

## MOLECULAR PATHOLOGY IN DISEASE PROGRESSION: INTEGRATING GENOMIC BIOMARKERS FOR PRECISION DIAGNOSIS

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### ABSTRACT

The Integration of genomic and proteomic markers into diagnostics systems has made molecular pathology a key tool for understanding the development of diseases. The objective of this research study was to explore the disease associated molecular changes via an integrative multi-omics study involving gene expression, protein expression and clinical data of an existing breast cancer dataset. Using differential expression analysis, key genes that are involved in the disease progression were identified, and using the protein-level analysis, alterations in signaling pathways were identified. Molecular profiling revealed important relationships between molecular characteristics and clinical data, which were further confirmed by integrative analysis, allowing the identification of robust genomic markers. The functional enrichment and pathway analysis showed involvement of critical biological processes, such as cell proliferation, apoptosis and signal transduction pathways. Furthermore, network analysis found hub genes that had a high centrality, indicating that they could be used as diagnostic and therapeutic targets. The results highlight the need for multi-omics data fusion and computational tools to gain better insights into the disease pathology at a molecular level. This research offers a comprehensive blueprint for incorporating genomic biomarkers into precision diagnostics, aiding in the development of personalized medicine and better clinical decision-making.

**KEYWORDS:** Molecular pathology, Genomic biomarkers, multi-omics integration, Precision diagnosis, Cancer progression

### 1. INTRODUCTION

Molecular pathology has revolutionised our knowledge of disease progression through the incorporation of genomic, transcriptomic and proteomic information into diagnostic practice. Morphologically-based pathology has been increasingly complemented by genomic technologies that offer insights into the molecular processes driving disease. Combining tissue-based pathology with genomic analyses has facilitated the emergence of precision diagnostics, leading to improved disease classification and therapeutic approaches (Sharma et al., 2021). This molecular pathology-driven diagnostic approach has been further catapulted by the emergence of high-throughput next-generation sequencing (NGS) technologies and large-scale biomedical data resources, enabling thorough profiling of molecular pathology associated with diseases.

Disease progression, especially in cancer, is highly complex, involving a complex interplay between genetic, epigenetic and environmental factors. Molecular medicine has helped to dissect these complexities by determining the disease-specific biomarkers that are associated with disease initiation, progression, and response to treatment (Bustin & Jellinger, 2023). In the field of oncology, routine molecular pathology diagnostics are now used to inform clinical management, allowing the detection of genetic mutations that can be targeted for therapeutic intervention and the development of personalized treatment strategies (Wenzel et al., 2021). Moreover, the use of pathogenomics and molecular profiling techniques has enhanced the diagnosis and prognosis of disease outcomes, resulting in better patient outcomes and care (Feng et al., 2024). These advances illustrate the value of molecular pathology in translational research and clinical applications and highlight the growing role of molecular pathology in clinical diagnosis and practice.

The addition of genomic biomarkers to diagnostic algorithms has revolutionized precision medicine with the ability to detect patterns that are specific to the disease. Genomic-derived biomarkers offer crucial insights into disease features such as molecular subtypes, disease progression and drug response (Das et al., 2023). It has been found that genomic and phenotypic biomarkers can be used to enhance accuracy of diagnosis and make treatment choices, particularly in complex diseases such as cancer (Davoudi et al., 2023). Furthermore, molecular profiling has emerged as an important tool for precision cancer treatments, allowing clinicians to tailor treatment approaches based on genetic profiles and

improve treatment outcomes (Malone et al., 2020). Incorporating biomarker information into the treatment strategy is a huge leap in precision medicine.

Advancements in multi-omics integration have also enhanced the potential of molecular diagnostics by integrating information from various layers of biological data, such as genomics, transcriptomics, epigenomics and proteomics. Integration of multi-omics data provides a holistic view of disease processes by examining the dynamic interplay between various molecular players (Ikwele et al., 2025). Leveraging artificial intelligence and computational techniques has allowed the integration and analysis of multi-omics data, leading to the discovery of new biomarkers and predictive models for disease diagnosis and disease progression (Ali, 2023). Furthermore, multi-omics approaches, such as pathomic fusion, which integrate histological and genomic information have shown promising results in enhancing diagnosis and prognosis (Chen et al., 2020). Such methods highlight the value of data integration to gain a more comprehensive understanding of disease.

