ULBP2 is Differentially Expressed in Breast Cancer with High Expression Associated with PoorSurvival

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Introduction

Cancer cells frequently express a variety of natural killer (NK) group 2D ligands (NKG2DL) and these ligands have been found to be associated with the sensitization of tumor cells for killing by cytotoxic T lymphocytes and the NK cells. UL16 binding protein 2 (ULBP2) is a stress-induced NKG2DL and a cell surface protein that is differentially expressed in cancer cells. However, little is known about its expression and function in breast cancer (BC). Its expression was found to be controlled by a tumor suppressive microRNA (miRNA) miR-34a/c in cancer cells. In this study we explored the expression and prognostic significance of ULBP2 in relation to immune infiltrates as biomarker for BC. This study extensively analyzed the expression level, clinical significance, possible pathways and immune interaction of ULBP2 in BC using in silico approach.

Methods

The relative and differential ULBP2 expression in BC were evaluated using publicly available gene expression profile databases (Oncomine, GEPIA, and UALCAN) and the R2 Platform, respectively. Comprehensive survival analyses (PrognoScan and Kaplan-Meier analysis) were performed to assess the prognostic value of ULBP2 for BC patients. Protein partners were carried out by STRING and GeneMANIA plugin Cytoscape software. Integrated bioinformatics analyses such as copy number alterations (CNA), mutation analysis, gene ontology, immune infiltration, and signaling pathway were conducted to explore the mechanisms and biological roles underlying ULBP2 dysregulation in BC.

Results

ULBP2 mRNA was enriched in BC compared to normal tissues ($P<0.05$). In addition, overexpression of ULBP2 not only correlated with elevated P53, estrogen and progesterone receptor statuses, major BC subclasses and advanced histologic grade and stage, but also had an independent prognostic value for the poorer survival of BC patients ($P<0.05$). Expression of ULBP2 was associated with worse prognosis in BC patients. Gene expression of ULPB2 was significantly associated with NK cell infiltration. The gene ontology analysis of the protein partners of ULPB2 showed that they are membrane bound protein (CC) and are involved in NK cell mediated cytotoxicity (BP) and NK cell lectin-like receptor binding (MF). ULBP2 was also enriched in pathways such as integrin signaling pathway, glycolysis, cadherin, Wnt, and P53 signaling pathways among others.

Conclusion

These findings showed that ULBP2 might be a potential prognostic and an attractive therapeutic target for BC.

Keywords: ULBP2; Breast cancer; Biomarker; Gene expression; Prognosis.