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Review Article

Advancing precision and personalized breast cancer treatment through multi-omics technologies

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Abstract: Breast cancer is the most common malignant tumour in women, with more than 685,000 women dying of breast cancer each year. The heterogeneity of breast cancer complicates both treatment and diagnosis. Traditional methods based on histopathology and hormone receptor status are now no longer sufficient. Recently, advances in multi-omics techniques, including genomic, proteomic, and transcriptomic analyses, have deepened our understanding of breast cancer. Combining these approaches allows for precise molecular subtyping, which is essential for the detection of key mutations, protein interactions and gene expression patterns that are highly relevant to different therapeutic strategies. Genomic analyses have been effectively identifying key mutations in cancer. Meanwhile, proteomics and transcriptomics complement by identifying new therapeutic targets and elucidating gene expression dynamics. Integrating multi-omics and conventional diagnostics improves tumour characterisation and enables prognostic accuracy comparable to established standards and treatment response. Existing and emerging technologies enable real-time enhanced tumour follow-up and data analysis through liquid biopsy and artificial intelligence, respectively. Despite these clinical implementation challenges, multi-omics including clinical phenotyping offers significant potential for precision breast cancer treatment. This article describes recent advances in molecular subtyping and multi-omics technologies that are driving key innovations to optimise patient outcomes and further develop personalised medicine in the context of breast cancer care.

Keywords: Breast cancer, precision medicine, molecular subtyping, multi-omics, personalized therapy

Introduction

Breast cancer is the most common malignancy among women worldwide, accounting for 24.5 per cent of all cancer cases and causing more than 685,000 deaths annually [1]. This high incidence underscores the urgent need for effective diagnostic and therapeutic strategies. Breast cancer demonstrates significant heterogeneity, with clinical presentation and response to treatment varying from patient to patient [2]. Treatment differs according to whether the lesion is localised, regional or metastatic. Despite advancements in early detection through imaging techniques like mammography, many cases are still diagnosed at advanced stages, increasing treatment complexity and worsening prognosis [3]. Current diagnostic approaches rely heavily on histopathological examination and hormone receptor status, which, while providing important insights, often fail to fully reveal the biological complexity of the disease [4]. For instance, based on hormone receptor status, breast cancers can be classified as luminal A, luminal B, HER2-enriched, and triple-negative breast cancers (TNBC), but this classification fails to adequately account for heterogeneity at the genetic and molecular levels [5]. Consequently, even patients with identical clinical and pathological features may have very different treatment outcomes and responses. This limitation highlights the need for more advanced diagnostic techniques, in particular the integration of multi-omics approaches (combining genomic, proteomic and transcriptomic data) to improve diagnostic accuracy and enable per-

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sonalised treatment strategies. Such integrated approaches are essential to address the complex biology of breast cancer and improve patient outcomes [6].

Recent advances in multi-omics technologies are greatly enhanced our understanding of breast cancer biology. With approaches like next-generation sequencing, genomic analyses are increasingly able to identify key mutations and driver genes that can be the foundation for novel targeted therapies [7, 8]. For example, in a comprehensive genomic analysis, high intra- and inter-tumor heterogeneity revealed in subgroups of luminal A, luminal B, HER2-enriched, and basal-like subtypes. These subtypes are crucial for determining prognosis and guiding personalized treatment plans [9]. Furthermore, proteomic analyses, including mass spectrometry, reveal protein interactions that aid in identifying new therapeutic targets and improving diagnostic accuracy [10]. Similarly, RNA-sequencing-based transcriptome analysis has been instrumental in elucidating gene expression fingerprints of breast cancer subtypes, thereby providing closer prediction of prognosis and more precise guidance of therapeutic decisions [11]. In summary, these advances in technology enhanced our molecular knowledge about breast cancer and showed the promise that multi-omics approaches hold for improvement in clinical outcomes (**Figure 1**) [12].

The integration of multi-omics techniques with conventional histological methods alone have significantly advanced in diagnosis and treatment for breast cancer [13]. The combination enables detailed molecular characterization of tumors, precise classification, and accurate dosing [14]. This review explores the state-of-the-art findings on molecular subtyping of breast cancer and their clinical relevance and underscores the need for continuous innovation in this fast-evolving domain. Optimizing of treatment regimens for breast cancer patient heterogeneity using multi-omics approaches will lead to better outcomes and personalized treatment. All of these offer tangible opportunity for integrating multi-omics findings into clinical utilities shortly and will no doubt pave the way for significant improvements in precision medicine and patient care. Further research and development in the coming years could revolutionize breast cancer diagnosis and treatment, ultimately improving patients' quality of life worldwide.

