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Review paper

Bridging Genomics and Oncology: Molecular Approaches to Personalized Medicine

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Abstract

Background and aim: Cancer treatment faces challenges due to intra-tumor heterogeneity and the need for better understanding of molecular mechanisms. Precision oncology aims to customize therapies based on accurate diagnostics, targeting specific molecules. Next-generation sequencing enables personalized treatment through identifying therapeutic targets and biomarkers. Comprehensive molecular characterization, including genomics, transcriptomics, proteomics, and the tumor microenvironment, is essential. This study addresses these gaps, investigating epigenetic changes, gene expression, and correction methods, with the potential for improved treatment outcomes and advancements in precision oncology.

Methods: This literature review explores advancements in oncology genomics and their implications for personalized medicine. A comprehensive search identified 35 relevant papers, covering topics such as genomic alterations, molecular profiling, biomarker identification, and clinical integration. Descriptive statistics summarize the distribution of publications by year, cancer type, and research focus. The findings demonstrate significant progress in oncology genomics, enabling tailored therapies based on individual genetic profiles and improving diagnosis, prognosis, and treatment outcomes. Integration of genomics into clinical practice holds promise for the future of precision oncology.

Results: The studies provide distinct perspectives on precision oncology, addressing challenges and advancements in the field. One study proposes the use of liquid biopsies as alternatives for monitoring molecular events in metastatic breast cancer, while another focuses on next-generation sequencing and organoid models for understanding the genetic landscape of individual cancer patients. Additionally, there are studies highlighting the significance of the cancer epigenome and the importance of targeting specific genomic alterations for personalized treatment strategies. These findings underscore the crucial role of genomic information in guiding effective precision oncology approaches.

Conclusion: In conclusion, the integration of oncology, molecular medicine, and personalized medicine holds great promise for improving cancer treatment outcomes. By utilizing genomic information, precision oncology enables tailored treatment approaches based on molecular features and epigenetic patterns, leading to more accurate and effective care. These findings have

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significant implications, offering personalized therapies that improve patient outcomes while minimizing adverse effects. Future research should focus on addressing challenges like equitable access to genomic testing and advancing multi-omics approaches. By refining personalized medicine in oncology, exploring new therapeutic targets, and leveraging innovative technologies, we can optimize treatment decision-making and unlock the full potential of molecular and personalized medicine in revolutionizing cancer care.
Keywords: *Oncology, Molecular, Personalized Medicine*

Introduction

Cancer is one of the leading cause of death in the world with the prevalence of >10 million mortalities annually. Current cancer treatments include surgical intervention, radiation, and taking chemotherapeutic drugs, which often kill the healthy cells and result in toxicity in patients. Therefore, researchers are looking for ways to be able to eliminate just cancerous cells. Intra-tumor heterogeneity of cancerous cells is the main obstacle on the way of an effective cancer treatment. However, better comprehension of molecular basis of tumor and the advent of new diagnostic technologies can help to improve the treatment of various cancers. Therefore, study of epigenetic changes, gene expression of cancerous cells and employing methods that enable us to correct or minimize these changes is critically important. In this paper, we will review the recent advanced strategies being used in the field of cancer research [1]. Carcinogenesis is a multistage process that etiologically involves mutations in a series of genes that play a role in maintaining the balance between cell proliferation and apoptosis, maintaining a stable cell mass (number) and also in regulating complex metabolic pathways, which ensure functional and structural integrity of cells and tissues [2], [3]. DNA replication is a crucial process that duplicates the entire genomic material. It occurs during the S phase of the cell cycle and involves the activation of specific DNA replication origins along chromosomes. Different origins are activated at different times, leading to bi-directional DNA synthesis. The replication timing is regulated by factors such as chromatin structure, chromosome conformation, and gene activity. Early-replicating regions are typically found in open chromatin regions and contain active genes, while late-replicating regions are gene-poor and more prone to mutations. The replication program is remodeled during development and differentiation, and disruptions can have severe consequences like cell lethality, developmental defects, and cancer [4]. Modern cancer treatment methods focus on targeting specific molecules involved in cellular signaling systems related to tumor initiation and progression. The success of these treatments relies on accurate diagnostic tests with high sensitivity to identify biomarkers and determine their levels in patients. This enables the selection of individuals who will benefit from the treatment. Advances in technology facilitate the molecular characterization of cancer, allowing for highly sensitive and specific detection of patients' mutational status [5]. Next-generation DNA sequencing has revolutionized clinical oncology by identifying therapeutic targets and molecular biomarkers, leading to personalized cancer treatment and improved outcomes. Recent advancements in tumor profiling allow detailed analysis of tumor molecular architecture and cellular phenotype. However, challenges remain in validating and implementing high-resolution tumor profiling and integrating multi-omics data into precision treatment. This review highlights recent advances in multi-omics tumor profiling, including spatial genomics, chromatin organization, spatial transcriptomics and proteomics, liquid biopsy, and ex vivo modeling of drug response [6]. Precision oncology, also called personalized medicine, is an emerging cancer treatment approach that customizes therapies based on an individual's molecular profile, including

