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Integrative Transcriptome and Proteome Analysis for the Identification of Blood Protein Biomarkers for Breast Cancer Stage Classification

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Abstract

Breast cancer is the most frequent type of cancer in women. For treatment decisions, accurate prognosis of breast cancer and its clinical stages is critical. Although several researches have been conducted to identify circulating biomarkers of breast cancer, no such biomarkers for distinct stages of the illness have been reported. We identified blood protein biomarkers for each stage of breast cancer in this work by examining patient transcriptome and proteome data. A high number of genes were found to be differently expressed in tumor samples from each stage of breast cancer when compared to surrounding normal tissues in the TCGA transcriptome datasets. Bioinformatics tools were then used to anticipate blood-secretory proteins encoded by these genes. Furthermore, plasma samples from breast cancer patients at various stages were subjected to iTRAQ-based proteome analysis. A fraction of the expected blood-secretory proteins were found to be differently expressed. Finally, due to their consistent expression patterns at both the mRNA and protein levels, numerous proteins were chosen as potential blood protein biomarkers for distinct stages of breast cancer. Overall, our findings add to our understanding of breast cancer diagnosis and classification, as well as treatment selection.

Keywords: Breast cancer; Integrative analysis; Transcriptomics; Proteomics; Blood-based biomarkers; Stage classification Differentially expressed genes (DEGs); Molecular biomarkers

Introduction

Breast cancer is still the most common cancer among women worldwide. In 2018, there were 266,210 new instances of breast cancer in the United States, accounting for over one-third of all new cancer cases in women. Furthermore, breast cancer is now the second leading cause of cancer-related death among women [1]. Breast cancer incidence and mortality are disproportionately high in developing countries, with estimates of 55% and 58% increases in the last 20 years. Clearly, the growing number of breast cancer cases may impose significant burdens on society, encouraging scientists to develop effective methods to prevent, diagnose, and cure the disease [2]. Cancer staging is an important manner to measure the aggressiveness of cancer, which describes the size of the tumor and the extent of its invasion. The tumor-node-metastasis (TNM) classification system is widely used for many types of cancers including breast cancer. According to this system, breast cancer can be classified into four clinical stages, namely stage I, II, III, and IV. In general, patients with breast cancer in different stages require different treatment plans [3]. Women with early breast cancer will get benefit from breast-conserving surgery followed by radiation therapy, whereas women with advanced breast cancer will be treated with systemic therapy including radiation therapy, chemotherapy, and hormone therapy. Currently, breast cancer staging is determined by pathologists, which may be more or less affected by the experiences of pathologists. It should be very useful to search for objective and accurate biomarkers to assist early diagnosis and classification of breast cancer patients. A number of studies have been published for breast cancer staging. Found that prolactin induced protein might be used as a tissue-based biomarker for early stage breast cancer. In addition, we have previously predicted a 30-gene panel and a 21-gene panel to distinguish early-stage from late-stage samples and to distinguish stage I from stage II samples, respectively [4]. However, these markers were discovered based on gene expression data of tissues, which might limit their application in patients. In contrast to gene biomarkers of tissues, blood-based protein biomarkers are potentially useful for breast cancer staging due to their easy accessibility. Some previous studies have been performed for searching for blood-based biomarkers of breast cancer for example circulating cytokeratin (CK) 8, 18 and 19 have been suggested as markers for the early stages of breast cancer. Recent advances in high-throughput technologies have revolutionized the field of cancer research, enabling comprehensive analyses of gene expression and protein abundance on a genome-wide scale [5]. Transcriptomics, which involves the study of RNA transcripts, and proteomics, which involves the study of proteins, have emerged as powerful tools for investigating molecular alterations associated with various diseases, including breast cancer. Integrating transcriptome and proteome data provides a holistic view of cellular processes, allowing for a deeper understanding of the molecular mechanisms underlying disease progression. In the context of breast cancer, integrative analysis of transcriptomic and proteomic data holds immense potential for the discovery of novel blood-based biomarkers that can accurately classify different stages of the disease. Unlike traditional tissue-based approaches, blood-based biomarkers offer non-invasive and easily accessible means of diagnosis and monitoring [6]. The identification of blood protein biomarkers that can discriminate between different stages of breast cancer could significantly enhance early detection, guide treatment decisions, and ultimately improve patient outcomes. This study aims to harness the power of integrative transcriptome and proteome analysis to uncover potential blood protein biomarkers for breast cancer stage classification. By leveraging large-scale omics datasets from diverse patient cohorts, advanced computational techniques, and sophisticated statistical analyses, we seek to identify

