The role of Fzd7 signalling in the epithelial-mesenchymal transition of cancer cells

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Video Byte

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Abstract

Epithelial-mesenchymal transition (EMT) is a cellular process critical to the spread of breast cancer. EMT leads to stem-cell like behavior, or stemness, and is largely responsible for distal lung metastasis. Many oncogenic pathways, including Fzd/Wnt-mediated pathways, contribute to this process. A new study explored the role of Fzd7 in EMT, stemness, and metastasis. Database searches found that Fzd7 expression was correlated with mesenchymal phenotypes and mesenchymal-associated genes. Fzd7 knockdown in vitro reduced the expression of mesenchymal-associated genes induced epithelial-like morphology and inhibited cell motility, impaired mammosphere formation, and decreased the Lgr5+ subpopulation. In mice, Fzd7 knockdown reduced lung metastasis of xenograft tumors while also delaying their formation and suppressing growth. To explore the mechanisms behind this, the researchers identified correlations between expression levels of Fzd7, Wnt5a/b, and Col6a1 in expression databases. In the laboratory, Fzd7 bound to Wnt5a/b and colocalized with Col6a1 and experimental alterations in Fzd7 expression led to parallel changes in Wnt5a/b and Col6a1 expression. Like Fzd7, Wnt5a/b and Col6a1 were associated with mesenchymal phenotype and stemness in silico and in vitro. These results demonstrate that Fzd7 contributes to EMT and stemness in breast cancer cells via a Wnt5b pathway mediated by Col6a1.