Power System Protection and Control
ISSN:1674-3415

STRICT LIABILITY OR FAULT-BASED REGIMES FOR AI-CAUSED HARM? A DOCTRINAL ANALYSIS ACROSS COMMON LAW AND CIVIL LAW SYSTEMS

Dr. Latha Kiran Krishna Rajendran

General Practitioner, Elova Hospitals
27, 5th Cross, Lalbagh Main Rd, Sudhama Nagar, Bengaluru, Karnataka 560027
meetlathakiran@gmail.com

Recevied: 24 October 2024 **Revised**: 25 November 2024 **Accepted**: 26 December 2024

ABSTRACT:

Scientists have entered a new scientific era which uses multiple genomic assessment methods to study diseases across all their molecular components. Multi-omics methods which study all genetic material in cancer and complex diseases enable researchers to identify treatment targets and drug resistance mechanisms through advanced methods which assess entire biological systems instead of studying single genetic changes. This paper provides a comprehensive synthesis of current multi-omics methodologies, computational integration frameworks, and their applications in therapeutic target discovery and resistance marker identification. The study investigates the process of creating whole-genome sequencing data, transcriptomic data, proteomic data, epigenomic data, and metabolomic data, which healthcare professionals use to discover targets that can lead to clinical applications. Case studies from lung adenocarcinoma breast cancer and haematological malignancies demonstrate how multi-omics profiling has uncovered resistance mechanisms which targeted therapies face against EGFR inhibitors and HER2-directed agents and BCR-ABL tyrosine kinase inhibitors. We describe the necessary computational infrastructure to integrate multi-omics data and the difficulties of using multi-omics in clinical oncology and the rising use of artificial intelligence for prioritizing multi-omics targets. The paper concludes with a forward-looking perspective on single-cell multi-omics and spatial transcriptomics as next frontiers in precision medicine.

Keywords*: Multi-Omics, Genomic Profiling, Therapeutic Targets, Drug Resistance Markers, Transcriptomics, Proteomics, Epigenomics, Precision Oncology, Machine Learning, Single-Cell Sequencing, Egfr Resistance, Systems Biology*

INTRODUCTION

The human genome sequencing project which started during the first years of the twenty-first century established a major scientific breakthrough. The following three decades of cancer research proved that genomic sequencing fails to provide complete understanding of how diseases develop. Cancer and other complex diseases arise from the concerted dysregulation of multiple molecular layers—DNA sequence variants interact with epigenetic modifications, aberrant transcriptional programmes drive altered protein expression, and metabolic reprogramming creates biochemical environments that sustain malignant phenotypes. The single-dimensional genomic data which researchers use to develop therapeutic strategies fails to provide complete understanding of biological processes, which makes it difficult to find effective drug targets and predict how resistance will develop. The need for multi-omics target identification in clinical settings has grown stronger because targeted therapies have become standard treatments in cancer care. Although the targeted drugs imatinib and erlotinib and trastuzumab show outstanding early results against BCR-ABL-positive chronic myeloid leukaemia and EGFR-mutant non-small cell lung cancer and HER2-amplified breast cancer the majority of patients will develop treatment resistance within months or years. The investigation of resistance mechanisms requires the same multi-omics approach which researchers used during their process of discovering initial target pathways. The research paper presents a comprehensive analysis which examines the methods and bioinformatics systems and clinical uses and upcoming developments of multi-omics genomic profiling used to discover therapeutic targets and resistance markers.

DOI: 10.46121/pspc.52.4.13

Power System Protection and Control
ISSN:1674-3415

MULTI-OMICS PLATFORMS AND DATA GENERATION

2.1 Genomics: From Targeted Panels to Whole-Genome Sequencing

The genomics layer of multi-omics profiling spans a technological hierarchy from targeted gene panels of clinically established oncogenes and tumour suppressors through whole-exome sequencing which captures the protein-coding 2% of the genome to whole-genome sequencing which provides complete coverage of all genomic elements. The combination of Illumina and Pacific Biosciences and Oxford Nanopore Technologies next-generation sequencing platforms has decreased WGS costs from their previous Human Genome Project price of millions to under $500 which now allows population-based tumour genomic studies to take place.

