

CBX2: A potential marker of HER2+ breast-to-brain metastasis

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Breast cancer Brain Metastases (BBM) represents a significant clinical challenge, with patients having a dismal 20% one-year survival. In the present study, we investigated the differential gene expression profile between tumor and normal samples by querying various public breast cancer cohorts, including TCGA BRCA, METABRIC, GSE11121, GSE17705, GSE12276 and CCLE. We compared the mean threshold in the breast cancer population, specifically in the ER+/HER2+ and TNBC, the more aggressive breast cancer subtypes. We further compared the expression levels across PAM50 subtypes to obtain unambiguous conclusions. The Kaplan-Meier (KM) analysis was performed to correlate overall survival curves based on gene expression data using the median as a threshold from TCGA and METABRIC breast carcinoma cohorts. Importantly, analysis done using TCGA-BRCA revealed elevated CBX2 mRNAseq gene expression in breast tumors than in normal tissue. Additionally, CBX2 mRNA seq expression showed a pattern of TNBC>HER2+>all tumor>ER+>normal tissue. Using Novartis/Broad Cancer Cell Line Encyclopedia (CCLE) for microarray and RNAseq gene expression profiling, we identified enhanced CBX2 mRNA expression in breast cancer cell lines compared to other cancer types. CBX2 mRNAseq expression was significantly greater among HER2+ (n=164) compared to normal (n=112) patients (FC=4.9; p=8.19e-36) and TNBC (n=115; FC=11, p-value=1.27e-6) from TCGA breast cancer cohort. Additionally, METABRIC cohorts also showed a significant correlation between higher CBX2 mRNA expression and poor overall survival outcome (Kaplan-Meier analysis, n=1904, p-value=0.0001). Thus, our investigation has identified CBX2 as a potential driver of HER2+ breast-to-brain metastasis and inhibition of CBX2 should be considered as a therapeutic target in breast-to-brain metastasis.

Biography

Rachana Garg, have been DoD postdoctoral fellow and Research Associate Scientist at the University of Pennsylvania, USA. Currently, she works as a Staff Scientist with City of Hope National Medical Centre, Duarte, California, USA. Her experience spans the field of cancer biology, neuroscience, clinical research, drug discovery, chemoprevention cellular and molecular biology, biochemistry, immunology, epigenetics. During her academic career, she has received multiple awards at international conferences and her research has been published in top journals: Cancer Research, Cell Reports, Oncogene, Carcinogenesis, Oncotarget, Journal of Biological Chemistry, Frontiers in Oncology, BBA Reviews in Cancer (1179 citations, H-index 14 & I-10 index 15). In addition to her passion and involvement in teaching, research and scholarship activities, she has mastered excellent communication, organizational and interpersonal skills.

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