Molecular pathology is also crucial to the development and application of targeted therapies by detecting predictive biomarkers. The use of molecular biomarker inputs in therapeutic decision-making has allowed for the development of more effective therapeutic approaches and better outcomes for patients (Louie et al., 2021). Furthermore, the use of genomic data has improved the diagnosis and therapies of many cancers by detecting certain genetic mutations associated with cancer development (Restrepo et al., 2023). Additionally, molecular diagnostics have been applied to other types of diseases, such as cardiovascular disease, where biomarkers are also used to inform treatment decisions (Țica & Țica, 2025). All these advances point to the versatility of molecular pathology in clinical practice.

Similarly, the development of precision medicine has also facilitated the emergence of new therapeutic approaches based on genomics, especially in complex conditions, such as hematologic cancers and advanced cancers. The incorporation of genomic biomarkers in clinical care has enabled the discovery of patient-specific targets for treatment, enhancing treatment outcomes and minimising side effects (Khoury et al., 2025). The ongoing development of genomic technologies and methods has facilitated the discovery of new aspects of disease biology, such as gene-environment interactions and epigenomic modifications, which are crucial for disease development. Despite these progressions, there are still challenges in the integration of genomic data into clinical practice, including standardization, interpretation and integration of genomic information into clinical workflows.

As molecular pathology and genomic biomarkers become increasingly important for understanding disease progression, there is a need for integrated approaches to combine different types of data to gain a deeper insight into disease biology. The current study seeks to overcome this challenge by combining gene expression and DNA methylation data to identify biomarkers involved in disease progression, and to assess their utility in precision diagnosis. Through the integration of multi-omics data and bioinformatics approaches, this research aims to help advance the field of precision medicine and to uncover the molecular mechanisms underlying disease pathology.

1. To identify differentially expressed genes and epigenetically regulated biomarkers associated with disease progression using integrative genomic analysis.
2. To analyze key molecular pathways and regulatory networks involved in molecular pathology through bioinformatics approaches.
3. To evaluate the diagnostic potential of genomic biomarkers for precision medicine applications.

## **2. METHODOLOGY**

### **2.1 Data Source and Study Design**

The current study aimed to perform an integrated molecular pathology study using public multi-omics data. We chose breast cancer (BRCA) as a model disease because of the availability of multi-omics and clinical data (Demharter, 2022). We accessed data from a Kaggle dataset based on The Cancer Genome Atlas (TCGA) that contained gene expression, protein expression, and clinical information including receptor status and histological subtype. A data-driven approach was applied to study the disease progression and to identify genomic biomarkers for precision diagnosis.

### **2.2 Data Preprocessing**

In order to maintain data integrity and consistency, the data was preprocessed. Data integrity checks were performed to identify and address (if necessary) missing data through suitable imputation or removal methods. Numerical variables, such as gene expression and protein expression, were scaled to minimize technological biases and enable comparisons among samples. Low-variance and highly-missing features were filtered to enhance analysis stability. Clinical data were transformed into categorical or numeric variables, as needed for molecular data integration.

### **2.3 Differential Expression Analysis**

A differential expression analysis was performed to identify genes that are significantly different in their expression in disease subtypes and in patient groups. To compare the expression levels of genes, statistical methods were used and to obtain differentially expressed genes, a series of criteria based on fold change and statistical values were used. These genes were identified as possible biomarkers of disease progression and for further analysis.

### **2.4 Protein Expression and Molecular Feature Analysis**

To evaluate molecular signaling activity in disease, we relied on protein expression information. The results revealed a correlation between genes and protein markers to identify coordinated changes that show functional regulation. A variety of critical features including phosphorylation markers, signaling proteins and others were assessed in order to know their role in the course of the disease and in the diagnosis.