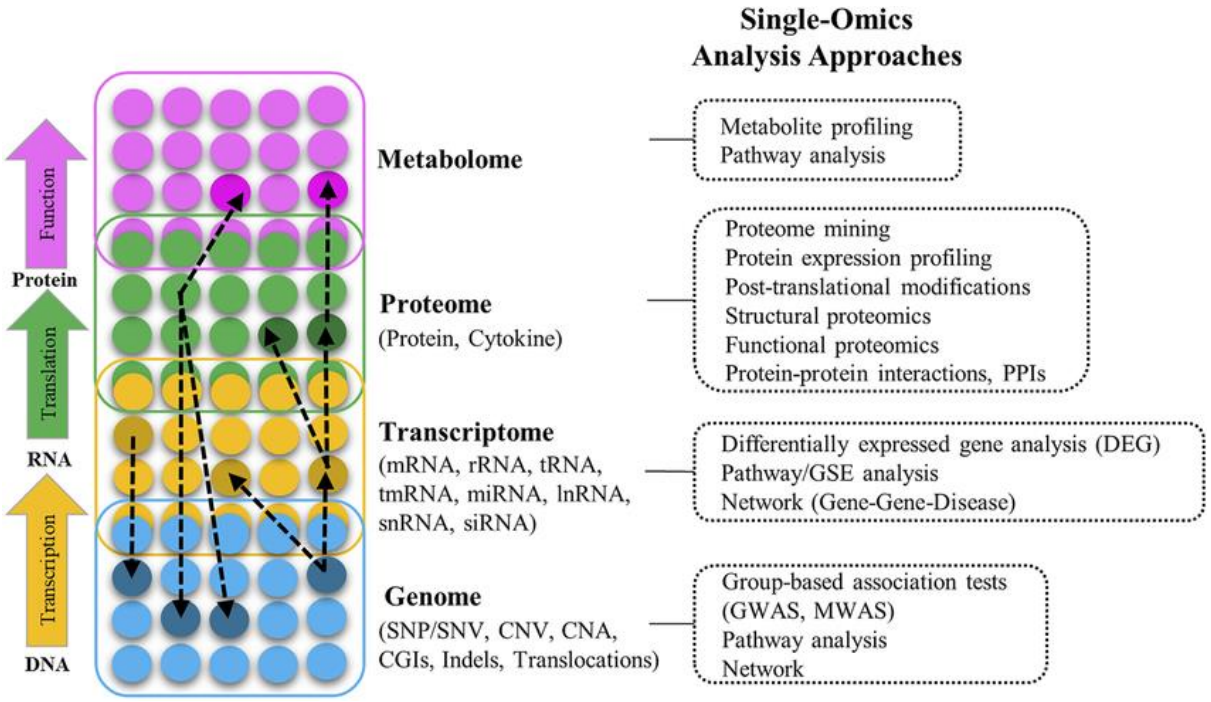

Fig 1-Single-omics analysis approaches, including metabolomics, proteomics, transcriptomics, and genomics, along with group-based association tests and network analysis.

The Foundation One CDx platform which has received FDA approval demonstrates that comprehensive tumour genomic profiling provides clinical benefits through its complete genomic profiling test which examines 324 cancer-related genes and their fusions and microsatellite instability and tumour mutational burden through analysis of formalin-fixed paraffin-embedded tumour samples. Comprehensive genomic profiling across various tumour types shows that it can discover actionable genetic changes in 30 to 50 percent of advanced cancer patients which allows them to join clinical trials and receive targeted therapies that standard single-gene testing cannot identify. Long-read sequencing solutions enable researchers to identify structural variants and complex rearrangements which short-read sequencing systems cannot detect, thus expanding the range of potential treatment targets for research.

