SOX and MALAT1: Understanding the Progression of Breast Cancer Metastasis

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Metastatic breast cancer affects more than 250,000 people every year. Interactions of SOX transcription factors (TFs) and MALAT1 lncRNA may induce breast cancer metastasis. This study's purpose is to (1) quantify reductions in breast cancer tumor organoid size/metastasis following SOX and MALAT1 knockdown, (2) find MALAT1 regulation of SOX expression via direct MALAT1-SOX binding, and (3) quantify the increase in metastatic gene expression post SOX-MALAT1 binding. Triple-negative-MMTV-tumor-organoids were constructed in MatriGel with ASO-knockdowns of SOX and MALAT1. RT-PCR quantified SOX expression following MALAT1 knockdown to confirm MALAT1 regulation of SOX. RNA-pulldown-assay and western blot were used to confirm SOX-MALAT1 binding. RT-PCR was utilized to quantify β-catenin and Wnt gene expression following MALAT1-SOX reduction to confirm increase in metastatic genes post SOX-MALAT1 binding. Triple-negative-tumor-organoid metastasis was significantly reduced by 51%, 69%, and 71% following SOX9, SOX2, and SOX5 knockdowns respectively, and by 75% following MALAT1 knockdown, indicating key roles of both in metastatic progression ($p<0.05$). MALAT1 knockdown reduced SOX by 65-73% confirming MALAT1 regulation of SOX expression ($p<0.05$). Western blot analyses from the RNA pulldown assay presented SOX2, SOX5, and SOX9 expression indicating SOX-MALAT1 binding in MDA-MB-231, triple-negative cell line exhibiting 70% SOX expression. Decreasing SOX-MALAT1 binding reduced β-catenin and Wnt gene expression by 57% and 52%, respectively, confirming the role of SOX-MALAT1 binding in metastatic progression ($p<0.05$). Elucidating stimulators of MALAT1-SOX binding and methods to disrupt SOX-MALAT1 binding will allow for synthesis of novel therapeutics to treat breast cancer metastasis.

Awards Won:
Third Award of $1,000