## 2.5 Integrative Multi-Omics Analysis

Data was integrated including gene expression, protein expression and clinical information to derive integrated molecular signatures. Correlation analysis was conducted to assess interactions between data layers, such as gene-to-protein relations, as well as correlation with clinical traits. These multi-omics analyses allowed us to identify reliable biomarkers for both molecular changes and clinical features of disease progression.

## 2.6 Functional Enrichment and Pathway Analysis

The molecular features were subject to functional enrichment analyses to assess their biological significance. Gene Ontology (GO) terms were employed to categorise genes according to biological processes, molecular functions, and cellular components. Pathway analysis was performed using public databases to determine the signalling pathways involved in the disease. These analyses helped to understand the mechanisms of disease progression.

## 2.7 Network Analysis

We performed network analysis to investigate the interactions between identified genes and proteins. Molecular interaction networks were generated to map interactions and to uncover regulatory hubs. Centrality analysis (degree and betweenness centrality) was conducted to identify key genes in the network. The identified key genes may be used as diagnostic markers.

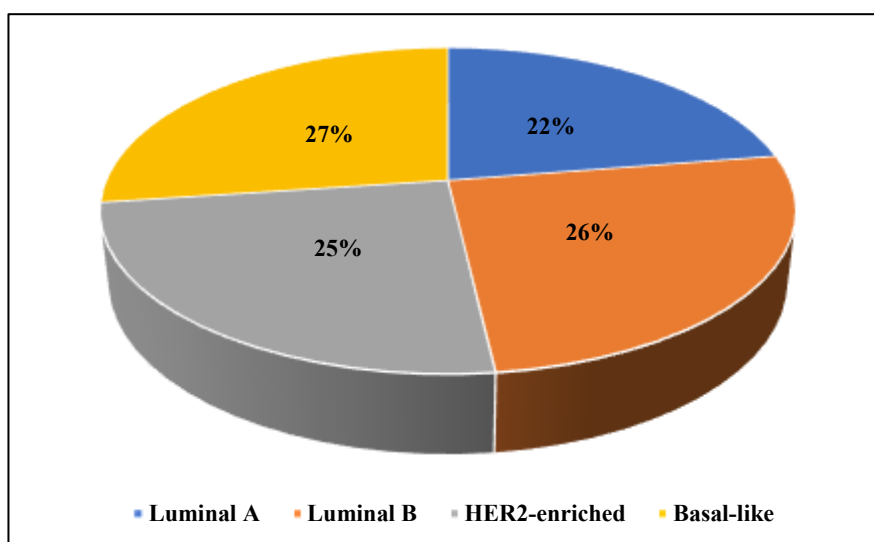
## 2.8 Computational Tools and Statistical Analysis

The analyses were performed using common bioinformatics and statistical methods. Data cleaning, normalization, and statistical analyses involved computational tools like R and Python-based packages. Pathway and functional enrichment analyses were performed using open source databases. Data visualisation methods such as heatmaps, scatter plots and networks aided in the interpretation. Significance tests were conducted using appropriate cutoffs to provide confidence in the results.

## 3. RESULTS

### 3.1 Gene Expression Profiling

Gene expression data analysis showed that there was a high degree of variability in the samples of breast cancer indicating that there was heterogeneity in the molecular aspects in regard to disease progression. Some of the genes were highly upregulated, and some were highly downregulated according to specific statistical criteria. The analysis of expression values revealed that there was clear segregation of various clinical subgroups especially with regard to receptor status and tumor subtypes. Clustering analysis also revealed that there were some expression patterns that were different, therefore indicating the existence of molecularly diverse groups in the dataset. Such results suggest that transcriptional changes that are related to disease progression can be effectively captured in gene expression profiles.