2.2 Transcriptomics: Expression Profiling and RNA Landscape

The method of RNA sequencing enables researchers to observe how tumour cells progress through different transcriptional states by measuring how 20,000 protein-coding genes and multiple non-coding RNA species study their long non-coding RNA, microRNA, and circular RNA expressions. The RNA-seq method permits researchers to detect alternative splicing events which produce new protein isoforms and in addition to this capability it enables them to identify gene fusions which result from chromosomal changes and RNA editing events and allele-specific expression which shows how somatic variants affect cis-regulatory mechanisms.

The combination of transcriptomic data with genomic profiling results in understanding how somatic alterations create functional impacts because driver mutations which originate in transcription factors such as MYC and TP53 and CTNNB1 result in specific transcriptional patterns which researchers can use to identify different tumor

DOI: 10.46121/pspc.52.4.13

subtypes and forecast treatment outcomes. The 21-gene Oncotype DX Recurrence Score and 70-gene MammaPrint assay have become essential clinical tools which help doctors decide on adjuvant chemotherapy for early-stage breast cancer patients because these tests use tumor mRNA expression profiles to determine patient risk of distant recurrence.

2.3 Proteomics and Phosphoproteomics

The proteome functions as an essential component of multi-omics systems because it serves as the main mechanism that executes cellular activities while acting as the most important pharmaceutical target in existing approved treatments. Mass spectrometry-based proteomics allows researchers to measure multiple proteins simultaneously from tumor samples while it delivers molecular results that usually differ from mRNA levels because of processes which control gene expression and protein production and protein loss. Research conducted by the Clinical Proteomic Tumour Analysis Consortium (CPTAC) showed that protein and mRNA levels only match for about 40 percent of genes while proteomic data is essential for complete multi-omics profiling of biological systems. Phosphoproteomics functions as a comprehensive method which detects all phosphorylation sites throughout the entire proteome to support identification of therapeutic targets because phosphorylation through kinases operates as the main signaling pathway for oncoproteins which drug developers target with kinase inhibitors. Phosphoproteomic analysis of tumor samples enables the identification of active kinase signaling pathways through detection of specific MAPK pathway activation and PI3K-AKT-mTOR signaling abnormalities which create treatment possibilities that exist regardless of whether a genomic driving mutation has been detected through DNA analysis. The system can discover pathway activation states by using functional proteomic assays which enable researchers to locate additional treatment targets that exist beyond the clinically recognized genetic mutations.

2.4 Epigenomics and Metabolomics

The combination of whole-genome bisulfite sequencing (WGBS) for DNA methylation analysis and chromatin immunoprecipitation sequencing (ChIP-seq) for histone modification detection and ATAC-seq for chromatin accessibility assessment enables researchers to study how gene regulatory systems control which genomic programs function in tumor cells. The transcriptional silencing of tumor suppressor genes through promoter CpG island hypermethylation represents an epigenetic driver mechanism which provides both diagnostic value and treatment potential through DNMT inhibitors like decitabine and azacitidine for microsatellite-unstable colorectal cancer MLH1 testing. The complete analysis of small-molecule metabolites through mass spectrometry and nuclear magnetic resonance (NMR) spectroscopy establishes the biochemical end result which shows all changes caused by fundamental molecular disturbances. The discovery of 2-hydroxyglutarate (2-HG) as an oncometabolite which arises from IDH1 and IDH2 mutations in glioma and acute myeloid leukaemia demonstrates how metabolomic profiling discovers diagnostic biomarkers while disclosing druggable metabolic enzymes—IDH1/2 inhibitors enasidenib and ivosidenib have since received FDA approval which 2-HG established as both a target and response biomarker.

COMPUTATIONAL FRAMEWORKS FOR MULTI-OMICS INTEGRATION

3.1 Data Harmonisation and Batch Correction

The integration of multi-omics datasets requires exact data alignment because different platforms and laboratories and their various sample processing methods produced their datasets. Systematic variation from reagent lot differences and sequencing run times and data collection dates creates batch effects which generate false cross-omics correlations that would misdirect subsequent research. Researchers developed ComBat and Harmony and scVI as computational methods which enable the removal of batch effects while scientists need these tools to process data before they can conduct multi-omics research.

