https://doi.org/10.29289/259453942023V33S1022

Breast cancer biomarkers of resistance to neoadjuvant chemotherapy

Martina Lichtenfels[1], Matheus Gibeke Siqueira Dalmolin[2], Marcelo Augusto Costa Fernandes[3], Caroline Brunetto de Farias[1]

[1]Ziel Biosciences – Porto Alegre (RS), Brazil.
[2]Laboratory of Machine Learning and Intelligent Instrumentation, Universidade Federal de Rio Grande do Norte – Natal (RN), Brazil.
[3]Department of Computer Engineering and Automation, Universidade Federal de Rio Grande do Norte – Natal (RN), Brazil.

Objective: The objective of this study was to identify possible biomarkers of resistance to neoadjuvant chemotherapy (NACT) in breast cancer (BC). **Methodology**: We evaluated microarray gene expression data of BC samples before NACT from three public datasets of the Gene Expression Omnibus database. We performed differential expression analyses comparing patients who presented partial versus pathological complete response (pCR) to NACT in each dataset. Differentially expressed genes with an adjusted p-value less than 0.01 and a logFC greater than 1 or less than –1, identified in more than one analysis, were selected as potentially relevant to tumor resistance. **Results:** The selected datasets were GSE25055, GSE25055, and GSE20194, containing 306, 182, and 178 samples. These datasets present heterogeneous data, with different subtypes of BCs (luminal, luminal/HER2, HER2, and triple-negative) and treatments used in the NACT, such as FACT and FECT in GSE20194 and Taxol and Taxotere in GSE25065. Our differential expression analysis identified 43 genes for the dataset GSE25055, 13 for GSE25055, and 30 for GSE20194. Despite the high heterogeneity of the datasets, we identified the genes CCND2, SNX15, and TTC4, which were common to at least two analyses. The CCND2 and TTC4 genes are upregulated, while SNX15 is downregulated in patients with partial response compared with those presenting pCR. The CCND2 gene has low expression in BC and is related to a worse prognosis. Our result showed an inverse relationship; CCND2 is overexpressed in patients with a partial response to NACT. The expression of the TTC4 gene is previously known in breast tumors, and the functions of the SNX15 gene in breast tumors are still poorly understood in the literature. **Conclusion:** These results can contribute to a better understanding of the mechanisms involved in intrinsic tumor resistance to NACT, allowing the development of personalized therapeutic strategies.

Keywords: breast neoplasms; neoadjuvant chemotherapy; drug resistance; gene expression.