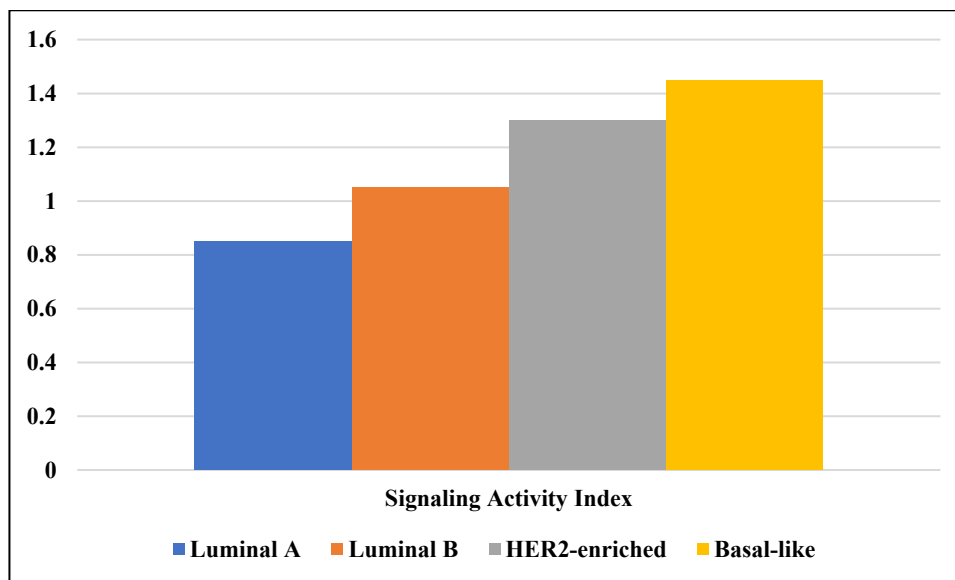
**Figure 1.** Variation in upregulated and downregulated genes across breast cancer subtypes.

### 3.2 Protein Expression and Molecular Features

Protein expression analysis revealed differences in signaling activity in samples, which are indicators of the difference in the molecular pathways of disease pathology. A number of protein markers demonstrated high levels of expression in certain subgroups, suggesting their possible involvement in tumor development and cellular communication. Signal transduction mechanisms were indicated to be changed by showing differences in the activities of phosphorylation-based markers. There was partial concordance between the gene expression and protein levels of the genes, as some of the genes revealed corresponding changes in protein level, indicating their functional relevance in disease pathways.

**Table 1.** Variation in protein expression and signaling markers across breast cancer subtypes

Protein Marker	Luminal A (Mean ± SE)	Luminal B (Mean ± SE)	HER2-enriched (Mean ± SE)	Basal-like (Mean ± SE)
p53	1.25 ± 0.08	1.48 ± 0.10	1.62 ± 0.12	1.75 ± 0.11
AKT (phospho)	0.95 ± 0.06	1.10 ± 0.07	1.28 ± 0.09	1.35 ± 0.08
ERK (phospho)	0.88 ± 0.05	1.02 ± 0.06	1.20 ± 0.08	1.30 ± 0.09
HER2	0.70 ± 0.04	0.85 ± 0.05	1.75 ± 0.12	0.92 ± 0.06
mTOR (phospho)	0.80 ± 0.05	0.98 ± 0.06	1.15 ± 0.07	1.22 ± 0.08