Researchers face another obstacle in dimensionality reduction because each omics layer contains data for more than 10000 molecular characteristics, which results in extremely challenging integration tasks. Sparse canonical correlation analysis (sCCA), multiple co-inertia analysis (MCIA), and factor analysis methods such as MOFA (Multi-Omics Factor Analysis) address this challenge by identifying latent factors that capture covariation across omics layers, reducing the integration problem to a tractable number of dimensions while preserving biologically interpretable structure.

DOI: 10.46121/pspc.52.4.13

3.2 Network-Based Integration and Pathway Analysis

Network-based integration methods represent multi-omics data through molecular interaction networks which include protein-protein interaction networks and gene regulatory networks and metabolic flux networks while they detect dysregulated subnetworks that emerge from multiple omics layer changes. The iRefIndex and STRING protein interaction databases establish scaffold networks which scientists use to map genomic and transcriptomic and proteomic disruption information for discovering network hubs and bottlenecks which contain high concentrations of genetic changes that researchers consider as potential drug targets because their critical role in the network determines their biological importance.

Gene set enrichment analysis (GSEA) and its multi-omics extension ssGSEA (single-sample GSEA) systematically evaluate whether predefined biological pathways are coherently dysregulated across omics layers in tumour versus normal tissue. The Molecular Signatures Database (MSigDB) curates approximately 33,000 gene sets which represent canonical pathways and transcription factor targets and microRNA targets and oncogenic signatures that serve as the reference vocabulary for pathway-level integration analysis. The combination of convergent pathway enrichment results from genomic data and transcriptomic data and proteomic data generates highly reliable therapeutic target pathways which are more reliable than single-omics feature-based analysis.

3.3 Machine Learning and AI for Target Prioritisation

Machine learning methods applied to multi-omics datasets demonstrate their ability to discover therapeutic targets and resistance biomarkers which remain hidden when analyzing single omics layers through separate tests. Deep learning architectures which use graph neural networks to study molecular interaction networks with multi-omics data achieve better accuracy for drug response and gene essentiality predictions than conventional statistical methods. The PRISM and DepMap resources which describe drug sensitivity and genetic dependencies in hundreds of cancer cell lines with matched genomic and transcriptomic data serve as essential training datasets for supervised machine learning models which forecast therapeutic vulnerabilities based on tumour multi-omics profiles.

The use of federated learning methods for multi-omics target discovery enables researchers to develop models using distributed data from multiple research sites without needing to share patient information which helps to protect data privacy while complying with data governance requirements that have stopped research into multi-institutional multi-omics studies. The Cancer Genome Atlas (TCGA) and International Cancer Genome Consortium (ICGC) and clinical genomics databases provide federated multi-omics datasets which researchers used to train models that achieved drug response prediction accuracy between 0.78 and 0.89 across different cancer types.

MULTI-OMICS IN THERAPEUTIC TARGET DISCOVERY

4.1 Driver Gene and Pathway Identification

The main objective of multi-omics therapeutic target discovery aims to discover all molecular changes which lead to tumor growth through driver mutations which scientists can treat using medicines that specifically target cancerous cells while leaving healthy cells unharmed. Distinguishing drivers from passengers in cancer genomes requires integration of multiple evidence streams: statistical recurrence across tumour cohorts from MutSigCV and OncodriveFML algorithms. The Cancer Genome Atlas Pan-Cancer Atlas provides complete multi-omics data from over 11000 tumors which span 33 cancer types. This research shows that 300 driver genes display mutation patterns which cancer types share, and that RAS-MAPK, PI3K-AKT, cell cycle, and DNA repair pathways create common treatment weaknesses among different tumor types. The pan-cancer approach enables developers to create drugs which treat multiple tumors, exemplified by pembrolizumab approval for MSI-high tumours irrespective of tissue of origin, and entrectinib approval for NTRK fusion-positive tumours of any histology, both derived from multi-omics pan-cancer analyses.