Advances in molecular subtyping technologies

Genomic profiling

Genomic profiling has greatly advanced our understanding of breast cancer, allowing for precise subtyping and the creation of targeted therapies. Comprehensive genomic profiling (CGP) through tissue-based and plasma-based assays identifies key pathogenic and driver mutations, providing essential data for personalized treatment strategies. A study conducted in Japan underscored the effectiveness of tissue-based assays over plasma-based assays in recommending matched therapies, likely due to the higher number of companion diagnoses available [15]. Additionally, gene-expression profiling has revealed significant inter- and intra-tumor heterogeneity, identifying intrinsic subtypes such as luminal A, luminal B, HER2-enriched, and basal-like, which are crucial for prognostic and predictive value in personalized treatment plans [16]. A recent study by Magbanua et al. emphasized the clinical utility of ctDNA-based genomic profiling in predicting response to neoadjuvant therapy and survival in early-stage breast cancer patients. They found that ctDNA dynamics could predict pathological complete response (pCR) and event-free survival (EFS), with significant alterations identified in genes such as TP53, PIK3CA, and ERBB2 [17]. Research on breast cancer brain metastases found that clinically relevant genomic alterations are more prevalent in brain metastases compared to local breast cancers, highlighting the potential for targeted therapeutic agents, including PARP inhibitors and immune checkpoint inhibitors [18]. Combining molecular subtyping with clinical parameters can identify high-risk patients who might otherwise be undertreated, stressing the importance of integrating molecular data with traditional clinical assessments [19].

A study on Chinese patients with breast cancer utilized targeted next-generation sequencing to identify common alterations such as TP53, PIK3CA, and BRCA2, which are essential for understanding tumor heterogeneity and developing effective targeted therapies [20]. Additionally, research on patient-derived xenograft models of metastatic breast cancer revealed

