

## Clinical Genome and Exome Sequencing (CGES) In Cancer Diagnostic

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### Editorial:

The human genome includes more than 3 billion base pairs and is built up of more than twenty thousand protein coding genes. As we are aware, decoding of DNA sequences is necessary for almost all divisions of biological research and specifically in cancer biology. With the noble discovery of capillary electrophoresis by Frederick Sanger and his colleagues in 1977, popularly known as “Sanger sequencing” the scientists in various research and diagnostic laboratories all over the world have adapted and expanded it in quality to improve the ability to resolve the investigations into the genetic disorders and to elucidate complete genetic information from any given biological system. Yet, this technology is not so efficient and accurate because it has always been hampered by inherent limitations related to high throughput, speed, noise, scalability and resolutions that often preclude from obtaining the essential information needed for the study.

We are now entering cancer targeting era, in which the cost of whole-genome sequencing with respect to the clinical aspects and targeted sequencing tests are important to resolve their application in the cost effective diagnostics for the cancer patient's care, especially in the developing countries. According to renowned molecular scientist Leslie G Biesecker, genomic test data are stupendously complex but so are a number of other medical tests. So, genomics is not so different because of its complexity. He concluded that clinical genomic data are the same as any other complex medical data and need to be interpreted and delivered to the patient by professionals (typically, a molecular geneticist, a clinical geneticist and genetic counselors) who have the skills to interpret these results in the context of the test methodology and the theoretical background of genetics [1].

Lately we have entered into a new era of complete genomics sequencing known as Clinical Genome and Exome Sequencing (CGES). Clinicians understand the diagnostic indications for CGES so that they effectively organize it in their practices. CGES is a useful diagnostic test for a number of clinical situations and it is already being used by clinical geneticists and other specialists, because the success rate of CGES for the identification of a causative variant is approximately 25% [2]. It is important to understand the basis of this testing and how to select the patients most likely to benefit from it.

A big question arises in our mind why Clinical Genome and Exome Sequencing (CGES) is important as a diagnostic approach? As we know, clinical exome sequencing is a test for identifying several disease-causing DNA variants within the 1% of the genome which codes for proteins, i.e., exons or flanks regions (splice junctions). This test is intended for use in conjunction with the clinical presentation and other markers of disease progression for the management of patients with rare genetic disorders. Translating Whole-Exome Sequencing (WES) may have great influence on molecular cancer diagnostics; however, numerous modernizations and improvements are necessary for accurate clinical implementation. For this prospective Van Allen et al describe a prospective clinical WES platform for archival formalin-fixed, paraffin-embedded tumor samples and used computational methods for effective interpretation of data and finally, this methodology have good

information and extensive applications for cancer cure. Maranhao et al. supported that use of exomeSuite software to analyze exome and whole genome variant data from diseased individuals and this software is the first freely available and useful [3,4].

Presently we are defining various mutations and patterns of mutations or epigenetic changes in different cancers. Except in genetic conditions strongly associated with cancer our list is awfully incomplete. Moreover a patient carrying a cancer causing mutation or cancer defining mutations does not necessarily develop clinical cancer over time, as cancer is a multistep process with multistep genomic alteration conspired by environment, diet, lifestyle, infections, habits (smoking) and epistatic factors. Moreover in all probability everyday many of us are developing some cancer defining gene mutations in somatic cells which are taken care of by our active immune system. Hence in the complex saga of neoplastic development a senescent immune system also plays its part.

Moreover, the cancer defining genetic change must involve a stem cell to be able to behave as they do. However there is also a large lacunae in our knowledge whether a cancer defining mutation while affecting a normally mitotically incapable well differentiated end cell can cause retro differentiation in this cell to become a cancer stem cell or all cancers arise from a mutation in relevant stem cell compartment? In the absence of all this information in a present manner of gene policing for cancer, will only increase the fear and anguish amongst population at large without any solid foundations and will only be of help in flourishing genepolicing industry further. We strongly feel that there is no case for large scale genetic screening for cancer for all and sundry at present. However specific subset of persons with strong family history of cancer needs to be screened and followed up as per standards which may emerge from time to time as the new knowledge is incorporated in the algorithm of investigation and management of such conditions.

In this era exome genome sequencing is well known and getting more popular tools use in clinical molecular diagnostics not only in cancer biology, it is also used in several diseases. Cabral et al. first reported and describing a novel homozygous missense mutation (c.229C > T, R77W) in CHST8 gene by using whole genome sequencing in autosomal recessive Peeling Skin Syndrome (PSS), this gene encodes a Golgi transmembrane N Acetylgalactosamine-4-O-Sulfotransferase

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(GalNAc4-ST1) and expressed throughout normal epidermis and localized to the Golgi membrane [5]. Dinwiddie et al. used exome sequencing tools to identify the gene fact behind Pediatric-onset Inflammatory Bowel Disease (IBD) of two brothers from a non-consanguineous relationship who presented before the age of one with severe infantile-onset IBD, failure to thrive, skin rash, and perirectal abscesses refractory to medical management. Finally, reported that these siblings had suffered with harbor compound heterozygous mutations in IL10RA (c.784C > T, p.Arg262Cys; c.349C > T, p.Arg117Cys). Therefore, on the basis this evidence, suggested that exome sequencing may be an effective and accurate molecular diagnostic tool to incorporate in pediatric-onset IBD [6].

Even though there are over 2,000 Mendelian diseases caused by known DNA variants, many patients who are suspected or have been clinically demonstrated to have rare genetic disorders do not receive a molecular diagnosis, often due to genetic heterogeneity and the relative inefficiency of the current sequencing technology. Recently Schuster et al exemplifies exome sequencing used a powerful diagnostic tool in Mendelian disorders and it accelerate better clinical comprehensive diagnosis [7]. It is widely accepted that about 85% of known disease-causing variants occur within the 1% of the genome containing the exons and splice junctions; thus, fathoming this region of the genome is a proficient and powerful clinical diagnostic tool for patients. Hence we think that though Clinical Genome and Exome Sequencing (CGES) has proven its diagnostic utility many clinician's geneticists have concerns regarding the interpretation of results and cost.

The author's only expressed his opinion in this clinical use of CGES in cancer biology and may not represent the any views of any scientist and institutions with which they are working or affiliated on this aspect.

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