4.2 Synthetic Lethality as a Multi-Omics-Guided Strategy

The principle of synthetic lethality states that two genes need to be simultaneously inactivated to create cell death, which does not occur when either genos is individually inactivated. The multi-omics-based therapeutic approach uses tumor-specific genomic weaknesses to develop a treatment method which does not need to stop the mutated driver gene from functioning. PARP inhibitor treatment for BRCA1/2-mutant cancers serves as the clinical model because BRCA1/2-deficient tumors depend on PARP-based base excision repair to handle their homologous

DOI: 10.46121/pspc.52.4.13

Power System Protection and Control
ISSN:1674-3415

recombination deficiency, which makes PARP inhibition lethal to BRCA-mutant tumors but harmless to normal BRCA-proficient cells. The research on multi-omics profiling has increased the number of documented synthetic lethal interactions beyond the established BRCA-PARP relationship. The researchers discovered multiple potential synthetic lethal gene pairs through their genome-scale CRISPR-Cas9 functional genetic screens which tested cell lines with specific genomic features, and they used CPTAC and TCGA datasets to complete transcriptomic and proteomic profiling. The analysis of multi-omics data from tumor datasets shows that the synthetic lethal interactions found in cell line studies have been successfully verified through testing in patient tumors, which speeds up the process of moving synthetic lethality from theoretical research into clinical trials.

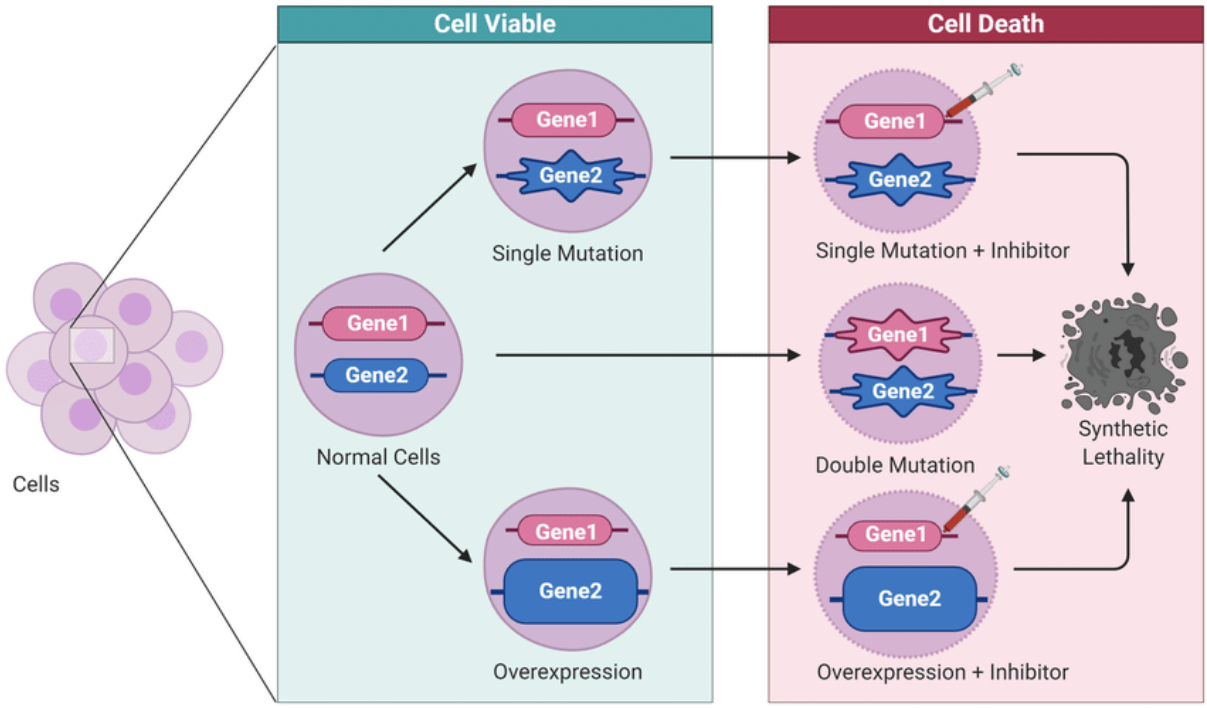

Fig 2-Conceptual Illustration of Synthetic Lethality—Cell Viability vs Cell Death under Gene Mutations and Inhibitor Treatment