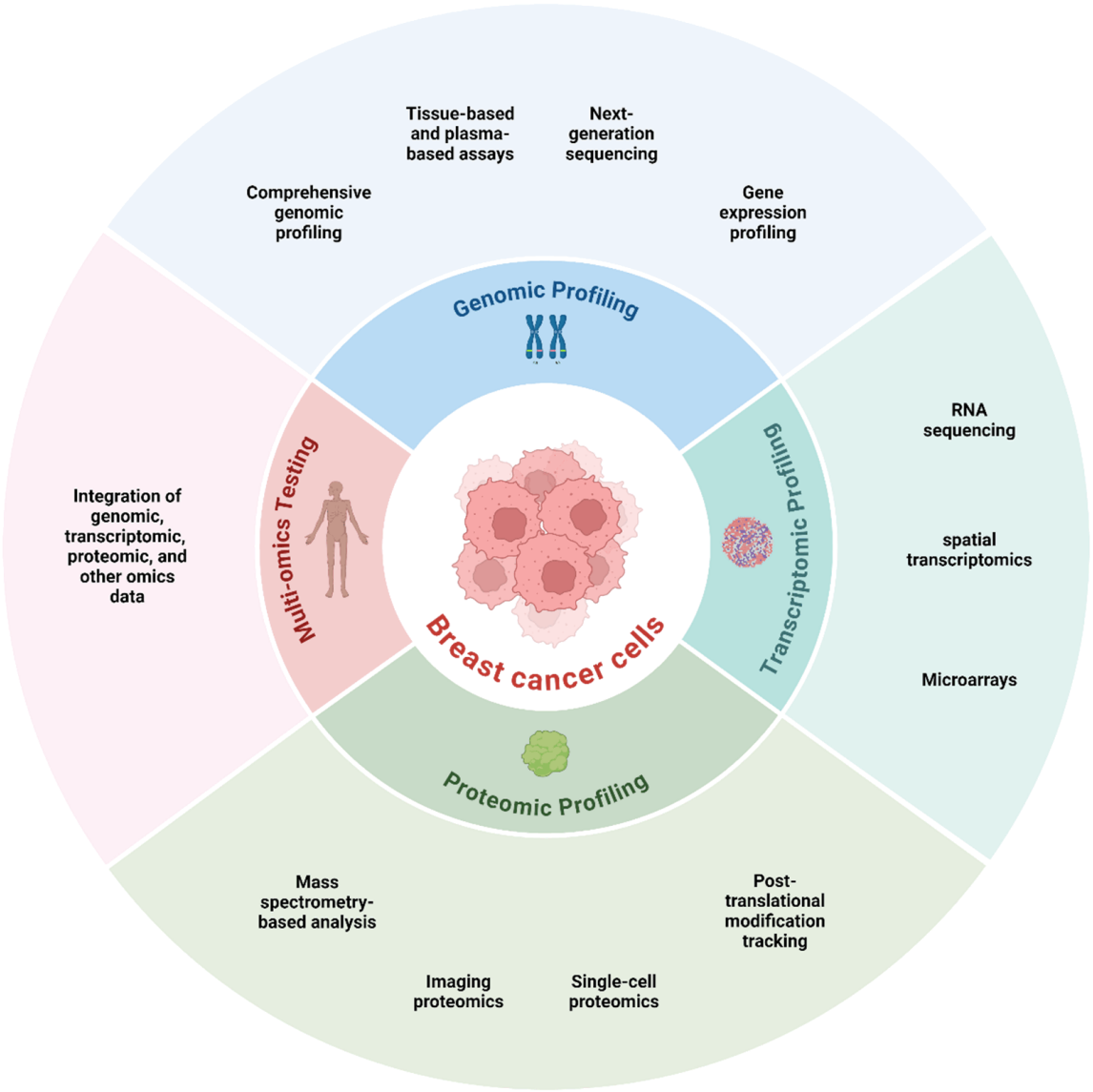

Figure 1. Multi-omics technologies in breast cancer diagnosis and treatment interruption.

both common and rare actionable alterations, highlighting the complexity of tumor evolution and the necessity for integrated analysis for optimal treatment selection [21]. Comprehensive molecular profiling has broadened treatment options by identifying novel genomic alterations and therapeutic targets, demonstrating the utility of next-generation sequencing in clinical practice for precision oncology [22]. In a cohort of Chinese patients, comprehensive genomic profiling identified significant genomic alterations, such as TP53 and BRCA1 mutations, and novel treatment targets, emphasizing the need for personalized treatment strategies in very early-relapsed TNBC patients [23]. Another study focused on the impact of genomic profiling in identifying estrogen-responsive genes in breast cancer, emphasizing the role of metabolic changes and their association with prognosis and therapeutic response [24]. A study utilizing cDNA microarray for genetic profiling of breast cancer further demonstrated the role of genetic alterations in diagnosis and personalized treatment strategies [25].

Additionally, integrating genomic and immune profiling has provided insights into the distinct

immune marker phenotypes of homologous recombination deficient breast cancers, suggesting potential susceptibility to immune checkpoint inhibitors [26]. The evaluation of CGP testing under the Japanese universal health insurance system highlighted significant actionable gene mutations, underscoring the utility of CGP in clinical practice [27]. Together, these studies demonstrate the transformative potential of genomic profiling in advancing breast cancer diagnosis, prognosis, and personalized treatment, thus paving the way for more effective, tailored therapies.

Genomic analysis crucial in breast cancer research and treatment, facilitating the development of precision medicine by revealing tumour heterogeneity and genetic mutations. Comprehensive genomic analysis of tissue and plasma can identify important disease-causing mutations and provide the basis for personalised treatment. Studies indicate that tissue analysis is more effective in recommending matched treatments, while the application of gene expression profiling further refines the classification of intrinsic subtypes of breast cancer, providing an important reference for prognosis and treatment options. Circulating tumour DNA analysis showed significant advantages in early breast cancer metastasis prediction, highlighting the clinical value of genomic dynamic surveillance. Research for subtypes such as triple-negative breast cancer revealed the predictive power of specific genetic alterations on chemotherapy response, highlighting the importance of individualised treatment. Integrating genomic and clinical data allows for the identification of high-risk patients and the optimization of treatment strategies. These advances demonstrate the potential of genomic analysis in the diagnosis, prognosis and treatment of breast cancer, paving the way for more precise and effective individualised treatment.

Proteomic profiling

Proteomic profiling is a crucial tool in breast cancer research, offering insights into cancer biology and identifying new therapeutic targets. One review emphasized the advancements in proteomics-based diagnostic and therapeutic options in breast cancer management, highlighting the role of imaging proteomics, single-cell proteomics, and post-translational modification tracking in enhancing diagnostic efficiency, prognostic value, and predictive response [28]. Additionally, mass spectrometry-based proteomic analysis of over 130 clinical breast samples revealed considerable intertumor heterogeneity across breast cancer subtypes, leading to the identification of a novel luminal subtype characterized by increased PI3K signaling. This subtype was validated using an independent protein-based dataset, underscoring the importance of comprehensive proteomic analysis for precise cancer treatment decision-making [29]. Another significant study focused on the proteomic profiling of ductal carcinoma in situ (DCIS), the most common type of non-invasive breast cancer, which accounts for about 15 to 30% of cases. This study used mass spectrometry to identify biomarkers that support prognosis and early detection. The proteomic analysis identified critical proteins such as VWF, MMP9, ITGAM, MPO, and PLG, which play key roles in cancer pathways like complement and coagulation cascades. These findings underscore the importance of protein regulation in cancer development and recurrence [30]. Furthermore, a study utilizing system-wide proteomic analysis of breast cancer proteomes identified novel prognostic markers for estrogen receptor-negative tumors, revealing stage-specific protein signatures and highlighting high levels of IDH2 and CRABP2 as well as low levels of SEC14L2 as prognostic markers [31].

