

GENE EXPRESSION ANALYSIS FOR PREDICTION OF EARLY BRAIN METASTASIS (BM) IN HER-2 POSITIVE BREAST CANCER PATIENTS (PTS)

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Background: BM is a common occurrence in HER2+ breast cancer pts. If the pts most likely to develop BM could be identified, prophylactic strategies might prevent or delay occurrence of this failure. We explored gene expression differences between HER2+ breast cancers with early versus late occurrence of BM.

Methods: Study group included 90 HER2+ breast cancer pts, 43 of whom developed BM (BM+): 22 and 21 pts with ≤ 3 and > 3 yrs in time from diagnosis to BM, respectively; 47 patients had not developed BM (BM-) at the last follow-up. We performed cDNA-mediated annealing, selection, extension, and ligation (DASL) assay (Illumina Corp) for expression of 502 known cancer genes using 200 ng RNA from archived FFPE. T-test with unequal variances was applied after sample median normalization. Differentially expressed genes were analyzed using ingenuity pathway analysis.

Results: A binary comparison of BM+ versus BM- revealed 25 differentially expressed genes (p-value < 0.05). For BM+ in < 3 yrs versus > 3 yrs comparison, 95 genes were differentially expressed with a p-value < 0.05 . Upregulated gene pathways included glucocorticoid receptor, PI3K/AKT and PTEN, IGF-1, P53, and NF- κ B. Downregulated gene pathways were cell cycle G1/S checkpoint regulation, cell cycle G2/M DNA damage checkpoint, vitamin D, and retinoic acid receptor signaling.

Conclusions: Early BM occurrence in HER-2+ breast cancer pts can be predicted by gene expression in primary tumors. Altered cell cycle regulation seems to be particularly important. Analyses are ongoing to generate a gene expression signature to predict development of BM.

This work was supported by the U.S. Army Medical Research and Materiel Command under W81XWH-06-2-0033.