardly a couple of years ago, gene expression profiling was the king. Then emerged the high-density geno-typing arrays, and efforts were made on the characterization of known variation within and across populations; and the association of these variations with human disease. Next generation sequencing has demonstrated a remarkable capacity for the characterization of the true variation between individuals and identification of the rare mutations responsible for disease," says Dr Rudd.

"We are going to see some profound effects of genomics, as it will be driven by advancement in sequencing technology. The biggest thing to look forward to is the $1,000 genome sequencing technology, which is likely to be achieved within the next two-to-three years. It will enable more people to sequence their genes; and babies at birth itself can be sequenced. It will cause a shift from preventive healthcare to a more managerial-based healthcare approach," adds Dr Siemering.

Personalized medication is set to gain more significance, particularly in Asia, with its ethnic diversity. Most drugs available in the market have been developed in the West, and have been tested on patients from there. The development and effects of drugs on various ethnic groups at the drug discovery stage, is largely unknown. This is an area of interest for bioinformatics analysis, as drug discovery and delivery involve methods for identifying new therapeutic molecules with specific biologic activities. These high-throughput techniques include combinatorial chemistry and genomics analysis, as the starting point.

Western countries are at the forefront of drug discovery, and have innovative technology platforms like genomics and broad-based screenings. As the global outsourcing of contract research services shifts to Asia; companies from the region will be able to offer specialized bioinformatics analysis services to companies worldwide, in need of this service. "In the next few years, many countries in Asia particularly India, China, Japan and Malaysia will be the major players in genomics-related field. Asian countries will gain momentum to be on par with the West, in terms of technology and its applications," adds Dr Pawel Suwinski of Frost & Sullivan.

Genomics will cause a shift from preventive healthcare to a more managerial-based healthcare approach

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Segregating data on various genomes will be a huge task. Many companies will take this up as a challenge, and devise ways to analyze the data and apply it in an efficient way. "We believe that like business intelligence, we need scientific intelligence for the life sciences industry," says Dr Chandru.

Genomics, as a promising sector, continuous to grow and evolve rapidly in the next few years. With greater emphasis on managing healthcare, instead of preventive healthcare, drugs will target specifically to the need of an individual. BS

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