Fusion Genes as Drivers of Breast Metastasis

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Metastasis causes 100% of deaths from breast cancer, the most common cancer in women worldwide. Fusion genes, a combination of two genes due to genetic structural variation, are potential drivers of breast cancer metastasis. Fusion genes are known cancer initiators and effective therapeutic targets, yet their role in cancer progression is largely unknown. Breast cancer has one of the most structurally variant and unstable genomes of all cancers, due to the cell's defects in DNA repair mechanisms. Thus, it is hypothesized that fusion genes mediate breast cancer metastasis. RNA-seq data from patient-matched primary and metastatic breast cancer pairs (n=7) were acquired from The Cancer Genome Atlas (TCGA) to discover fusion genes not found in normal tissue that were preserved or acquired in metastatic disease. STAR (sequence alignment) and Salmon (transcript quantification) programs were used to align reads and check differential gene expression respectively, and a custom R-script curated the resulting fusions. This same pipeline was applied to breast cancer cell lines (n=78). The full list of cancer-specific fusions (n=400) was subset to metastatic-specific or preserved fusions present in both patient tumors and cell lines, resulting in a final set of seven fusions. The PREX1-CPNE1 fusion was selected for in vitro verification in a human metastatic breast cancer cell line since PREX1 is an RAC1 pathway mediator and implicated in metastasis/invasion. Future studies will focus on such fusion genes for metastatic phenotypes (i.e. invasion, migration) within in vitro models, as well as functionally characterizing this fusion.

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