genetic alterations and biomarkers. By targeting specific molecular changes that fuel cancer growth and developing drugs tailored to these changes, precision oncology aims to deliver more effective and less harmful treatments compared to traditional chemotherapy. Precision oncology has the potential to improve cancer treatment outcomes and enhance patient quality of life. However, there are challenges that need to be addressed, such as developing new anti-cancer agents targeting genetic changes, identifying effective biomarkers to select patients for targeted therapies, and overcoming therapy resistance [7], [8]. This filed is based on tailoring cancer treatment strategies to the unique molecular characteristics of a tumor. While genetic mutations have historically defined these characteristics, understanding the transcriptome, proteome, and tumor microenvironment is also crucial. High-throughput genomic technologies have provided opportunities to unravel disease biology at different stages, including cancer initiation, prevention, early detection, adjuvant therapy, minimal residual disease monitoring, drug resistance, and cancer evolution. This review explores the impact of genomics on these aspects and identifies areas for improvement in cancer outcomes. Complementary approaches are needed to address knowledge gaps in the field [9].

Methods

This literature review paper investigates the advancements in oncology genomics and their implications for personalized medicine. A comprehensive search was conducted on PubMed, Scopus, and Google Scholar using relevant keywords such as oncology, genomics, molecular, and personalized medicine. After applying predefined inclusion and exclusion criteria, 35 papers were included in the analysis, while 20 papers were excluded. The selected papers covered a diverse range of topics, including genomic alterations in different cancer types, molecular profiling for targeted therapies, biomarker identification, and the integration of genomics into clinical practice. Descriptive statistics were employed to summarize the characteristics of the included papers, providing insights into the distribution of publications by year, cancer type, and research focus. The findings highlight the significant progress made in oncology genomics and its potential to revolutionize personalized cancer treatment approaches. By understanding the molecular basis of cancer through genomics, tailored therapies based on individualized genetic profiles can be developed, leading to improved diagnosis, prognosis, and treatment outcomes. The integration of genomics into clinical practice holds promise for the future of oncology, offering new avenues for precision medicine in the fight against cancer.

Literature of Review

In a 2013 study [10], it was emphasized that the development and translation of high-throughput molecular classifiers in oncology require sophisticated bioinformatic and statistical procedures. The challenges of experimental design, data preprocessing, and high-dimensional statistical analysis were highlighted. The study provided recommendations for good practice in the translation of classifiers to clinical practice.

The same year, a study by Garraway et al. [11] stated that precision medicine, with its focus on personalized treatments based on genomic information, is particularly relevant in oncology. Cancer being a genomic disease, understanding the molecular pathways through mutated oncogenes and tumor suppressors is crucial for effective treatment.

In 2015, Thill [12] discussed the use of biosimilar monoclonal antibodies (mAbs) in the treatment of breast cancer. The approval process for biosimilar mAbs, including trastuzumab, raised new concerns in the cancer setting. The requirements for the approval of biosimilar mAbs published by

the EMA were examined, highlighting potential controversies.