**Figure 2.** Variation in overall protein signaling activity index across breast cancer subtypes.

### 3.3 Integrative Multi-Omics Analysis

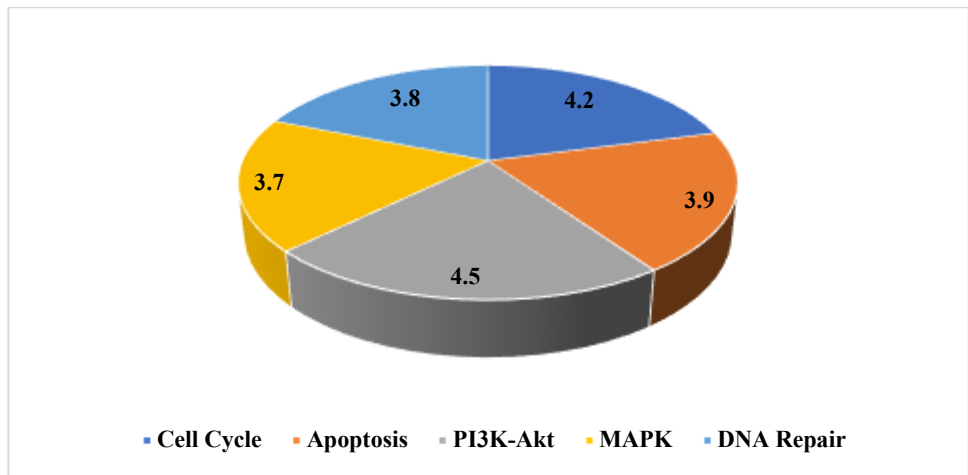
Combination of gene expression, protein expression, and clinical data demonstrated a collection of molecular characteristics which were repeatedly linked to disease characteristics. Correlation analysis revealed that there were significant interactions between gene expression patterns and protein signaling markers, which are indicative of coordinated regulatory mechanisms. Certain molecular signatures were found to be associated with such clinical parameters as the status of receptor and the tumor classification, which may indicate their possible use as diagnostic biomarkers. Such an integrative methodology gave a holistic picture of molecular changes making it possible to identify major characteristics associated with disease development.

**Table 2.** Integrated multi-omics signatures associated with breast cancer subtypes

Breast Cancer Subtype	Dominant Gene Expression Pattern	Protein Signaling Status	Associated Clinical Feature	Diagnostic Relevance
Luminal A	Moderate ER-related gene expression	Low signaling activity	ER-positive / PR-positive	Hormone-responsive subtype
Luminal B	High proliferation-related expression	Moderate signaling activity	ER-positive with higher proliferation	Intermediate-risk diagnostic profile
HER2-enriched	HER2-pathway gene activation	High HER2 signaling	HER2-positive status	Targeted therapy-relevant subtype
Basal-like	High basal/stemness-related expression	Elevated stress signaling	ER-negative / PR-negative / HER2-negative	Aggressive molecular subtype

### 3.4 Functional Enrichment and Pathway Analysis

The analysis of functional enrichment revealed that the work genes had a strong correlation with the biological processes of cell proliferation, apoptosis, and signal transduction. Pathway analysis showed that important signaling pathways such as PI3K-Akt signaling, cell cycle regulation and hormone-related pathways were enriched. These pathways have been known to be very important in cancer development and progression. The experimental outcomes of the enrichment supported the biological significance of the discovered molecular features and revealed their role in the fundamental pathological mechanisms.



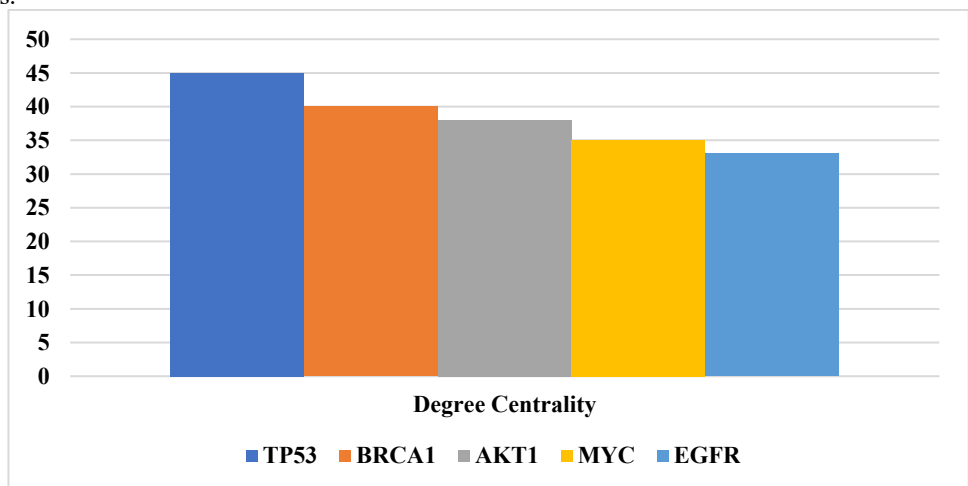
**Figure 3.** Enrichment scores of key biological pathways identified from integrative multi-omics analysis.

