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Stable isotope resolved metabolomics to interrogate the interactions between stroma and desmoid tumors

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Desmoid tumors (DT) are locally invasive soft tissue growths with no directed therapies and high rates of recurrence. Spontaneous desmoid tumor are derived from *CTNNB1* mutations, primarily T41A and S45F variants of the β-catenin protein. Pancreatic tumors are like desmoid tumors, in that they consist of an abundance of desmoidic stromal tissue, are driven by mutations of K-ras, another Wnt protein, and accumulate β-catenin. It was described that the activated fibroblasts cells in pancreatic ductal adenocarcinoma (PDAC) release alanine to fuel the TCA cycle, rather than glucose and glutamine-derivatives, which therefore facilitates tumor survival and growth. It was our hypothesis that the desmoid tumor fibroblasts have altered metabolism similar to PDAC. We are using stable isotopic resolved metabolomics.

(SIRM) to better define the desmoid tumor and adjacent normal fibroblast metabolism through the TCA cycle, glycolysis, and the synthesis of non-essential amino acids. By using ^{13}C-labeled glucose and glutamine in cell media and a targeted panel by GC-MS, we are using primary cell lines from patient tumor and normal fibroblast to investigate metabolite concentration differences and isotopic flux through the energy metabolic pathways. We are starting to understand metabolite concentration and isotopic differences in T41A and matched normal fibroblast when incorporating these both ^{13}C glucose and glutamine and will be evaluating the differences between S45F and T41A cell lines next. It will be important to evaluate how TCA is fully functioning through citrate, pyruvate, and oxaloacate concentrations, in addition to the flux of ^{13}C isotopes from 13C glutamine for evidence of anapleortic flux.