RESISTANCE MARKER IDENTIFICATION THROUGH MULTI-OMICS

5.1 Mechanisms of Acquired Resistance: EGFR Inhibitors as a Case Study

The primary clinical obstacle that precision oncology faces comes from the development of acquired resistance to targeted therapies. The use of multi-omics profiling on tumor samples obtained before treatment and after resistance development has helped researchers discover the molecular pathways that lead to resistance development. All patients with EGFR-mutant non-small cell lung cancer who receive first- and second-generation EGFR tyrosine kinase inhibitors gefitinib and erlotinib will develop treatment resistance within 9 to 12 months. Resistant tumors show various resistance mechanisms through multi-omics profiling which demonstrates that tumors use different methods to achieve resistance. The T790M gatekeeper mutation which causes approximately 50 percent of acquired resistance together with MET amplification and ERBB2 amplification and HER2 exon 20 insertions and KRAS mutations and PIK3CA mutations and phenotypic epithelial-to-mesenchymal transition and small-cell transformation, made up the complete spectrum of resistance mechanisms which were discovered in the study.

Osimertinib third-generation EGFR TKI was specifically developed to combat T790M resistance, and its clinical effectiveness shows better progression-free survival results than first-generation TKIs according to FLAURA trial results which demonstrate its efficacy as a first-line treatment. The drug osimertinib encounters multiple resistance mechanisms which include C797S tertiary EGFR mutations and EGFR amplification and non-EGFR bypass signalling through MAPK and AXL and MET pathways. The discovery of each new resistance mechanism results in two outcomes: the first outcome establishes a diagnostic resistance marker while the second outcome establishes a therapeutic hypothesis for combinatorial intervention.

DOI: 10.46121/pspc.52.4.13

5.2 Epigenetic and Transcriptional Resistance Mechanisms

Scientists have shown that multi-omics profiling research proves epigenetic plasticity functions as a main resistance mechanism which DNA sequencing methods cannot detect. Researchers found that drug-tolerant persister (DTP) cell populations which survive initial targeted therapy became different from drug-sensitive cells through their unique chromatin accessibility patterns (ATAC-seq) and histone modification states (ChIP-seq) and their specific transcription factor activity profiles. Researchers have discovered that ID proteins and EZH2-mediated H3K27 methylation alterations and BRD4-dependent super-enhancer remodelling functions as epigenetic mechanisms which help persister cells survive through different tumour types and treatment methods. The combination of transcriptomic cell state data with epigenomic chromatin landscape data shows that cancer cells use phenotypic plasticity to switch between epithelial and mesenchymal cell states and between differentiated and stem-like transcriptional programmes as a common resistance mechanism. The mechanisms which drive transcriptional-epigenomic resistance remain hidden from genomic profiling methods because their detection requires scientists to use multiple omics techniques. EZH2 inhibitors and BET bromodomain inhibitors and LSD1 inhibitors which target epigenetic resistance mechanisms, which scientists discovered through multi-omics profiling, currently undergo clinical testing as combined treatments with targeted therapies.

5.3 Metabolic Reprogramming as Resistance Marker

Tumour metabolic reprogramming functions as a drug resistance marker which researchers can exploit as a targetable weakness according to metabolomic profiling evidence. The metabolic shift towards OXPHOS dependency in melanoma BRAF inhibitor resistance becomes evident through metabolomic profiling which shows increased mitochondrial biogenesis in transcriptomic data. The metabolic phenotype serves as a resistance biomarker because pre-treatment high OXPHOS metabolic activity predicts shorter response time to BRAF-MEK combined treatment. Clinical trials currently test the OXPHOS targeting approach which combines metformin or IACS-010759 with BRAF-MEK inhibition based on findings from multiple omics studies.