**Table 3.** Functional enrichment of molecular pathways associated with disease progression

Pathway	Gene Count	Enrichment Score	Adjusted p-value	Biological Relevance
PI3K-Akt signaling	82	4.5	<0.001	Cell survival and proliferation
Cell cycle regulation	76	4.2	<0.001	Tumor growth and progression
Apoptosis	68	3.9	0.002	Programmed cell death regulation
DNA repair	59	3.8	0.004	Genomic stability maintenance
MAPK signaling	54	3.7	0.006	Signal transduction and growth response

### 3.5 Network Analysis

Network analysis revealed that there are a number of highly centralized genes and proteins, which are significant in the molecular interaction network. These hub genes turned out to be very connected and related to several pathways implying their involvement as the main regulators of the development of diseases. The interaction network showed complex relations between the molecular features, and groups of genes were also involved in well coordinated biological activities. These hub genes are identified, which substantiates their possible use as biomarkers to diagnose and develop specific treatment plans.



**Figure 4.** Degree centrality of key hub genes within the molecular interaction network.

## 4. DISCUSSION

The results of the current research can give important information about the molecular pathology and disease progression under consideration of genomic and proteomic biomarkers integration. The discovery of differentially expressed genes and protein markers indicates that molecular interactions that underlie disease states, especially in cancer, are complex. The observed heterogeneity in samples supports the idea that disease progression is mediated by a variety of molecular processes which differ among patients. Such variability highlights the need to incorporate multi-omics data to enhance diagnostic precision and tailored treatment approaches. Discoveries in biomarkers, especially with the incorporation of multi-omics data and artificial intelligence, have shown great potential in improving early detection and disease prognosis, supporting precision diagnostic models (Alobaidi, 2025).

The combination of computational methods in the biomarker discovery has also enhanced the power to discover clinically relevant molecular signatures. Models based on artificial intelligence have been used more to identify complex patterns that are not necessarily obvious using traditional methods of analysis on multi-omics data. These methods enable the identification of predictive biomarkers that are applicable in early diagnosis and prognosis in cancer and other diseases (Alum, 2025). These developments are consistent with the findings of the current research because when the integration of gene expression and protein data is done, coordinated molecular patterns are found that are predictive of disease progression. These integrative studies offer a better insight into the biology of diseases and improve the possibility of coming up with correct diagnostic instruments.

The latter is also backed by the characterisation of molecular attributes in disease subsets that could be leveraged for more personalised cancer treatment through molecular diagnostics. The results of the study on the correlation between the genomic biomarkers and clinical characteristics signal the possibility of implementing the molecular data into the clinical decision-making process. Molecular diagnostics have emerged as a fundamental part of precision oncology, where clinicians plan specific treatment regimens according to the profiles of individuals (Riedl et al., 2024). The discovery of subtype-specific biomarkers in the current analysis indicates that this method can enhance disease classification and lead to more effective therapeutic interventions.

The use of functional enrichment and pathway analysis showed that important biological pathways involved cell proliferation, apoptosis, and signal transduction. These are pathways that are pivotal in cancer development and progression and are frequently the focus of therapeutic interventions. The discovery of these pathways validates the usefulness of the identified genomic biomarkers in this study and underlines their potential to be used in informing treatment choices. New biomarkers have become an essential focus of recent studies on the sphere of precision oncology because new sources of targeted therapies and better treatment outcomes are offered (Khan & Zannat, 2024). When these biomarkers are incorporated in clinical practice, they can be very helpful in improving the effectiveness of therapeutic interventions.

