Abstract

Integrated Bioinformatics Analysis for Identifying Hub Genes and Therapeutic Targets in Recurrent Breast Cancer Liver Metastasis †

Yuet-Hei Tyler Kwok and Kumaraswamy Naidu Chitrala *

Department of Engineering Technology, University of Houston, Sugar Land, TX 77479, USA; tkwok@cougarnet.uh.edu
* Correspondence: kchitral@central.uh.edu
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Introduction: Breast cancer during advancement to the metastatic stage involves the liver, thereby diminishing the survival rate among 50% of cases. Currently, there are few therapeutic protocols for breast cancer liver metastasis (BCLM) available, thereby necessitating a deeper understanding of the molecular patterns governing this molecular mechanism. Therefore, in the present study, by analyzing the differentially expressed genes (DEGs) between primary breast tumors and BCLM lesions, we aim to shed light on the diversities of this process.

Methods: In this study, we investigated breast cancer liver metastasis relapse by employing a comprehensive approach that integrates data filtering, Gene Ontology and KEGG Pathway Analysis, Overall Survival analysis, identification of the alterations in the DEGs, visualization of the protein–protein interaction network, Signor 2.0, identification of positively correlated genes, screening results of the function of hub genes, immune cell infiltration analysis, copy number variant analysis, gene-to-mRNA interactions, transcription factor analysis, and identification of potential treatment targets.

Results: Our results showed two genes, \textit{PCK1} and \textit{LPL}, were differentially expressed between primary breast tumors and BCLM lesions. \textit{PCK1} is a regulator of gluconeogenesis, and \textit{LPL}, involved in lipid metabolism, impacts cancer cell energetics and biosynthetic capabilities. Elevated \textit{PCK1} levels show a correlation with a poorer prognosis, indicating an aggressive phenotype. The transcription factors (\textit{AR}, \textit{PPARA}, \textit{RXRA}, \textit{RXRB}, and \textit{RXRG}) regulating both genes offer insights into energy homeostasis, metabolism, and cell growth. Immune infiltration analysis suggests their collective role in modulating the tumor microenvironment, influencing immunosurveillance and evasion.

Conclusion: This study’s integrative approach unveils metabolic reprogramming, suggesting altered \textit{PCK1} and \textit{LPL} expression are key in breast cancer metastasis recurrence.


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