Editorial

Prostate cancer bioinformatics analysis: emerging genomic profiling techniques

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Diagnosis techniques

Serum prostate-specific antigen (PSA) level measurement has been used as a diagnosis and prognostic measure for prostate cancer (PCa) (1,2). Catalona *et al.* reported that serum PSA measurement is a useful adjunct to rectal examination and ultrasonography in PCa diagnosis (1). Cooper *et al.* studied PSA levels in metastatic PCa cohorts of patients. They reported that 44 of 60 patients had a decrease of PSA to ≤10 ng/mL at period of 3 to 6 months after the EORTC trial of Zoladex plus flutamide versus orchidectomy (2). The European Association of Urology (EAU) suggested using a systematic prostate biopsy under ultrasound guidance and local anesthesia as a preferred diagnostic method than measuring PSA level (3). However, this method comes with underdetection and under-grading of clinically significant (4). ElKarami *et al.* applied a machine learning approach to magnetic resonance imaging-guided targeted biopsy (MRI-TB) on a cohort of patients who upgraded to significant PCa on MRI-TB was defined as upgrading to Gleason score (3+4) to Gleason score (4+3) (5). MRI-TB works with a visual diagnosis of lesions or the shape of the cell in the tissue (6).

Wei *et al.* introduced a bioinformatics pipeline that identified potential hub genes biomarkers for PCa diagnosis and prognosis. The methods were applied to four Gene Expression Omnibus (GEO) datasets that contain 123 PCa samples versus 76 normal. A panel of 368 differentially expressed genes (DEGs) was identified, including 120 up-regulated DEGs and 248 down-regulated DEGs. Pathway analysis showed that those DEGs were enriched in focal adhesion, chemical carcinogenesis, drug metabolism, and cytochrome P450 pathways. Then protein-protein interaction (PPI) analysis identified 11 hub genes network of the DEGs. While the work is comprehensive, DEG from microarray can be a starting point for biomarker identification (7). However, modern next-generation sequencing (NGS) allows deeper throughput into genomic insights. Hamzeh *et al.* proposed a machine learning approach to identify Gleason stages biomarkers based on NGS data. Genes transcripts from RNA-Seq data could determine a Gleason stage from the rest of the stages (8). The transcriptomics method identified biomarkers related to genes strongly associated with the progression of PCa, including PIAS3, UBE2V2, and EPB41L1.

The technical advancement in biomedical engineering technology allowed various measures from various omics areas, including genomics, transcriptomics, epigenomics, proteomics, metabolomics, and many other biomedical fields. The authors in (9) proposed a deep learning approach to predict the relapse in PCa. The multi-omics model integrates five different omics: mRNA, miRNA, DNA methylation, copy number variations (CNVs), and long non-coding RNA (lncRNA) by utilizing H2O package. Gholami *et al.* highlighted the importance of utilizing

