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Understanding the Genetic Basis of Cancer and its Implications for Precision Medicine

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Perspective

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DESCRIPTION

Cancer is a disease caused on by an abnormal growth of clonal cells brought on by DNA anomalies. These result in aberrant proteins and functions and can be observed as mutations, deletions, substitutions, rearrangements, or amplifications. These genetic changes may be inherited or acquired as a result of exposure to carcinogens, diseases, a certain lifestyle, etc.

The functional unit of inheritance in humans is thought to consist of 80,000-100,000 genes, according to the human genome project. Our understanding of the onset and progression of cancer has been fundamentally changed by genomic information. Giving the appropriate diagnosis at the appropriate time to select the appropriate therapy is the primary goal of genomics and precision medicine. Genomic sequencing enables the understanding of the genetic basis of cancer patients and resolves the diagnostic conundrum in challenging histopathological situations.

In patients with advanced metastatic illness, DNA sequencing of the tumor is increasingly employed. By allowing us to identify mutations, copy number variants (CNV), and translocations while simultaneously generating data in

terabytes of millions of reads of genomic DNA, next generation sequencing has given us an unmatched opportunity to study the biological basis of many cancer kinds. One can correctly anticipate who will respond better to a medication and who will experience adverse effects by using genomic data and machine learning techniques.

Recent advancements in bioinformatics and robotic technologies increase accuracy and speed up the procedure by automating DNA sequencing and gene mapping. As the same type of cancer may behave differently to various medications, pharmacogenomics can also serve to describe the behavior of the tumor in response to a specific therapy and find genomic biomarkers of drug response and resistance. Precision medicine also referred to as better diagnostic and treatment methods that are adapted to the patient's tumor, has resulted from this.

For cancer patients who are diagnosed at a young age or who have multiple family members who have the same or related cancers, genetic counseling and germline testing (done on cells that do not have cancer to determine if a person has a gene mutation known to increase the risk of developing cancer) are advised.

A number of germline malignancies, such as hereditary breast and ovarian cancers (HBOC), Hereditary Non-Polyposis Colorectal Cancers (HPNCC), BRCA 1 and 2, etc., have been reported to be fairly prevalent in India. By the time they reach the age of 70, those who test positive for hereditary mutations in the BRCA1 or BRCA2 genes have a 45%-65% risk of developing breast cancer and a 10%-20% risk of developing ovarian cancer. A variety of illnesses affecting many organ systems, including the female genital tract, breast, pancreatic, prostate, etc., are caused by mutations in the BRCA1 and BRCA2 genes.

The identification of acquired somatic or inherited germline variations in the patient can aid in the selection of a systemic therapy and, when used as a screening tool in the patient's relatives, may aid in preventative surveillance. It can also encourage the patient to lead a healthy lifestyle by avoiding risk factors.

However, somatic and germline biomarker testing-tests conducted on cancer cells to learn more about the malignancy are complementary, and each can yield a different set of recommendations. Olaparib, a poly (ADP-ribose) Polymerase (PARP) inhibitor that has been approved by the FDA, has been successfully used to treat HBOC. Targeted medications disrupt gene expression, signaling pathways, or abnormal protein expression by acting as tiny molecules, antibody-based, or direct inhibitors.

When tissue biopsy is not an option, liquid biopsy (cell free (cf) DNA) can be done to analyze Circulating Tumor Cells (CTCs), which are lost from the main tumor site into the circulation. It is common practice to use these genetic hallmarks of cancer cells for cancer diagnosis and long-term monitoring of cancers with resistance mutations.

This simplifies the process of monitoring patients receiving radiotherapy and chemotherapy. Understanding the response to targeted therapy is aided by the monitoring of Minimal Residual Disease (MRD) by RT-PCR in hematological malignancies (cancer in blood-forming tissues).

A therapeutic response to immune checkpoint inhibitors may be predicted by genomic approaches that measure Tumour Mutational Burden (TMB), Microsatellite Instability (MSI), and Programmed Cell Death (PDL-1) in addition to identifying targetable changes. The therapeutic approach to tumors at various places has been revolutionized by tumor agonistic or histology agonistic therapy for specific genetic fusions or mutations.