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Humanized Monoclonal Antibody to Secreted Frizzled-Related Protein 2 Inhibits Triple Negative Breast Cancer Metastases

Introduction:
A novel target for breast cancer is secreted frizzled-related protein 2 (SFRP2), which is anti-apoptotic and pro-angiogenic. We aim to evaluate SFRP2 protein prevalence in human TNBC and evaluate efficacy of hSFRP2 mAb in metastatic TNBC.

Methods:
A tissue microarray (87 cores) of human TNBC was stained with antibody to SFRP2 and quantified using spatial analysis. Results were analyzed as negative (0%); low positive (0-10%), positive (>10%). PY8119 or E0771 TNBC cells were injected intravenously into C57BL/6 female mice. Mice were treated with IgG1 or hSFRP2 mAb iv q3 days. After four weeks, lung surface metastases were counted. Differences were analyzed with Poisson distributions. FFPE sections of lungs were stained with ApopTag kit. Apoptotic cells were counted and differences analyzed with two-tailed T-test.

Results:
Of 87 TNBC cores, 83 cores were positive and 4 cores were low positive for SFRP2. For E0771 cells, surface metastasis counts were 8.9 ±2.8 in IgG1 treated and 4.9 ± 1.1 in hSFRP2 mAb treated group ($p<0.05$, n=15). The number of apoptotic cells/HPF was 9.8 ± 1.8 for controls and 21.0 ± 4.6 for hSFRP2 mAb group ($p<.01$, n=15 per group). For PY8119 cells, there were 6.4 ± 1.0 surface metastases in IgG1 treated and 3.6 ± 0.9 in hSFRP2 mAb treated group ($p<0.05$, n=11). The number of apoptotic cells/HPF was 6 ± 1.8 for IgG1 and 14 ± 1.3 for hSFRP2 mAb group ($p<0.001$, n=10).

Conclusions: SFRP2 protein is abundantly expressed in TNBC. hSFRP2 mAb reduces TNBC lung metastases and increases tumor apoptosis.