Investigating the difference in the gene expression profile of breast cancer metastasis to the brain with the lung, liver and bone tissues

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Abstract: Breast cancer is the most common malignancy in women. The relatively high mortality rate in these patients is not due to initial tumors, but, rather, to process of metastasis, followed by formation of subsequent tumors at distant organs. Therefore, this study aimed to compare the microarray gene expression profiles of different tumors formed in the brain, liver, lung and bone tissues using bioinformatics tools to find the specific markers. Our findings showed that 9 brain-specific genes functioning as protectors of the fork replication complex as well as the positive regulators of topoisomerase, both active in the function of the tumor cells, showed increased expression in comparison with those expressed in liver, lungs and bone. Furthermore, 14 other brain-specific genes involved in regulation of cellular differentiation and tumor necrosis factors were expressed in lower levels. In this study, for the first time, Col2A1 gene, playing role in fetal skeletal connective tissue, reported to show increased expression in brain tumors subsequent to the breast cancer metastasis in comparison to those expressed in liver, lung and bone tissues. Data was extracted from the Gene Expression Omnibus database (GEO) with access number GSE14018 from the NCBI database. The database is comprised of a total of 36 expression profiles of metastatic breast cancer tumors to various organs, including 7 expression profiles to the brain, 8 to the bone, 5 to the liver as well as 16 to the lung (Barrett et al., 2013). The expression profile of 7 brain samples with those in 8 bone samples, 16 lung samples and 5 liver samples were compared using GEO2R software. Those genes with increased and decreased expression were extracted from all those commonly expressed in brain and other tissues. Finally, *Gene Ontology* Analysis was performed by DAVID and EnrichR tools (Huang da et al., 2009).The results of comparison of gene expression of metastatic tumors showed 53 and 140 genes with respectively increased and decreased expression in brain compared to the lung, as well as 72 and 215 genes with respectively increased and decreased expression in brain, in comparison to the liver and finally , 97 and 179 genes underwent respectively upregulation and downregulation in brain in relation to the those of bone. Together, among all overexpressed and downregulated genes, only 9 and 14 were respectively commonly expressed in the brain and the given tissue. Therefore, we investigated these genes with respect to Gene Ontology, suggesting embryonic skeletal joint morphogenesis and replication fork protection activities for the genes with increased expression, as well as functions in bone development and tumor necrosis factor-mediated signaling pathway for those with lower expression in the breast cancer metastasis tumor in the brain. Also, this study for the first time reported that of the commonly expressed genes in the brain and the bone, *COL2A1* (Collagen type II alpha1 chain), together with *LOC101928* show altered expression in brain tumors due to breast cancer metastasis.