EDITORIAL

Molecular Pathology: A Paradigm Shift towards Precision Medicine

Fouzia Shaikh[1], Talat Mirza[2]
[1]Department of Pathology, Ziauddin University [2]Department of Research, Ziauddin University, Karachi, Pakistan.
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Healthcare system is experiencing a paradigm shift to precision medicine. Genotypic–phenotypic affiliation has been found to be a fundamental percept in biology after the completion of Human Genome project. The first era of precision medicine is split into groups and subgroups, making it a meaningful strategy concurrently throughout the clinical phases of drug designing and development. It likewise recommends healthcare reshaping that suggest disease perceptivity or remedial treatment. Thus, translational genomics addresses bench to bedside approach to achieve P4 medicine (*personalized, predictive, preventive, and participatory*), i.e., early disease diagnosis and specifically designed treating plans instead of one size fits all[1].

The ever-increasing importance of targeted therapy in the management of cancerous as well as non-neoplastic diseases calls for novel, advanced techniques of diagnostic pathology. Understanding of tumor development and acquiring information regarding the genetics, transcriptomics, proteomics, metabolomics and epigenetics of pathological lesions, especially cancers, is central to the development of precision medicine. The next generation sequencing (NGS) techniques have proved to be invaluable for gaining insights into molecular profiles of tumors and development of targeted therapies. Even though genomic characterization of tumors has been of immense value, DNA aberrations do not give a clear picture of the related biological pathways. This gap has been very efficiently filled by transcriptomic studies, which have emerged as one of the essential techniques in molecular diagnostics. Moreover, transcriptomics studies have paved the way for the development of bioinformatic tools improving the understanding of differential gene expression concerning biological functions. 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 the genomic profiles of breast cancers including single nucleotide pleomorphism, copy number variations and driver muations[2].

An increasing number of miRNAs are being identified by transcriptomic studies and to date nearly 8600 miRNA genes have been identified. miRNAs play various roles in cell proliferation, fate determination, and differentiation. These appear to contribute to transitions from stem (precursor) cells to differentiated cell types by refining/reinforcing desired gene expression profiles, rather a process of mapping molecular signatures[3]. Further recent field of 'molecular pathological epidemiology' (MPE) is now being recognized for personalized medicine along with public health all through using 'omics' data in population-based studies also. The proposed integration of microbiome (viruses, bacteria, fungi and parasites) into MPE to highlight the reactions and responses of tumor cells, the microbiome, immune cells and other factors of the tumor microenvironment is a step forward[4]. Current advances in tumor microenvironment has accomplished an era of immunotherapies which has proved to be valuable in various tumors e.g. lymphomas. Advancement in understanding complex tissue microenvironment has been accomplished by single-cell analysis to provide useful perceptions on tumor biology and progress.

Liquid biopsy involves the evaluation of circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and tumor-derived exosomes. Although DNA appears a promising prognostic marker, it cannot supersede biopsy or radiographic assessment. Liquid biopsies can be used as a supplementary standard to follow patients by monitoring the progressive genomic alterations in response to medication[2,3]. Rapid drops in cfDNA concentration and lack of ctDNA in plasma after commencement of therapy indicate treatment response linked with survival[5].

Moreover, digital and telepathology has broadened the scope for diagnostic precision. Infrared microscopy used for the assessment of tumor characteristics has been established as a key technique in the biomedical research promising better patient management. Moreover, Spectral histopathology (SHP) is a new promising tool; though, its use has not been authenticated for clinical practice yet, still the practical implications are expected.

The familiarity with the instructional manual of the master molecule of DNA is now completely sequenced in the form of a chip as an amazing identity card. The present hub of recent advances revolves around molecular signature, microenvironment, liquid biopsy and computational pathology. The mega achievements related to the high-profile diagnostics has amplified in depth understanding of disease processes with advent of targeted therapies. Moreover, the specific approaches for personalized medicine have further revolutionized the strategies and therapeutic outcomes, based on tailored treatment. However, in this era of precision medicine the developed countries are the major beneficiary as compared to resource deficient populations due to financial constraints. The high expenses for molecular diagnostics with lack of supportive infrastructure and expertise is a deprivation of recent advances in technology for the developing countries.

The debate remains that in depth knowledge of molecules altering diseases can lead to mental stress and can have a huge impact on a patient's life. The hidden budget could be potentially lower with the focus on preventive care rather than therapeutic strategies. Precision medicine has the predictive potential in healthcare, but that requires massive infrastructure investments and time to implement. According to a recent analysis, many newly discovered so-called disease-carrying mutations may have limited or no meaningful effect on future illness. Over diagnosis happens when people are diagnosed with a disease that would never actually harm them. Therefore, huge unanswered questions are around to interpret results of genomic testings. Carrying the gene chip is not the total answer to cure through precision medicine, which is, customized approach tailored to the individual patient.

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