Editorial

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Diagnostic Pathology in the Era of Precision Medicine

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The ever-increasing importance of targeted therapy in the management of cancerous and non-neoplastic diseases calls for novel, advanced techniques of diagnostic pathology. The past decade has witnessed substantial changes in how cancer patients are managed, with a pronounced focus on precision medicine based on genomic profiles and gene expression analysis, thus discarding the "one-size-fits-all" approach[1]. Understanding tumor development and acquiring information regarding the genetics, transcriptomics, proteomics, and epigenetics of pathological lesions, especially cancers, is central to precision medicine[2]. Several state-of-the-art techniques, especially those directed towards the molecular characterisation of diseases, have been developed to meet these challenges. Completing the Human Genome Project and the advent of pharmacogenomics, disease management has changed drastically, especially that of cancers. Oncology is now considered to be the first choice for targeted therapeutics. In cancer therapeutics, precision medicine aims to develop tailored therapies for patients according to the molecular pattern of the tumor.[3,4]

More recently, cancer researchers have focused on non-invasive methods for diagnosing molecular profiles of tumors. One such diagnostic tool, "liquid biopsy," relies on circulating tumor cells and cancer cell-derived circulating components like ctDNA and exosomes. These components are isolated from peripheral blood and can be utilized for genomic and proteomic diagnostic techniques.[5,6] Liquid biopsy is being recognized as an effective non-invasive, real-time approach for detecting biomarkers in body fluids for screening, diagnosing, and predicting various cancers. Potential clinical applications of liquid biopsy include genomic profiling of tumors, recognizing molecular targets for therapy, response to therapy, and assessing minimal residual disease.[7] Role of liquid biopsy in cancer screening is still undecided and is an open arena for future research.

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Advancement in molecular diagnostic techniques and data processing have made possible analysis of large amounts of data and has provided opportunities for suitable and effective interventions. Next-generation sequencing techniques have proved invaluable for gaining insights into tumor molecular profiles and the development of targeted therapies.[8] Sequencing and array technologies generate extensive data and make it possible to unravel the potential mechanism underlying the alteration in morphology and function of tumors. These techniques can identify multiple and epigenetic alterations including, insertions and deletions, copy number variation, chromosomal rearrangements, and single nucleotide mutations. These techniques can be applied to specific genes, entire protein-coding regions of DNA (whole-exome sequencing) or the entire genome (whole genome sequencing). The advent of computational biology and bioinformatics has made it possible to handle, store and analyse the extensive data generated by next-generation sequencing. Diagnosing cancers and predicting cancer behaviour and progression has become more precise owing to these advancements. Thus modern molecular techniques like NGS have become an inevitable tool in cancer diagnostics. The same results would be impossible with the conventional pathological diagnostic methods that rely on morphological changes and can predict only a general need for therapy. However, it will give little insight regarding the precise target therapy based on the underlying genetic alteration and its functional consequences.

Even though the genomic characterisation of tumors has been of immense value, DNA aberrations alone do not picture the related biological pathways. This gap has been very efficiently filled by transcriptomic studies that have emerged as essential techniques in molecular diagnostics.[9] Moreover, transcriptomic studies have paved the way for developing bioinformatics tools, improving the understanding of differential gene expression regarding biological functions.[10] RNA sequencing (RNA seq), a type of whole-genome transcriptomic technique, is utilized to characterize and quantify the entire RNA content in a cell or tissue. This technique has improved immensely since its early development, especially regarding data quality related to translated and non-translated RNA molecules and gene fusions.[11] RNA seq has also revolutionized differential expression analysis in specific cell types. More recently, single-cell RNA sequencing methods have been developed

that enable accurate gene expression profiling with a limited number of reads.[12] Targeted breast cancer therapeutics is one of the success stories in the achievements of transcriptomics in cancer management in the near past. Whole-genome sequencing has provided substantial knowledge of, breast "cancers' genomic profiles, including single nucleotide pleomorphism, copy number variations, and driver mutations.[13] One of the significant achievements in this regard is the advent of RNA sequencing, especially mRNA sequencing. This technique has been effectively utilized to characterise receptor-negative breast cancers (triple-negative breast cancers). It has been a valuable aid in evaluating differential gene expression between TNBCs and non-TNBCs hence characterisation of TNBCs and their subclassification.[14] This classification has opened avenues for developing precision medicine for triple-negative breast cancers with specific molecular subtypes, a ray of hope for patients with this aggressive tumor. siRNA screening has also uncovered genetic variants participating in cancer development and progression.[15] An increasing number of miRNAs (microRNAs) are being identified by transcriptomic studies, and many of these play critical roles as tumor suppressors and promoters.[16] MicroRNAs are often dysregulated in cancers, and profiling miRNAs has given insights into the complex mechanisms underlying oncogenesis. miRNA expression may be used to classify tumors and design effective therapies, and multiple clinical trials have shown promising outcomes.

While there has been a boom in developing new and more precise molecular diagnostic techniques worldwide, we lack behind with regards to utilizing these advancements to develop even a basic genetic profile of cancer patients in our population. There is an extreme shortage of knowledge regarding the mutational profiles of cancer patients in the Pakistani people. To develop targeted therapies directed at treating the prevalent cancers in our part of the world, it is imperative first to understand our genetically diverse population's genomic and expression profiles of our genetically diverse population. In the same regard, trained individuals in molecular pathology, molecular medicine, and bioinformatics are indispensable assets. Qualified individuals in molecular pathology, molecular medicine, and bioinformatics are essential assets, trained individuals in molecular pathology, molecular medicine, and bioinformatics. It is high time that we take advantage of the rapidly emerging advancing diagnostic techniques to identify the biological hotspots and networks in various prevalent cancers in our population for effective drug development and design.

Authors Contribution:
Summaya Shawanna: Idea Conception, writing
Yasmeen Taj: Literature Review

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