LIQUID BIOPSY AND DYNAMIC MULTI-OMICS MONITORING

The combination of multi-omics profiling with liquid biopsy platforms enables researchers to study circulating tumor DNA and circulating tumor cells and exosomes and cell-free RNA from blood samples to track therapeutic target changes and resistance marker development without needing tissue samples that multiple tumor biopsies would require. ctDNA profiling through ultra-deep targeted sequencing and low-pass whole-genome sequencing enables real-time monitoring of resistance mutation development because it can detect resistance clone growth which happens weeks to months before radiological signs become evident.

Multi-analyte liquid biopsy platforms that simultaneously profile ctDNA mutations cell-free methylation patterns and plasma proteomics have shown better sensitivity for early resistance detection than single-analyte methods. The CancerSEEK multi-analyte liquid biopsy assay integrates ctDNA profiling with eight protein biomarkers which demonstrates this multi-omics liquid biopsy approach. Longitudinal multi-omics liquid biopsy monitoring creates a dynamic molecular portrait of tumour evolution under therapeutic pressure which enables adaptive treatment strategies from drug holiday protocols to combination therapy escalation and therapeutic switching which doctors guide through real-time multi-omics resistance signals instead of using delayed radiological indicators.

TRANSLATIONAL CHALLENGES AND CLINICAL IMPLEMENTATION

The process of integrating multi-omics profiling into clinical routine treatment face multiple technical and computational and regulatory and healthcare system challenges which are all interrelated. The need for high-quality tissue samples which must include fresh-frozen material to meet the requirements of complete multi-omics profiling causes a fundamental problem because standard clinical biopsy procedures do not provide enough tissue samples needed for simultaneous WGS and RNA-seq and proteomics and methylation profiling. The development of ultra-low input and single-cell multi-omics technologies is progressively reducing minimum tissue requirements, with some platforms now enabling comprehensive profiling from fewer than 1,000 cells. The healthcare system needs two essential components which include bioinformatics expertise and computational infrastructure to successfully implement multi-omics data integration but these requirements create greater challenges for clinical settings which have fewer resources. Cloud-based genomics platforms including Terra, DNAnexus, and the European Genome-phenome Archive provide accessible scalable multi-omics analysis infrastructure which allows clinical genomics programs to operate at facilities without access to local high-

DOI: 10.46121/pspc.52.4.13

performance computing resources. Standardised bioinformatics pipelines such as nf-core/sarek for somatic variant calling and nf-core/rnaseq for transcriptome analysis establish uniform data processing standards which enable laboratories to share multi-omics data. This standardisation process establishes a foundation which allows cross-institutional data integration and multi-omics biomarker validation.

The development of multi-omics companion diagnostic regulations has made progress although they still need to develop complete systems which can handle the complexities of multiple biomarker tests. The FDA's Breakthrough Device Designation pathway has accelerated regulatory review for several comprehensive genomic profiling assays and new adaptive clinical trial designs which include basket trials that use multi-omics target profiles for patient selection and umbrella trials that test multiple targeted treatments in one tumour type have established new regulatory standards which use multi-omics data to guide treatment decisions.

FUTURE DIRECTIONS

8.1 Single-Cell Multi-Omics

Single-cell multi-omics technologies enable researchers to study the complete set of DNA, RNA, proteins, and epigenetic changes that exist in each individual cell of a sample. The two platforms CITE-seq and scATAC-seq and multi-ome ATAC + Gene Expression (10x Genomics) enable researchers to create single-cell molecular atlases which transform bulk tumor profiles into their individual cell components, which include drug-resistant subclones that become undetectable through standard bulk sequencing methods.

8.2 Spatial Transcriptomics and Tumour Microenvironment Profiling

The spatial transcriptomics technologies which include Visium from 10x Genomics and MERFISH and seqFISH+ enable researchers to measure gene expression in tissue sections while maintaining the original spatial coordinates for all measurements. The spatial dimension plays a vital role in studying the tumour microenvironment which consists of non-malignant immune cells and stromal cells and vascular cells and neural cells that develop together with tumour cells and have a major impact on treatment results. The study combines spatial multi-omics data with tumour immunophenotyping and ligand-receptor interaction mapping to reveal immune response mechanisms which remain hidden from bulk multi-omics analysis.