Roychowdhury and Chinnaiyan [13] emphasized the importance of translating cancer genomes and transcriptomes into precision oncology. They discussed various applications, including molecular classification of cancer, heritable risk assessment, eligibility for targeted therapies, and genomic-based clinical trials. The review outlined key opportunities and new directions for integrating genomic information into patient care. A 2017 study by Kamps et al. [14] focused on next-generation sequencing (NGS) technology and its applications in oncology. The advancements in NGS, such as improved reliability, sequencing chemistry, and data interpretation, have made it feasible for clinical practice. The review described various clinical applications of NGS, including mutation detection, risk prediction, cancer classification, and pharmacogenetics. In 2017, Sheikine et al. [15] discussed the clinical and technical aspects of genomic diagnostics for precision oncology. They highlighted the significance of next-generation sequencing in enabling precision medicine. The review presented strategic decisions for optimizing genomic testing programs and summarized the technical considerations for different technologies.

In a 2017 study, Schwartzberg et al. [16] emphasized the importance of resampling and retesting tumors using liquid biopsy technology to make treatment decisions in the face of resistance to targeted therapies. They highlighted the value of molecular profiling in improving outcomes for patients when used appropriately. Senft et al. [17] conducted a study in 2017 summarizing computational approaches to detect novel drivers and genetic vulnerabilities for therapeutic exploration in precision oncology. They also reviewed clinically relevant platforms for testing predicted drugs in individual patients and highlighted technological advances in single-cell analysis for overcoming genetic and phenotypic heterogeneity in current anticancer therapies.

A 2018 study by Ziogas et al. [18] discussed the potential and challenges of next-generation sequencing (NGS) integration into appropriately designed studies for achieving predictive, preventive, and therapeutic clinical implications. They differentiated between conventional NGS and breakthrough NGS, which includes multi-regional and serial liquid biopsy analyses.

In another 2018 study, Ziogas et al. [19] highlighted the need for discovering novel valid biomarkers and drugs in patient-centric genomic trials in the era of precision surgical oncology. They discussed the potential of genome analysis in overcoming unmet needs and improving outcomes for patients with early-stage aggressive tumors. Kurnit et al. [20] emphasized the importance of sophisticated precision oncology decision support services in 2018. They reviewed existing tools and strategies for optimizing decision support, including molecular testing assays, interpretation of alteration information, and matching patients to clinical trials. Madhavan et al. [21] conducted a study in 2018 on the art and challenges of interpreting and integrating genomic data into clinical practice in precision medicine. They discussed the complexity of incorporating and interpreting precision medicine sequencing results and highlighted the need for collaboration, such as molecular tumor boards or virtual tumor boards, to process and interpret the growing volumes of omics data. Recent studies have highlighted the significant advancements in precision oncology, which has revolutionized cancer treatment approaches. The emergence of molecular tumor boards (MTBs) has played a crucial role in bridging genomic platforms and clinical practices by establishing actionable connections between drugs and molecular alterations [22]. Furthermore, genomic-based immuno-oncology has provided insights into the genetic foundations governing tumor immunity and identified molecular determinants associated with clinical benefits from immunotherapy [23].

In the realm of urothelial cancer, precision oncology has demonstrated promising clinical implications, including molecularly matched therapies and predictive biomarkers that inform

responses to chemotherapy and immunotherapy [24]. Additionally, comprehensive genomic profiling of Chinese breast cancers has revealed prevalent mutations in p53 and Hippo signaling pathways, leading to the identification of potentially actionable targets for treatment [25]. Similarly, in mesothelioma, a thorough understanding of molecular heterogeneity has paved the way for precision oncology-based therapies [26]. The implementation of precision oncology faces various challenges, including the efficient transition of next-generation sequencing from research to routine clinical practice, data management, interpretation of molecular findings, and multidisciplinary coordination [27]. However, the integration of high-throughput technologies, decision support applications, and patient databases has optimized disease management and improved patient outcomes [28]. The combination of genomic profiling and organoid development has emerged as a powerful approach in precision oncology. This integration allows for accurate genetic characterization of individual patients, enabling personalized treatment strategies based on molecular matching [29]. In conclusion, precision oncology has transformed cancer treatment by integrating genomics, molecular profiling, and clinical decision-making. The advancements in molecular tumor boards, genomic technologies, and organoid models have opened new avenues for targeted therapies, improved patient outcomes, and a deeper understanding of drug resistance mechanisms. However, further research and collaborative efforts are necessary to overcome challenges and fully realize the potential of precision oncology in routine clinical practice.

