GENOME SCIENCES

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ABSTRACT

Rehman Medical Institute (RMI) recently inaugurated the Center for Genomic Sciences, where, in addition to currently practiced molecular genetic techniques, the addition of Next Generation Sequencing ushers in the era of modern high throughput genomics for diagnostic and prognostic use. This paper provides a brief review of the historical development of this field till the present era.

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INTRODUCTION

Genomics is a science that studies the genetic material of humans, animals, plants, microbes and other living organisms. It deals with the genes and how they work together. Any error in such network of genes can lead to various problems in internal communication and result in genetic diseases.

Brief History of Genomics

Sequencing started as soon as Sanger et al.[1] and Maxam and Gilbert[2] published their article using P^{32} labeled double de-oxynucleotide bases (ddNTPs). Sequencing by this technique was very tedious, expensive and cumbersome and thus scientists continued their search for better and economical methods. Eventually fluorescent based sequencing techniques were developed .[3] ABI took the lead and developed a machine as well as used various dyes attached to ddNTPs. Colours not only eliminated the dangerous use of P^{32} but also made it possible to run four lanes in one. The first human genome was mainly sequenced using dye attached ddNTPs using ABI sequencers at a cost of 3 billion dollars and over 2000 scientists. The last state-of-the-art Sanger sequencing based ABI machine utilised in genome sequencing was 3730 DNA Sequencer and was capillary based. Currently, 3730 machine is being used mostly for validation purpose.

New Era of Genomics

Sequencing technologies are developed to decode the genes involved in various functions. Error detections in genes can be helpful in determining various diseases such as cancer and can lead to better and robust treatment. Not long ago, Roche announced 454 DNA Sequencer machine and Illumina announce their ever first GA sequencer then known as Solexa machine. Solexa/Illumina GA were only capable of generating 20 bp read. In short span of time, now we have a variety of sequencers. There are a few major players with their hold on the market, maintained by Illumina, ABI (Lifetech), and Pacific bioscience. Nanopore is weighing their option to make their first mark and release a machine real soon. All the current machines are single molecule sequencers and are now collectively named as NextGen sequencers or machines.

NextGen sequencing technologies such as Miseq machine can be effectively deployed in developing countries to counter genetic diseases. Cancer and other genetic diseases detection and personalizing its treatment is now possible using NextGen sequencing technologies. RMI Peshawar has recently acquired such machine to effectively deal with many known and unknown genetic diseases and provide world class treatment to its patients. RMI will become the first institute in Pakistan to deploy Miseq, a cutting edge machine to train new scientists, provide diagnostic services to its patients, and further explore unknown genetic diseases and management.

NextGen sequencing is a paradigm shift in prevention, detection, and treatment. Such technology is at the forefront in making personalised medicine a possibility. NextGen sequencing provides a clear picture of genes involved in specific diseases and provides an opportunity to design drugs for accurate and precise treatment at a personalised level. Currently such technologies are used to ascertain the landscape of

30 genetic diseases out of 49 including majority of the cancers.

Pharmacogenomics/Personalized medicine

A living cell or a living being functions by using genetic material for transcribing to RNA and then translating to protein. Proteins are the driving force of life. Therefore, any error in the genetic material located in the coding region (gene) may lead to a change in protein. Such error in protein can create complications and thus become a genetic disease. Genetic changes can be inherited (germ cells) or can be accumulated later in life (somatic). Germ cell changes can be passed on from generation to generation unless lethal; however, somatic changes on the other hand may not be passed on.

Some epigenetic changes are now known to be remembered by chromosomes and may in a sense be passed on by unknown mechanism. Current flow of genetic diagnostic and/or studies seems like:

Genetics > cells > genes > RNA > proteins > cancer/diseases physiology

The diagram below provides a quick snap shot of various genetic makeups and how a drug may be personalized using genetic screening.[4]

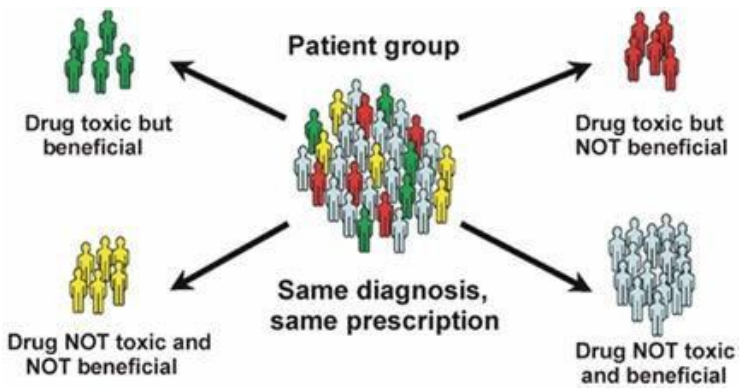

Figure 1: Genomic Variation[4]

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