Sorting Nexin 27, a Novel Target Gene to Prevent Tumor Metastasis in Highly Aggressive Breast Cancer Cells

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Sorting Nexin 27 (SNX27) belongs to a super family of sortin nexins which mediate protein-protein interaction in intracellular trafficking, membrane remodeling, organelle motility, tight junction formation and receptor recycling. However, its role in tumor metastasis and differentiation remains unknown. Epithelial-mesenchymal transition (EMT) is a cellular program that allows polarized, immotile epithelial cells to convert to motile mesenchymal cells in promoting carcinoma invasion and metastasis. I hypothesized that SNX27 regulates the EMT to affects tumor metastasis. I used a stable SNX27 knockdown (KO) clone in a highly aggressive breast cancer cell line MDA-MB-231. Wound healing data and a growth curve assay showed that SNX27-KO significantly decreased the cell motility and proliferation. Morphologically, SNX27-KO cells differentiated into round cells, whereas the parental cells had many spikes. Depletion of SNX27 also changed the extracellular matrix. This change made cells adhere together and move collectively and decreased cell motility. Western blots and immunostaining showed that SNX27-KO led to increased E-cadherin, ß-catenin, and F-actin protein expression, which facilitates the adhesion formation and inhibits EMT. Furthermore, the expression levels of Vimentin and slug, the critical transcription factors of EMT, were significantly diminished in the SNX27-KO cells. The data at morphological, translational, and transcriptional levels have demonstrated that SNX27 plays a crucial role in tumor cell metastasis and differentiation. SNX27 is a potential molecular target for controlling metastasis and inhibiting EMT, thus possibly turning malignant tumors into benign tumors.

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