Cancer is a multifactorial disease with increasing incidence, encompassing over 100 different cancer types characterized by location, cell of origin, and genomic alterations. Tumor heterogeneity, both between different patients and within the same patient's tumor, presents a significant challenge in cancer treatment [30]. To address this challenge, various approaches have been explored to study tumor heterogeneity longitudinally and latitudinally, with the goal of tailoring individualized treatment regimens [30]. The detection and classification of structural variants (SVs) in cancer genomes are computationally challenging due to inconsistencies in breakpoints, variant types, and biological complexity. Integrating multiple algorithms and sequencing technologies is necessary to achieve high recall and precision in full-spectrum SV detection, enabling the use of tumor-specific SVs in precision oncology [31]. Aberrant activation of the RET proto-oncogene is implicated in various cancers. RET gain-of-function point mutations drive multiple endocrine neoplasia 2 (MEN2) syndrome and sporadic medullary thyroid cancer, while RET rearrangements are driver events in non-medullary thyroid cancers. Selective RET inhibitors, such as selpercatinib and pralsetinib, have shown promising efficacy and tolerability in treating RET-mutated cancers. The identification of rare RET alterations, including deletions and insertions (indels), raises questions about their functional effects and potential as targets for RET inhibitors [32].

Functional precision oncology, a personalized approach, involves exposing live tumor cells to drugs to gather immediate, individualized information for guiding therapy. This approach complements traditional precision oncology, which relies on static tumor features. Functional precision medicine provides insights into tumor vulnerabilities and can enhance treatment outcomes. However, further clinical trials are needed to assess its impact on patient outcomes and establish its role as a standard tool in clinical oncology [33]. In the future, advanced multi-omics tumor profiling will play a crucial role in shaping precision oncology. Preclinical models, such as patient-derived xenograft (PDX) models, offer a dynamic platform for studying cancer evolution and identifying response predictors [34]. In recent years, there have been significant advancements in precision oncology, aiming to tailor cancer treatment based on individual characteristics. The use of cancer genomic profiling (CGP) has shown promise in guiding the treatment of malignant

head and neck tumors [35]. Additionally, streamlined digital systems, such as the Molecular Tumor Board Portal (MTBP), have been developed to support clinical decisions and facilitate collaborative discussions in precision oncology [36]. While genomics has played a crucial role in precision medicine, it has certain limitations in analyzing the molecular phenotype of cancer. To overcome these limitations, proteogenomics, which combines proteomics and genomics, has emerged as a valuable approach. Proteogenomics offers new insights into precision oncology and has the potential to enhance our understanding of cancer at a molecular level [37]. Translating precision oncology into clinical practice poses several challenges due to the biological complexity and diversity of cancer. Technological advancements in genomics have contributed to our understanding of various aspects of cancer, including initiation, prevention, early detection, therapy resistance, and metastasis. However, addressing these translational challenges requires further research and innovative strategies [38]. Multimodal data integration is another area of focus in advancing precision oncology. Integrating diverse data types, such as molecular diagnostics, imaging, and clinical information, can provide comprehensive insights for personalized cancer care. However, the sparse nature of medical datasets and the need for improved machine learning techniques present challenges to fully harness the potential of multimodal data integration [39]. In conclusion, precision oncology holds great promise in improving cancer treatment outcomes. The integration of CGP, proteogenomics, digital platforms, and multimodal data can enhance our understanding of tumor biology and guide personalized therapies. However, further research, technological advancements, and collaboration among researchers and clinicians are essential to overcome the existing challenges and fully realize the potential of precision oncology.