Research also demonstrated the influence of biospecimen variables on the evaluation of PI3K/Akt/mTOR pathway markers. This study found significant correlations between central and peripheral tumor specimens, with specific markers like pAkt S473 showing higher levels in core-needle biopsies compared to surgical specimens, indicating potential loss of phosphorylation during surgical manipulation [32]. Moreover, proteomics-based techniques applied to invasive ductal carcinoma, the most common subtype of malignant breast cancer, have improved diagnosis, prognosis, and treatment monitoring. LC-MS/MS and MALDI-MS techniques have facilitated the identification of early-stage IDC biomarkers and emphasized the role of PTMs in revealing specific molecular mechanisms [33]. A pilot study comparing saliva and serum samples using proteomics

approaches identified potential early markers for breast cancer, involving proteins related to exocytosis, secretion, immune response, and cytokine-mediated signaling pathways. This study suggests that saliva and serum proteomics provide a non-invasive platform for early breast cancer diagnosis [34]. A comprehensive systematic review synthesized existing prognostic biomarker data in male breast cancer, spanning genetics, transcriptomics, proteomics, and epigenetics. This review identified knowledge gaps, discussed study limitations, and highlighted underexploited markers of prognostic value, such as STC2, DDX3, and DACH1, along with well-studied predictors of poor survival like TP53 and c-Myc [35].

Proteomics is pivotal in breast cancer research, driving diagnostic and therapeutic advances by revealing tumour heterogeneity and identifying novel therapeutic targets. Technologies such as mass spectrometry and single-cell proteomics have improved diagnostic accuracy and prognostic prediction. Particularly in ductal carcinoma in situ and invasive ductal carcinoma, proteomics identifies key biomarkers that contribute to early detection and therapeutic decisions. Furthermore, studies of circulating tumour DNA and small extracellular vesicles demonstrate the potential for non-invasive diagnostics. These advances underscore the importance of proteomics in precision medicine and provide strong support for the development of personalised treatment strategies.

Transcriptomic profiling

Transcriptomic profiling, utilizing techniques like RNA sequencing and microarrays, offers detailed insights into gene expression patterns, facilitating molecular subtyping of breast cancer and identifying potential therapeutic targets. A recent study on metastatic breast cancer performed extensive genomic, transcriptomic, and proteomic profiling, identifying common mutations such as TP53 and PIK3CA, as well as novel biomarkers like NF1, PTEN, and ARID1A mutations. RNA sequencing validated the expression levels of these mutations and identified new antibody-drug conjugate targets, such as LIV-1 and B7-H3, paving the way for personalized treatments [36]. In a study focusing on the genomic and transcriptomic differences between inflammatory breast cancer and non-inflammatory breast cancer (non-IBC), researchers used whole exome sequencing and RNA-seq to identify somatic mutations specific to IBC in Asian women, such as ZNF74 and DYNC2H1 mutations. The study also discovered more frequent gene fusions in IBC samples, such as CTC-786C10.1-RP11-680G10.1 and TULP4-RP11-732M18.3, which may explain the aggressive biological behavior of IBC. Mutations and enhanced signaling in the RAS pathway were significant features of IBC, suggesting potential efficacy of RAS pathway inhibitors in treating IBC [37].

