

Title: Role of Frizzled 7 in melanoma development and metastasis

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Scientific Abstract:

The frizzled (Fzd) family of proteins are 7-transmembrane G-protein coupled receptors (GPCRs) that transduce signals mainly for Wnt ligands. There are 10 Fzds identified in mammals, and they are involved in multiple cellular and biological functions via signaling through the canonical Wnt/beta-catenin, planar cell polarity, and calcium signaling pathways. Our previous work revealed a pro-metastasis role of Fzd6 in melanoma. This project focuses on Fzd7, a homolog of Fzd6, in melanoma. We found that *FZD7* is highly expressed in multiple melanoma cell lines. siRNA knockdown of *FZD7* does not affect cell proliferation but significantly reduces cell invasion in A375, Hs294T, and SK-MEL28 cells *in vitro*. To determine the *in vivo* role of Fzd7 in melanoma, we generated Fzd7 knockout YUMM1.7 cell lines for xenograft experiments using CRISPR. All three Fzd7 knockout clones showed a significant reduction in primary tumor growth when xenografted in C57BL/6 mice. To determine the potential mechanism of Fzd7 in melanoma growth and invasion, we performed bulk RNA-Seq on the YUMM1.7 knockout cell lines and identified 215 downregulated and 31 upregulated genes (with a fold change of 2, $p < 0.05$). We are in the process of confirming these transcriptional profile changes. Further functional analysis will be performed using gain- and loss-of-function approaches to determine the downstream mechanisms of Fzd7 in melanoma growth and invasion.

Written Lay Abstract:

In melanoma (skin cancer) cells, frizzled (FZD) proteins affect Wnt proteins, which impact how cancer cells grow and spread in the body. In humans and other mammals, there are 10 types of FZD proteins. Scientists have already found that FZD6 increases the spread of melanoma cancer.

In this study, the scientists looked at FZD7. They found that melanoma cells have a lot of FZD7. When the scientists changed cell DNA to remove FZD7, the melanoma cells still grew but did not spread as much. The scientists then changed mice DNA to remove FZD7 and found that these mice had smaller melanoma tumors. The scientists also studied the DNA of these mice and found over 200 genes (pieces of DNA) that are affected by FZD7.

This research tells us that the protein FZD7 may be important in stopping the growth and spread of melanoma. In future studies, the scientists will look more closely at how FZD7 proteins affect growth and spread of melanoma.

Visual Lay Abstract:



Research on Skin Cancer

What did we study?

Melanoma (skin cancer) cells have 10 types of frizzled proteins (FZD). We wanted to see how one of the proteins, FZD7, affects cancer. We studied FZD in cells in a lab and in mice.

What did we find?

Melanoma cells have a lot of FZD7 protein. FZD7 proteins may be increasing growth and spread of melanoma cancer.

What's next?

We will study how FZD7 proteins make melanoma grow and spread in the body.



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