Using SUMO Proteases (SENPS) as a Potential Cancer Biomarker for Future Drug Therapies

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The small ubiquitin related modifier, SUMO, is a protein that is conjugated to other proteins through an enzymatic cascade of E1, E2, and E3 enzymes. SUMO can also be removed from proteins through the activity of SUMO proteases, called SENPs. Many cellular processes regulated by SUMOylation are essential for human cancers. Therefore, inhibitors of SUMOylation are being developed by drug companies to treat cancer. TAK-981 is one such drug currently in human clinical trials and inhibits the SUMO E1 enzyme. Interestingly, SENPs are often misregulated in human cancers. Therefore, we aim to test the hypothesis that cancer cells with higher levels of SENPs are more sensitive to TAK-981 compared to normal cells with lower levels of SENPs, and thus establish SENP expression as a biomarker for TAK-981 therapy. As a step towards testing our hypothesis, we conducted a bioinformatics analysis of cancer cell line mRNA expression data and identified naturally existing cancer cells with varying SENP expression levels. In future experiments, we will use these identified cancer cell lines to test our hypothesis that cells with higher levels of SENP expression will be more sensitive to TAK-981.

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