Furthermore, transcriptomic profiling has identified distinct gene expression patterns across different breast cancer subtypes. For instance, Luminal A/B, HER2-enriched, and basal-like subtypes exhibit unique transcriptomic characteristics that can predict prognosis and treatment responses. A study of Luminal B subtype indicated higher expression of cell proliferation genes, correlating with poorer prognosis [31]. RNA-seq analysis of Luminal A subtype revealed gene expression patterns closely linked to estrogen receptor (ER) pathway activation, suggesting potential therapeutic benefits of ER pathway inhibitors in this subtype [36]. One important study discusses how tumor-infiltrating lymphocytes (TILs) and gene expression signatures are used to predict clinical outcomes and the efficacy of immunotherapy in breast cancer. The findings emphasize the prognostic value of immune-related gene expression signatures over TILs, particularly in early-stage HER2-positive breast cancer [38]. Another study demonstrated that transcriptomic profiling could identify differentially expressed genes in palbociclib-resistant ER+ MCF7 breast cancer cells, uncovering pathways related to cell cycle, DNA replication, DNA repair, and autophagy, which are critical for developing new therapeutic targets against drug-resistant tumors [39]. A study identified multiple genes and ECM-receptor interaction pathways associated with breast cancer through transcriptome profiling of invasive ductal carcinoma and adjacent tissues. Researchers found 937 differentially expressed genes, including 487 upregulated and 450 downregulated genes, underscoring the ECM-receptor interaction pathway as a significant player in breast cancer development [40]. Another study utilized transcription factor profiling to develop a nine-TF signature that sig-

nificantly predicted recurrence-free survival in breast cancer patients, indicating its potential as a prognostic biomarker [41].

Comprehensive transcriptomic profiling has been utilized to identify breast cancer patients who could avoid adjuvant systemic therapy. A study evaluated transcriptomic signatures from a randomized phase III trial and found that most signatures were highly prognostic for distant metastasis, identifying a low-risk subgroup with a 95% metastasis-free rate at 15 years without adjuvant endocrine therapy, highlighting the potential of transcriptomic profiling in guiding treatment decisions and avoiding overtreatment [42]. Another study demonstrated the limited impact of intra-tumor heterogeneity on transcriptomic-based molecular profiling, suggesting that a single biopsy can reliably represent the overall transcriptomic landscape of a breast tumor [43]. Recent transcriptomic studies have also focused on lncRNAs. One study identified a three-lncRNA signature (AK291479, U79293, and BC032585) predictive of pathological complete response following neoadjuvant chemotherapy in breast cancer patients. The study highlighted the potential of lncRNAs in predicting treatment response and their role in chemoresistance [44]. Another study developed a three-lncRNA signature (CAT104, LINC01234, and STXBP5-AS1) that could predict breast cancer patient survival, underscoring the clinical significance of lncRNAs as prognostic biomarkers [45].

Spatial transcriptomics has demonstrated significant potential in breast cancer research, particularly in revealing tumor heterogeneity and understanding the tumor microenvironment. Studies using technologies like 10× Visium have identified differences in drug sensitivity between the core and peripheral regions of tumors, emphasizing the importance of considering spatial characteristics in treatment planning [46]. Furthermore, the integration of spatial transcriptomics with single-cell RNA sequencing enables a more comprehensive analysis of cell interactions and spatial organization, providing deeper insights into the complexity of tumors [47]. Advanced methods such as Slide-seq and High-Definition Spatial Transcriptomics (HDST) allow for subcellular-level gene expression analysis, offering a more precise understanding of the distinct regions within breast tumors [48]. Another key study demonstrated how spatial transcriptomics could map intratumor heterogeneity, which is critical for the accurate diagnosis of breast cancer. By analyzing gene expression at high resolution across tumor samples, researchers could distinguish between areas with varying levels of malignancy and identify early signs of metastasis that are spatially localized within the tumor microenvironment [49]. These advancements not only enhance our understanding of the biological underpinnings of breast cancer but also provide new avenues for personalized treatment approaches.

Transcriptomic analysis, using RNA sequencing and microarray techniques, reveals the gene expression characteristics of different breast cancer subtypes, potential therapeutic targets, and prognostic information. Studies have shown that transcriptomic profiling can identify common mutations such as TP53 and PIK3CA, as well as novel biomarkers like NF1 and PTEN, and discover new targets suitable for personalized treatment. It plays a crucial role in understanding genetic differences between inflammatory breast cancer and non-inflammatory breast cancer, predicting the efficacy of immunotherapy through immune-related gene expression, and identifying key pathways in drug-resistant tumors. Spatial transcriptomics further reveals tumor heterogeneity and the complexity of the tumor microenvironment. By integrating with single-cell RNA sequencing, it offers deeper insights into personalized treatment approaches.

