A Humanized Monoclonal Antibody to Secreted Frizzled Related Protein-2 as a Targeted Therapy for Triple Negative Breast Cancer

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BACKGROUND: Secreted frizzled related protein-2 (SFRP2), a glycoprotein in the Wnt pathway, has shown increased expression in multiple tumor types, including breast cancer. SFRP2 expression has been linked to increased tumor growth and angiogenesis. We developed a humanized monoclonal antibody to SFRP2 (hSFRP2) and hypothesized that it would specifically target the tumor tissue and decrease tumor growth in triple negative breast cancer *in vivo*. We also hypothesized that hSFRP2 would decrease tumor growth in vitro in doxorubicin-resistant triple negative breast cancer.

METHODS: Nude mice were injected with MDA-MB-231 cells in the mammary fat pad and treated with either hSFRP2 mAb (n=10) or IgG1 control (n=9) via tail vein injection at 4 mg/kg for 11 weeks. Tumor volumes were measured every 3 days. *In vivo* Maestro imaging was used to evaluate the tissue biodistribution of NIR-conjugated hSFRP2 and IgG1 control over 72 hours after injection and in the organs after euthanasia, which was compared to non-tumor-bearing mice. MDA-MB-231 cells were cultured for increasing doxorubicin resistance to 10 µM and treated with either hSFRP2 mAb or IgG1 control for two hours.

RESULTS: At experiment endpoint, mice treated with hSFRP2 had significantly smaller tumor volumes ($p<0.001$) with a mean of 1159 mm^3 (95% CI 800-1519 mm^3) compared to 2998 mm^3 (95% CI 2619-3376 mm^3) in the IgG1 control. In the NIR-conjugated hSFRP2-treated mice, the fluorescence signal was highest in the tumor compared to all other organs. Doxorubicin-resistant MDA-MB-231 cells showed significantly increased apoptosis with hSFRP2 treatment compared to IgG1 ($p<0.0001$).

CONCLUSION: The biodistribution of hSFRP2 in a triple negative breast cancer model *in vivo* shows specificity for the tumor tissue and inhibits tumor growth *in vivo* and in doxorubicin-resistant cells identifying it to be a potential targeted therapeutic.