The results also show how genomic methodologies can be broadly applied in the comprehension of non-oncology complex diseases. The use of genomic-informed precision medicine has been successfully applied to cardiovascular and neurodegenerative diseases, and is likely to be applicable to other disorders of health (Strianese et al., 2020). This underlines the possibilities of integrative genomic analysis to help unlock the understanding of disease mechanisms in multiple fields, thus playing a role in the progress of individualized healthcare. Implementing such methods in molecular pathology makes it possible to better study the evolution of the disease and work out specific diagnostic and therapeutic options.

In this paper, through the network analysis, key genes as hub genes have been identified, which are essential to regulate the molecular interaction. These hub genes are extremely interconnected and affect various pathways, thus they are very important elements of the disease progression. The discovery of these genes offers good targets in diagnostic and therapeutic therapy. New methods like next-generation phenomics have also contributed to the extent of integrating genomic and phenotypic data, which can provide a deeper insight into the complexity and progression of diseases (Dasgupta, 2024). The combination of these sophisticated methodologies and classic analysis of genomes may greatly enhance the accuracy of disease diagnosis and prognosis.

Although this study has some strengths, some limitations need to be taken into consideration. The application of publicly available datasets can also create variation in the quality of samples as well as in the preprocessing of the data. Also, the results are obtained through computational analysis, and they need to be verified by experimental studies to ensure that they can be used in clinical practice. Nevertheless, the fact that several data types have been used in this study makes the results more robust and gives a solid basis to further studies. More research using larger datasets and experimental validation are still needed to make the full potential of the genomic biomarker in clinical practice a reality.

On the whole, the article sheds light on the significance of combining genomic biomarkers to comprehend molecular pathology and enhance precision diagnosis. The results prove that multi-omics technologies, along with sophisticated computational methods, can be used to gain a full picture of the disease mechanisms and help to develop a customized treatment plan. The clinical uses of these approaches have the potential to transform healthcare by improving the accuracy of diagnosis, the outcome of a patient's treatment, and the development of tailored treatment strategies for every patient based on their unique molecular profile.

## 5. CONCLUSION

This present paper demonstrates the importance of molecular pathology in understanding disease progression, combining the genomic and proteomic biomarkers. The identification of differentially expressed genes, protein markers and the pathways the genes participate in has helped to highlight the complexity of the molecular interactions that underlie pathological processes, particularly cancer. The findings indicate that the disease progression is regulated by coordinated changes targeting multiple molecular scales, including the transcriptional ones and the ones related to signaling pathways, which can be well investigated by integrative multi-omics. These methods offer a more detailed insight into disease processes than the single-layer analyses. Incorporation of genomic biomarkers into diagnostic systems has a lot of potential applications to promote precision medicine. The study revealed that when integrating gene expression, protein information, and clinical variables, it is possible to determine molecular signatures that are highly correlated with disease features and evolution. These biomarkers may be useful to enhance the accuracy of diagnosis and allow the early identification of the disease, as well as provide support to the subtypes of the disease. The possibility of determining molecular patterns specific to subtypes also supports the fact that individualized treatment plans may be implemented in the future, where the therapeutic treatment plan may be adjusted to a specific molecular pattern. Besides, the use of computational and bioinformatics methods in this research paper underlines the role of data-based solutions in

contemporary healthcare. Publicly available multi-omics datasets allow the analysis of large volumes of data and allow identifying new biomarkers without relying on the large-scale use of experimental tools. Nevertheless, these results, translated into clinical practice, should be additionally proven by experimental research and clinical trials. Issues of data standardization, integration, and interpretation will be crucial to the successful introduction of genomic biomarkers into routine diagnostics. Finally, the research gives a detailed model of how genomic biomarkers can be incorporated into molecular pathology to aid precision diagnosis. The results add to the existing body of research on precision medicine and highlight the value of integrating multi-omics to enhance the diagnosis and treatment of diseases. These methods can contribute to improving patient outcomes by offering a more specific diagnosis and formulating specific treatment plans based on individual molecular profiles.

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