Discussion

The two studies offer distinct perspectives on precision oncology. The first study highlights the logistical difficulties of monitoring molecular events in metastatic breast cancer and proposes the use of liquid biopsies, such as circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA), as easily obtainable alternatives. It emphasizes their potential to provide informative evidence for better precision oncology care. Discusses the limitations of genomic analysis and introduces proteogenomics as a merging field of proteomics and genomics, emphasizing its importance in gaining a comprehensive understanding of precision oncology. It briefly mentions the application of proteogenomics, related public data projects, and the challenges that need to be addressed. Overall, both studies contribute to the advancement of precision medicine by exploring different avenues of molecular analysis for improved cancer management [37], [40]. The studies examined different aspects of precision oncology. Highlighted the need for robust computational tools to handle and analyze large volumes of genetic and molecular profiling data, providing a guide for the implementation of a precision oncology pipeline. Demonstrated the positive clinical benefits of integrating RNA expression and genome data in treatment decision-making. It supported the use of comprehensive whole-genome transcriptome analysis (WGTA) in clinical cancer care. Finally, provided a comprehensive overview of omics data sources, cancer "omics" projects, and pathway analysis tools, emphasizing their potential applications in cancer research and precision oncology. Collectively, these studies contribute valuable insights into the computational aspects, treatment efficacy, and knowledge bases involved in precision oncology, enabling improved patient care and decision-making [41], [42], [43]. The studies provide distinct perspectives on precision oncology. This study addresses the challenges in implementing precision oncology, emphasizing the need for equal access to genomics tests, robust evidence generation, physician interpretation of genomics data, and patient empowerment in shared decision-making. It

emphasizes the importance of a multi-stakeholder approach to translate advances in precision oncology into global benefits for cancer patients. In contrast, another study focuses on the current state of personalized cancer medicine, highlighting the role of next-generation sequencing and organoid models in understanding the genetic landscape of individual cancer patients. It discusses the clinical implications and limitations of genomic profiling and organoid models, with a specific focus on breast and ovarian cancer. Furthermore, it explores the integration of these approaches for applications in precision oncology. Together, these studies shed light on the challenges, advancements, and potential clinical applications in precision oncology, contributing to the overall understanding and progress of personalized cancer care [29], [44]. The other study offers a complementary perspective on precision oncology. The overview emphasizes the significance of the cancer epigenome in predicting therapeutic response and discusses advanced technologies available for decoding epigenetic patterns at a genomic level. It highlights the potential applications of these technologies in precision oncology. In contrast, another study highlights the paradigm shift in cancer treatment towards patient-specific approaches based on tumor-specific molecular features, including oncogenic driver mutations and cancer-signaling pathway activities. It emphasizes the significance of targeting these specific genomic alterations for personalized treatment strategies. Collectively, these studies underscore the importance of genomic information in precision oncology, whether through epigenetic patterns or tumor-specific molecular features, in guiding effective and tailored treatment approaches for cancer patients [45], [46]. In summary, these studies underscore the importance of genomic information in precision oncology for guiding personalized treatment approaches. They highlight the need to address challenges, advance research, and promote global collaboration to ensure the widespread implementation of precision oncology across disciplines. By leveraging genomic data, precision oncology has the potential to revolutionize cancer treatment and improve outcomes globally.

Conclusion

In conclusion, the integration of oncology, molecular medicine, and personalized medicine holds great promise for improving cancer treatment outcomes. The studies discussed underscore the significance of utilizing genomic information in precision oncology to guide personalized treatment approaches based on molecular features and epigenetic patterns. The findings highlight the potential to enhance the accuracy and effectiveness of cancer care through targeted therapies tailored to individual patients. The implications of these findings are far-reaching, as they pave the way for more precise and tailored treatment strategies that can improve patient outcomes and minimize adverse effects. However, further research is needed to address challenges such as equitable access to genomic testing, robust evidence generation, and the integration of multi-omics approaches. Future studies should focus on refining and expanding the application of personalized medicine in oncology, exploring novel therapeutic targets, and developing innovative technologies to optimize treatment decision-making. By advancing research in this field, we can unlock the full potential of molecular and personalized medicine in revolutionizing cancer care and improving patient outcomes.

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Conflict of interests

The authors declare that there are no competing interests.

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