Medicon Microbiology
Volume 1 Issue 4 May 2022
Short Communication

Multi Omics Based Approach to Tackling Cancer

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Received: April 18, 2022; **Published:** April 21, 2022

Introduction

Cancer is the second most fatal disease faced by Indians and it takes the lives of around 2.5 million people annually. Around 70% of the cases have been treated but survival rates remain diminished. Indian context dictates that the most prominent cancers have been lung cancer, breast cancer, stomach and cervical cancer and are attributed to poor to moderate living conditions, improper dietary and lifestyle choices, inadequate medical facilities and pollution. Hence, India faces a grave public health concern in the form of cancer with growing pollution and attitudinal shifts in the population.

Current Diagnostic Landscape

Various cancers are diagnosed at late stages mostly and the techniques used can fall under the following windows:

1. Molecular techniques: These are biomarker-based techniques and include Microarrays (DNA, RNA, and Tissue), PCR and its variants, Liquid biopsy that looks for biomarkers in blood and FISH.
2. Radiological techniques: These are mostly imaging based and include X-ray, Ultrasound, Immunomagnetic capture/ immunofluorescence, CT scan, MRI and are important as noninvasive detection techniques.
3. Cytological techniques: These are invasive techniques that include Fine needle aspiration cytology (FNAC) and generally looks at palpable tumors, Frozen Sectioning, Biopsy (Needle and Surgical) and Endoscopy.
4. Immunological techniques: These include RIA, ELISA, Immunohistochemistry and various immune assays like Microparticle enzyme immunoassay.
5. Other techniques: Includes various sequencing methods like deep sequencing, Sanger, Pyrosequencing, RNA-Seq, NGS etc.

Exisiting Inconsistencies

Albeit the former techniques are immensely helpful in the detection of cancer, the diagnostic landscape has many gaps. These gaps owe their existence to the inconsistencies that characterize cancer as a complex disease defined by heterogeneity, genomic instability, resistance to treatment and recurrence. Keeping these in mind, the relatively young fields of genomics, proteomics, transcriptomics were hailed as the batons of hope.

These focus on deep and targeted sequencing of the entire genome and includes techniques that rely on Next Generation Sequencing like Whole genome Sequencing (WGS) and Whole Exome Sequencing (WES). Such a thorough combing of the genome leads to information of gene mutations, gene signatures and gives information about the differences in gene expression (DEG Analysis), driver v. passenger mutations etc. Following the DEG analysis with Enrichment Studies yield a wealth of molecular, biological and cellular information.

Yet even they have not managed to develop a consistent and accurate picture of the disease.

Upcoming Solutions

Biomarkers are the most important of the information obtained by various Omics analysis as they are central to early detection of cancer. Use of biomarkers would improve the characterization of risk stratification of patients, detection, early diagnosis and better prognosis of the cancer. These are identified using methods like Genome wide association studies (GWAS) that relies heavily on Bioinformatics tools like Gene Ontology Terms and Database Matching (there are many relational databases that are used like GEO, Human Protein Atlas).

This kind of integrated Bioinformatics based approach is the cornerstone of screening novel prognostic biomarkers and a brief overview is given below:

a. RNA-SEQ is done and the data is collated. If novel data is not used microarray data can be obtained from HTP databases like Gene expression Omnibus (GEO).
b. Conversion into cDNA libraries and amplification followed by NGS.
c. Identification of the biomarker by developing a bioinformatics workflow that includes LC-MS/MS techniques and followed by-open Mass spectrometry Search Algorithm in conjunction with splicing datasets derived by cancer proteome studies available in specific databases.
d. Screening of DEGs using CDiff and R package Limma.
e. Enrichment Analysis using GO and KEGG pathway analysis using DAVID database.
f. Construction of PPI (protein-protein network) module using STRING tool.
g. Analysis of PPI module using Cystoscope database.
h. Survival Analysis (used to check the cluster of gene expression against the survivability of patients). This uses many tools like GEPIA, Cancer Genome Atlas etc.
i. RT-qPCR for confirmation and further construction of the biomarkers.

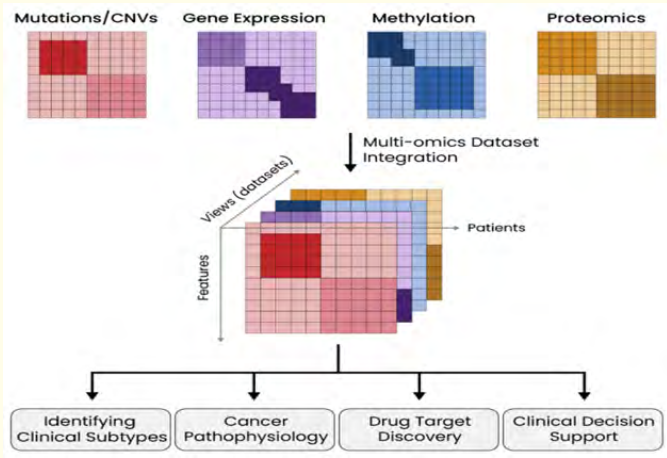
Such a discovery is of long non-coding RNA (lncRNAs) as they are propelling the future advancement of biomarker development. E.g. Zheng et al. identified a survival-related gene-based ceRNA (competing Endogenous RNA) network using the WGCNA algorithm, and the constructed lncRNA–miRNA–mRNA ceRNA interactive network to provide novel insights into the treatment of gastric cancer.

Other upcoming solutions also include anti-cancer treatments like Chimeric antigen receptor (CAR)-modified natural killer (NK) cell therapy and Biosensor based technologies.

Roadmap for the Future

The above technologies and techniques are still not enough to tackle cancer as it is based on the homeostatic interactions of the body with environmental stimuli which can manifest in myriad ways, sometimes even showing considerable differences in the tumor genome in the same patient. Hence, only an overarching approach that combines all of the above can effectively manage the disease. Such an approach is classified by the infant field of Multi Omics Systems. A multi-omics study is a high throughput data-driven scientific investigation that conducts at multiple levels by combining the datasets from Genomics, Proteomics, Transcriptomics and bioinformatics-based results from Wet Lab techniques to reveal the complexity of cells and their environment. It then provides novel frameworks to untangle biological phenomena or models to test certain hypotheses using various datasets.

The various combining datasets have their parentage in WES, WGS, DEGS, Methylation profiles (Epigenomics), Single cell technologies and are all fed into Omics platforms like iCluster, iOicsPASS or SALMON ((Survival Analysis Learning with Multi-Omics Neural Networks) that generate cancer subtypes, cancer pathophysiology and patient subgroups.



Essentially this systems and computation biology platform based on Bayesian statistics is the next frontier of cancer diagnostics as it is able to bypass the current complexities genetic and phenotypic heterogeneity.

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