CONCLUSION

Multi-omics genomic profiling has developed into the most complete and pathway-based method for discovering therapeutic targets and determining resistance markers which cancer researchers and oncologists utilize for their work. Multi-omics profiling establishes systems-level tumor biology understanding which goes beyond single-dimensional molecular testing because it combines genomic, transcriptomic, proteomic, epigenomic, and metabolomic data to show targetable weaknesses and resistance patterns which individual omics testing cannot detect. The clinical impact of multi-omics profiling is already manifest in the approval of tumour-agnostic targeted therapies guided by molecular target profiles, the characterisation of resistance mechanisms enabling next-generation therapeutic development, and the identification of epigenetic and metabolic resistance mechanisms that expand the combinatorial intervention landscape. The advancement of single-cell and spatial multi-omics technologies will enable researchers to identify specific targets and resistance patterns at the cellular level within their surrounding environmental conditions which will create new possibilities for precise therapeutic development.

The complete operational capacity of multi-omics profiling research needs additional funding to build its necessary computational capabilities and establish bioinformatics standards and develop regulatory systems while ensuring equal access to clinical services. The foundational promise of precision medicine will be achieved through multi-omics genomic profiling when its required enabling conditions are fulfilled. The individual molecular characteristics of each patient's disease will determine their therapeutic strategies which will include methods to prevent resistance that has historically limited targeted therapy effectiveness.

DOI: 10.46121/pspc.52.4.13

REFERENCES

1. Cancer Genome Atlas Research Network. (2013). The Cancer Genome Atlas Pan-Cancer analysis project. Nature Genetics, 45(10), 1113–1120.
2. Mertins, P., Mani, D. R., Ruggles, K. V., Gillette, M. A., Clauser, K. R., Wang, P., ... & Carr, S. A. (2016). Proteogenomics connects somatic mutations to signalling in breast cancer. Nature, 534(7605), 55–62.
3. Baylin, S. B., & Jones, P. A. (2011). A decade of exploring the cancer epigenome — biological and translational implications. Nature Reviews Cancer, 11(10), 726–738.
4. Ward, P. S., Patel, J., Wise, D. R., Abdel-Wahab, O., Bennett, B. D., Coller, H. A., ... & Thompson, C. B. (2010). The common feature of leukemia-associated IDH1 and IDH2 mutations is a neomorphic enzyme activity converting alpha-ketoglutarate to 2-hydroxyglutarate. Cancer Cell, 17(3), 225–234.
5. Lackner, M. R., Wilson, T. R., & Settleman, J. (2012). Mechanisms of acquired resistance to targeted cancer therapies. Future Oncology, 8(8), 999–1014.
6. Argelaguet, R., Velten, B., Arnol, D., Dietrich, S., Zenz, T., Marioni, J. C., ... & Stegle, O. (2018). Multi-Omics Factor Analysis — a framework for unsupervised integration of multi-omics data sets. Molecular Systems Biology, 14(6), e8124.
7. Subramanian, A., Tamayo, P., Mootha, V. K., Mukherjee, S., Ebert, B. L., Gillette, M. A., ... & Mesirov, J. P. (2005). Gene set enrichment analysis: A knowledge-based approach for interpreting genome-wide expression profiles. Proceedings of the National Academy of Sciences, 102(43), 15545–15550.
8. Huang, K. L., Mashl, R. J., Wu, Y., Ritter, D. I., Wang, J., Oh, C., ... & Ding, L. (2018). Pathogenic germline variants in 10,389 adult cancers. Cell, 173(2), 355–370.
9. Stuart, T., & Satija, R. (2019). Integrative single-cell analysis. Nature Reviews Genetics, 20(5), 257–272.
10. Cohen, J. D., Li, L., Wang, Y., Thoburn, C., Afsari, B., Danilova, L., ... & Papadopoulos, N. (2018). Detection and localization of surgically resectable cancers with a multi-analyte blood test. Science, 359(6378), 926–930.

DOI: 10.46121/pspc.52.4.13