Multi-omics testing and molecular staging of breast cancer

Multi-omics testing, which combines genomic, transcriptomic, proteomic, and other omics data, has greatly advanced the molecular staging of breast cancer. This comprehensive approach reveals the complex biological mechanisms behind breast cancer heterogeneity. A recent study utilized multi-omics data to identify a novel hybrid breast cancer subtype, termed Mix_Sub, characterized by poor survival prognosis and specific molecular features, including lower inflammatory response and higher T-cell dysfunction. This subtype exhibited distinct cellular functional states and was more sensitive to targeted therapies, demon-

strating the clinical relevance of multi-omics approaches [50]. Another study emphasized the integration of exon expression, RNA-seq, and methylation data to classify breast cancer subtypes more accurately than traditional methods, improving survival predictions for luminal A and B subtypes [51].

The application of multi-omics in breast cancer research has also provided insights into the molecular landscape of various breast cancer models. For instance, patient-derived xenografts and organoids have been shown to closely resemble the molecular characteristics of primary tumors, making them suitable for drug screening and molecular analysis. This comparison highlights the importance of multi-omics in validating and refining breast cancer models [52]. Additionally, integrated multi-omics analysis has identified key biomarkers associated with breast cancer prognosis, such as RPL31 and ZNF273, which are crucial for understanding the molecular mechanisms and developing targeted therapies [53].

Barriers to practical clinical application

Despite significant advancements, several barriers hinder the practical clinical application of multi-omics testing in breast cancer. The high cost and complexity of multi-omics technologies, along with the need for specialized infrastructure and expertise, limit their broader adoption in clinical settings. Additionally, the integration and interpretation of large-scale omics data require robust bioinformatics tools and standardized protocols, which are still under development [54]. Furthermore, the variability in sample quality and data processing methods can affect the reproducibility and reliability of multi-omics studies, posing challenges for clinical translation [50].

Recent research on causal discovery algorithms and language models aims to address some of these challenges by enhancing the reliability of multi-omics data interpretation. These algorithms can identify causal relationships between genetic changes and patient outcomes, thus enhancing the clinical utility of multi-omics data [55]. However, the implementation of such advanced computational methods requires substantial computational resources and expertise, which may not be readily available in all clinical settings.

Diversity and complexity of research methods

The diversity and complexity of research methods in multi-omics studies present an additional challenge. Omics technologies, such as genomics, transcriptomics, proteomics, and metabolomics, each offer unique insights into the molecular characteristics of breast cancer. However, integrating these diverse datasets to form a cohesive understanding of tumor biology is challenging and requires advanced computational methods. Recent advancements in multi-omics single-cell analyses have offer insights into addressing these challenges by providing high-resolution data on cellular heterogeneity and interactions within the tumor microenvironment [53]. However, the development of integrative analytical frameworks that can handle the complexity and scale of multi-omics data remains a critical area of research [54].

A new tool, ioSearch, has been developed to tackle these challenges by integrating multi-omics data and identifying disease-related interacting omics. This tool employs a principal regression framework to explore inter-relationships among omics datasets, providing a more interpretable inference for clinical applications [56]. Such advancements highlight the ongoing efforts to create robust methods for integrating and analyzing multi-omics data, which are essential for the successful clinical application of these technologies. In conclusion, while multi-omics testing has transformed the molecular staging of breast cancer, several challenges must be addressed to fully realize its clinical potential. Ongoing advancements in technology, data integration, and standardization, along with efforts to reduce costs and increase accessibility, are essential for the broader application of multi-omics approaches in personalized breast cancer care.

Clinical applications and implications of molecular subtyping in breast cancer

Diagnosis

Molecular subtyping has greatly improved the diagnostic accuracy of breast cancer, offering detailed molecular profiles that extend beyond traditional histopathological and clinical methods. For instance, immunohistochemistry-based protein markers have been utilized to sub-

type triple-negative breast cancer into categories such as luminal androgen receptor, immunomodulatory, basal-like immunosuppressed, mesenchymal-like, and unclassifiable subtypes. This classification not only aids in prognosis but also in identifying potential therapeutic targets, with the BLIS subtype associated with the poorest overall survival [57].

Advances in DNA profiling, particularly through next-generation sequencing, have further refined the identification of tumor subtypes with different prognoses. A comprehensive study evaluated DNA copy number profiles in breast cancer, demonstrating that DNA classifiers could accurately classify RNA expression subtypes. This stratification power is expected to increase with the integration of multidimensional DNA factors, promising more precise and actionable diagnostic insights [58]. Comparing IHC with molecular subtyping has shown significant discrepancies, especially in hormone receptor-positive breast cancers. A study from South Africa highlighted the challenges of using IHC as a surrogate for molecular subtyping, emphasizing the need for molecular assays to improve diagnostic accuracy [59]. Similarly, a study from Taiwan showed that molecular subtyping via multigene assays such as MammaPrint and BluePrint significantly influenced treatment decisions compared to traditional pathological subtyping [60].