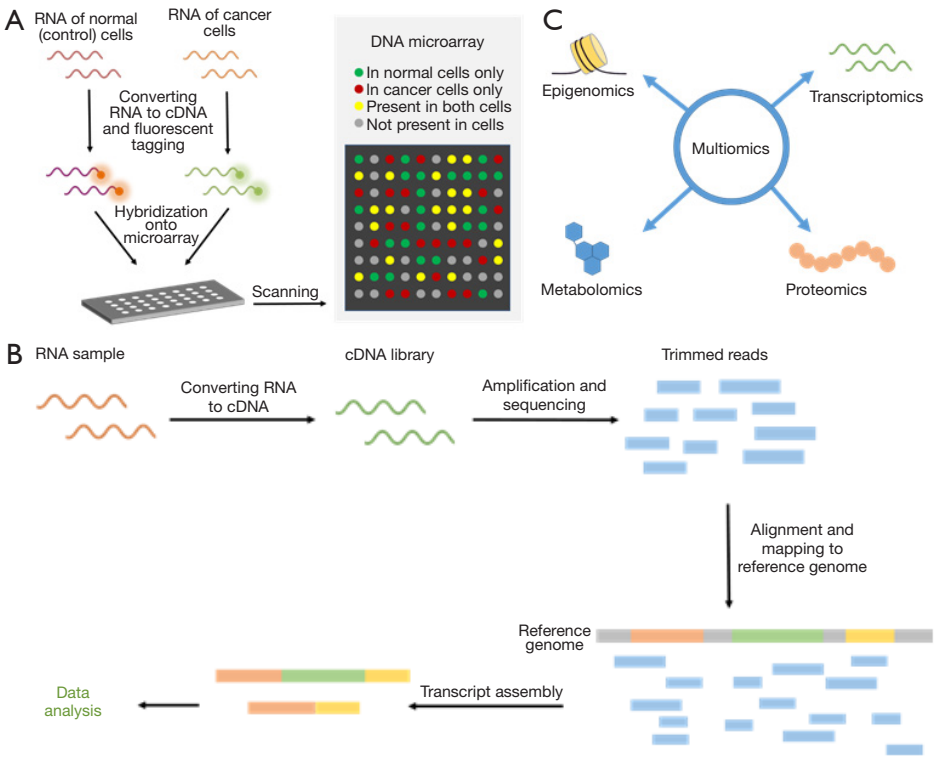

Figure 1 Different genomic profiling technologies. (A) Miccroarray gene technology. (B) RNA-Seq next generation sequencing. (C) Multi-omics data integration.

multi-omic approaches to improve outcomes in treating PCa patients. They survey recent works that applied a multi-omics data integration model to analyze PCa. The authors highlighted the challenges of using multi-omics approaches; it is an invasive biopsical practice to collect data with many side effects. The heterogenity nature of the various multi-omics data may result in a biased model. The resulting different molecular characteristics of tumor cells lead to effective screening methods for early cancer detection, patient selection strategies, or treatment response assessment (10).

Technology reflection

While microarray technology may provide relative gene expressions affordably, it comes with many drawbacks, including identifying only known transcripts with low sensitivity and providing no alternative splicing information. Conversely, RNA-Seq throughout NGS technology brought more high-intensity transcriptomics events and measurements. It can also identify unknown transcripts throughout *de novo* reads alignment technique (11). The NGS technology is becoming cheaper and expected to be affordable by the next couple of years for genomic profiling.

Similar to RNA-Seq library preparation, microarray requires converting RNA to cDNA. However, it requires an additional step, hybridization into microarray, before scanning, as seen in *Figure 1*. While RNA-Seq requires amplification before sequencing and extra data processing after sequencing, including reads alignments to the human genome and transcript assembly, as seen in *Figure 1*. Multi-omics data integration studies rely on integrating data from different omics measurements, which yields to comprehensive analysis of the disease that can extract various types of biomarkers. However, it is an expensive approach and complicated to analyze (10). *Table 1* highlights the strengths and drawbacks for different techniques of studying PCa.

While microarray and RNA-Seq technology provide insight into gene expressions in the tumor tissue, the current trend of PCa bioinformatics analysis is to integrate different omics to find various biomarkers for the diagnosis

Table 1 Genomic analysis studies strengths and drawbacks

Properties/technology	Microarray	RNA-Seq	Multi-omics
Strengths	Low cost	High sensitivity	Comprehensive analysis
	Well-known hybridization protocol	Transcription level biomarkers	Various types of biomarkers
		De novo assembly for unknown transcripts	
Drawbacks	Low sensitivity	Costly	Very costly
	Only gene level biomarkers	Preprocessing is required before data analysis	Each omic requires it's own protocol
	It works for only known transcripts		Still no well-formulated integrative model
	Low variance expression		

and prognosis of the disease. With the power of artificial intelligent methods, the future direction is to integrate omics data with other types of medical data, including medical images including MRI, to predict the outcome of the PCa. The fusion of various health data may unveil the potential of the prohibition and treatment of the disease.

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