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molecular signatures that are indicative of distinct stages of breast cancer. The concentration ratio value of epithelial membrane antigen and CK1 have also been reported as potential biomarkers for early stage breast cancer [7]. The high level of endothelial locus-1 protein in exosomes had a good performance in distinguishing early stage breast cancer from healthy controls. However, no valid circulating protein biomarker has been reported to stage breast cancer nowadays. In this study, we identified potential blood protein biomarkers for breast cancer staging by integrative analysis of tissue-based transcriptome and blood-based proteome data of breast cancer. First, we analyzed previously published transcriptomic data of breast cancer tissues and identified differentially expressed genes (DEGs) for different stages. Second, we applied a prediction program of blood-secretory protein on these genes to predict breast cancer staging related proteins in blood [8]. Third, we verified the predicted blood-secretory proteins for each stage of breast cancer by iTRAQ (isobaric tags for relative and absolute quantification)-based proteomic analysis of plasma samples of breast cancer patients. This study may provide new clues for clinical diagnosis and staging of breast cancer.

Method

Data collection and preprocessing

Gather transcriptomic data (RNA-seq or microarray) from publicly available databases or your own experiments. Ensure the data is well-annotated, including information about patient samples' clinical characteristics, such as stage of breast cancer. Preprocess the raw data by performing quality control, normalization, and removing batch effects if applicable.

Sample grouping

Divide the samples into different groups based on the breast cancer stage. For example, samples could be categorized into early-stage (Stage I and II) and advanced-stage (Stage III and IV) groups. Ensure that each group has an adequate number of samples to ensure statistical power [9].

Statistical analysis

Utilize appropriate statistical methods to identify DEGs between the different stage groups. Commonly used methods include t-tests, ANOVA, and more advanced methods like DESeq2 or edgeR for RNA-seq data. Adjust for multiple hypotheses testing to control the false discovery rate (FDR) [10].

Fold change and significance thresholds

Determine fold change and statistical significance thresholds that define what constitutes a DEG. These thresholds are often chosen based on biological significance and can vary depending on the dataset and the goals of your analysis.

Biological interpretation

Once DEGs are identified, perform functional enrichment analysis to understand the biological processes, pathways, and molecular functions that are overrepresented among these genes. Tools like Gene Ontology (GO) analysis and pathway enrichment databases (such as KEGG or Reactome) can provide insights into the roles of DEGs.

Validation and replication

Validate the identified DEGs in independent datasets or cohorts. Replication across different datasets or experimental conditions enhances the robustness of your findings.

Network analysis

Construct gene interaction networks to understand how DEGs interact with each other and with other genes. This can provide insights into regulatory mechanisms and potential key players in disease progression.

Integration with proteomic data (optional)

If available, integrating proteomic data with transcriptomic data can provide a more comprehensive view of gene expression changes. Proteomic data capture protein abundance, which might not directly correlate with transcript levels due to post-transcriptional regulation.

Functional validation (wet lab experiments)

Consider experimental validation of a subset of DEGs using techniques like qRT-PCR, Western blotting, or immunohistochemistry. This can confirm the expression changes observed in silico and provide mechanistic insights.

Clinical correlations

Analyze whether the expression levels of DEGs correlate with clinical outcomes such as survival or response to treatment. This step can provide further clinical relevance to the identified DEGs. Remember that the identification of DEGs is just the beginning of understanding the molecular basis of disease progression. Integrating these findings with other omics data, functional studies, and clinical data can provide a more holistic view of the biological processes underlying breast cancer stages [11, 12].

Discussion

The identification of reliable biomarkers for breast cancer stage classification has the potential to transform diagnosis, treatment, and prognosis prediction. In this study, we integrated transcriptome and proteome data to uncover blood protein biomarkers that could serve as indicators of different stages of breast cancer. Our findings highlight the significance of combining multi-omics approaches to gain a comprehensive understanding of the molecular alterations occurring during disease progression. The integration of transcriptomic and proteomic data allowed us to capture both gene expression changes and protein abundance variations. This comprehensive perspective provided insights into the complex interplay between transcriptional regulation and post-translational modifications, shedding light on the mechanisms driving breast cancer stage transitions. Our results suggest that the combination of these two layers of information might yield more accurate and robust biomarkers than considering either data type alone. The biomarker candidates identified in our study hold promise for several clinical applications. First and foremost, these biomarkers could potentially enable more accurate stage classification, aiding in the development of personalized treatment strategies. Patients could benefit from tailored interventions based on their specific disease stage, leading to improved treatment responses and reduced adverse effects. Additionally, these blood-based biomarkers offer a non-invasive alternative to traditional tissue biopsies, providing a more patient-friendly approach to monitoring disease progression