Prognosis

Molecular subtyping provides subtype-specific prognostic indicators, which are essential for risk stratification and predicting disease outcomes. The PAM50 gene expression subtypes are central to in breast cancer classification, incorporated into risk prediction models to guide treatment decisions. However, a study on a cohort of 6233 primary breast tumors highlighted the variability and stability of PAM50 subtyping, revealing that subtypes represent a continuum rather than discrete classes. This finding is vital for interpreting tumors with conflicting PAM50 classifications compared to clinical biomarkers, underscoring the importance of considering underlying biological processes [61].

Additionally, new methodologies in molecular subtyping are expanding prognostic capabilities. One notable advance is the development of the IntClust model, which integrates genomic and transcriptomic data to provide a more comprehensive understanding of breast cancer heterogeneity. The IntClust model has been shown to improve patient stratification and predict clinical outcomes more effectively than the PAM50 system, highlighting the importance of incorporating multiple data types for more accurate prognostication [62]. The clinical significance of these subtypes has also been validated in specific contexts, such as triple-negative breast cancer (TNBC). TNBC, a particularly aggressive subtype, lacks hormone receptors and HER2 expression, limiting therapeutic options. Molecular subtyping has proven instrumental in identifying high-risk patients within the TNBC cohort who could benefit from targeted therapies, thereby improving prognostic accuracy and potentially guiding therapeutic decisions [63].

Personalized treatment approaches

Molecular subtyping has revolutionized personalized treatment approaches by enabling the development of targeted therapies based on specific molecular characteristics of breast cancer subtypes. The identification of HER2 overexpression in certain subtypes has led to the successful use of HER2 inhibitors, significantly improving patient outcomes. Reviews of molecular subtypes highlight the need for flexible and robust bioinformatics frameworks to integrate diverse data types (e.g., microarray and RNA sequencing) and address technical and biological variability. Such frameworks are essential for implementing molecular profiling in clinical settings to guide treatment decisions [64].

Moreover, molecular subtyping has facilitated the identification of predictive markers for therapy resistance. Discovering specific gene expression patterns linked to tamoxifen resistance in estrogen receptor-positive breast cancer has highlighted pathways like the PI3K-AKT pathway as potential targets for overcoming resistance [65]. Studies indicate that combining genetic and epigenetic data enhances the prediction of treatment outcomes and helps identify new therapeutic targets [42]. The heterogeneity of triple-negative breast cancer has been further examined, revealing at least four major omics-based subtypes. This classifica-

tion facilitates the design of clinical trials targeting specific molecular subtypes, which may lead to better survival outcomes [66]. Early surgical outcomes based on molecular subtypes have shown varying preferences for surgical intervention, highlighting the importance of subtype-specific treatment plans [67]. Additionally, new biclustering algorithms, such as the mutually exclusive spectral biclustering, have been developed to identify novel subtypes and improve patient stratification for personalized therapies [68]. These advancements in molecular subtyping and data integration are paving the way for more precise and effective treatment strategies in breast cancer management.

Emerging technologies and future trends

Liquid biopsy

Overview of Technical Principles and Applications Liquid biopsy is a minimally invasive technique that allows the detection of circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and other tumor-derived biomarkers in the blood. This method provides real-time insights into the tumor's genetic landscape without the need for tissue biopsies. Advanced technologies like digital PCR and next-generation sequencing (NGS) are used to extract and analyze nucleic acids from blood samples. Recent advancements in liquid biopsy technologies have greatly enhanced their sensitivity and specificity for breast cancer management. Novel microfluidic devices have improved CTC isolation and characterization, allowing for downstream molecular analyses and single-cell sequencing to reveal intratumoral heterogeneity [69]. Simultaneously, highly sensitive digital PCR and next-generation sequencing techniques have enabled the detection of cancer-specific mutations in cfDNA at very low allele frequencies, showing promising results in early breast cancer detection and treatment response monitoring [70].

The integration of multiple circulating biomarkers (CTCs, cfDNA, and exosomes) has demonstrated improved sensitivity and specificity in breast cancer detection and monitoring, with recent studies showing that combining CTC enumeration with cfDNA mutation analysis significantly enhances the ability to predict treatment response in metastatic breast cancer patients [71]. As research in this field progresses, future directions include the development of highly sensitive multi-marker panels for early detection and minimal residual disease monitoring, integration of liquid biopsy data with other multi-omics technologies for comprehensive patient profiling, and exploration of novel circulating biomarkers such as tumor-educated platelets [72]. These advancements in liquid biopsy technologies hold great promise for advancing personalized breast cancer treatment by providing real-time, non-invasive monitoring of tumor dynamics and treatment response.