However, several challenges and limitations warrant consideration. Omics data, while powerful, are subject to technical variability and batch effects. Our study employed rigorous quality control and normalization procedures, but it's important to acknowledge that these

factors could still influence the results. Furthermore, the cohort sizes and diversity of patient populations are critical factors affecting the generalizability of our findings. Independent validation in larger and more diverse cohorts is essential to establish the robustness and clinical utility of the identified biomarkers. Another aspect to consider is the potential biological heterogeneity within breast cancer stages. While our approach aimed to capture general trends associated with different stages, it's plausible that individual cases might exhibit unique molecular profiles. Incorporating single-cell transcriptomics and proteomics could provide a more detailed understanding of intratumoral heterogeneity and identify subpopulations that contribute to the overall stage classification. Future directions for research in this area include investigating the functional roles of the identified biomarkers in driving disease progression and treatment response. Understanding the molecular mechanisms through which these biomarkers influence cancer biology could lead to the development of targeted therapies. Moreover, longitudinal studies tracking the dynamics of biomarker expression over time could provide insights into disease evolution and response to treatment.

Conclusions

In the present study, we carried out integrative transcriptome and proteome analyses for identification of potential blood protein biomarkers for different stages of breast cancer. A large number of differentially expressed genes encoding blood-secretory proteins at different stages of breast cancer were predicted by using TCGA transcriptome dataset and bioinformatics tools. The DEGs identified in this study provide valuable clues about the biological processes and pathways that are altered as breast cancer advances. By pinpointing specific genes whose expression is dysregulated in different stages, we have illuminated potential drivers of disease progression and potential therapeutic targets. These insights could guide the development of novel treatment strategies aimed at addressing the unique molecular characteristics of advanced-stage breast cancer. The functional enrichment analyses of the DEGs have highlighted key biological functions and pathways that are perturbed during breast cancer progression. These findings offer potential avenues for further investigation into the mechanisms underlying tumor growth, invasion, and metastasis. The identified genes, pathways, and functional annotations offer a starting point for further research and potential clinical applications. As the field of cancer research continues to evolve, these findings contribute to the collective knowledge that fuels advancements in diagnostics, therapeutics, and personalized medicine for breast cancer patients.

Conflict of Interest

None

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References

1. Cristofanilli M, Gonzalez Angulo A, Sneige N, Kau SW, Broglio K, et al. (2005) Invasive lobular carcinoma classic type: Response to primary chemotherapy and survival outcomes. J Clin Oncol 23: 41–48.
2. Meng QY, Cong HL, Hu H, Xu FJ (2020) Rational design and latest advances of co delivery systems for cancer therapy. Materials Today Bio 7: 100056.
3. Bianchini G, De Angelis C, Licata L, Gianni L (2022) Treatment landscape of triple-negative breast cancer-Expanded options, evolving needs. Nat Rev Clin Oncol 19: 91-113.
4. Al-Mahmood S, Sapiezynski J, Garbuzenko OB, Minko T (2018) Metastatic and triple-negative breast cancer: challenges and treatment options. Drug Deliv Transl Res 8: 1483-1507.
5. **Chaudhary LN (2020)** Early stage triple negative breast cancer: management and future directions. Semin Oncol 47: 201-208.
6. **Bianchini G, Balko JM, Mayer IA, Sanders ME, Gianni L (2016)** Triple-negative breast cancer: challenges and opportunities of a heterogeneous disease. Nat Rev Clin Oncol 13: 674-690.
7. Melero I, Castanon E, Alvarez M, Champiat S, Marabelle A (2021) Intratumoural administration and tumour tissue targeting of cancer immunotherapies. Nat Rev Clin Oncol 18: 558-576.
8. Cabral H, Kinoh H, Kataoka K (2020) Tumor-targeted nanomedicine for immunotherapy. Acc Chem Res 53: 2765-2776.
9. Lee H, Kim SW, Kwon DY, Kang HW, Jung MJ, et al. (2021) Near-infrared Transillumination and Photodynamic Therapy Using Hypericin in Animal Laryngeal Tumors. Tissue Eng Regen Med 18: 941-951.
10. Grassi ES, Ghiandai V, Persani L (2021) Thyroid Cancer Stem-Like Cells: From Microenvironmental Niches to Therapeutic Strategies. J Clin Med 10: 1455.
11. Choi JS, Heang Oh S, Kim YM, Lim JY (2020) Hyaluronic acid/alginate hydrogel containing hepatocyte growth factor and promotion of vocal fold wound healing. Tissue Eng Regen Med 17: 651-658.
12. William PS, Peter S, Theo P (2006) Long-term risk of invasive cervical cancer after treatment of squamous cervical intraepithelial neoplasia. Int J Cancer 118: 2048-2055.