Application of artificial intelligence in molecular staging

Data Analysis and Pattern Recognition Artificial intelligence and machine learning have become integral to analyzing the vast amounts of data generated by molecular profiling. These technologies excel in pattern recognition and uncovering complex relationships within the data that may not be apparent through traditional analytical methods. AI algorithms classify breast cancer subtypes based on gene expression profiles, predict clinical outcomes, and uncover novel biomarkers for early detection and treatment [73]. AI tools can integrate multi-omics data - such as genomics, transcriptomics, and proteomics, providing a comprehensive view of tumor biology and aiding in the development of personalized treatment plans [51]. The recent advances in AI-driven histopathology show its potential to in automating routine pathology investigations, enhancing diagnostic accuracy and efficiency [74].

Predictive Modelling and Treatment Optimization AI-driven predictive models hold significant promise in optimizing treatment strategies for breast cancer patients. By analyzing historical data from clinical trials and real-world patient outcomes, these models can predict the most effective therapies for individual patients based on their molecular profiles. For instance, predictive modeling can identify patients to benefit from specific chemotherapy regimens or targeted therapies, thereby minimizing side effects and improving overall treatment efficacy [75]. AI applications are also being developed to monitor treatment responses in real time, adjusting therapy protocols

dynamically to maximize therapeutic benefit and reduce resistance [76].

Furthermore, integrating AI with imaging technologies like PET/CT and MRI has enhanced the precision of breast cancer staging and prognosis. AI-based models can analyze radiomic features from medical images, enhancing the detection and characterization of tumor lesions [77]. Studies indicate that AI can improve the prediction of distant metastasis using MRI data, demonstrating its potential in non-invasive risk assessment and treatment planning [78]. The combination of radiomics and AI holds promise for future clinical applications, enabling more accurate and personalized treatment strategies [79].

Conclusion

The integrated role of advanced genomic, proteomic, and transcriptomic analyses in molecular subtyping is further implicated in the study and treatment of breast cancer. Such approaches will better unravel the disease heterogeneity and, consequently, characterize improved classification with individualized treatment strategies. In turn, genomic analysis helps identify the leading mutations and driver genes as the basis for developing personalized hubs. Proteomic analysis techniques identify key protein interactions and pathways, improving diagnostic accuracy and prognosis prediction. Transcriptome analysis has greatly enhanced understanding of gene expression patterns across breast cancer subtypes and identified new therapeutic targets and biomarkers.

The emergence or advent of multi-omics approaches has further increased the importance of having a perception of the molecular landscape of breast cancer. Integrating genomics, transcriptomics, and proteomics data can provide comprehensive insights into the complex biological mechanisms involved. It may enhance molecular staging, hence providing for more precision in treatments. Although there has been significant advancement, successful clinical use of these technologies remains challenging: such approaches are costly, complex, and require infrastructure and knowledge specialization. Overcoming these barriers requires further investment in technology development, data integration, and standardization, along with efforts to reduce costs and improve accessibility. Emerging technologies, such as liquid biopsy and artificial intelligence, are holding the fort in improving molecular staging and the accuracy of the personal treatment approach. Liquid biopsies provide a minimally invasive possibility of tracing tumor dynamics and treatment response in real-time, supplying valuable information for adjusting treatment plans. Artificial intelligence and machine learning have emerged as essential tools that can be applied to derive insights into big histological data, identify the complex patterns of different phenotypes expressed in these patient populations, and optimize treatment strategies. Integration with imaging technologies allows artificial intelligence to improve the accuracy of breast cancer staging and prognostication.

Moving ahead, multi-omics technologies will be developed and integrated into breast cancer care. This progress will be supported by the development of robust computational methods and bioinformatics tools capable of managing the complexity and scale of multi-omics data. Further integration of artificial intelligence and machine learning techniques with clinical practices is expected to improve diagnostic accuracy and treatment outcomes. The era of such advances in treatment will pave the way for more precise, personalized, and hence more effective treatment strategies that will ultimately improve patient outcomes and quality of life. Hence, molecular subtyping and multi-omics analysis have greatly revolutionized the field of breast cancer investigations and therapeutics. These approaches offer substantial potential for personalized therapies by providing deeper molecular insights into breast cancer heterogeneity. In times to come, as we face the challenges and potential of these innovations, we shall be nearer to a future with breast cancer management individually effective and improving patient care.

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Disclosure of conflict of interest

None.

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