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A Metabolomics Pilot Study on Desmoid Tumors and Novel Drug Candidates

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Abstract

Desmoid tumors (aggressive fibromatosis) are locally invasive soft tissue tumors that lack the ability to metastasize. There are no directed therapies or standard treatment plan, and chemotherapeutics, radiation, and surgery often have temporary effects. Most desmoid tumors are related to T41A and S45F mutations of the β-catenin encoding gene (*CTNNB1*). Using broad spectrum metabolomics, differences were investigated between paired normal fibroblast and desmoid tumor cells from affected patients. There were differences identified, also, in the metabolomics profiles associated with the two β-catenin mutations, T41A and S45F. Ongoing drug screening has identified currently available compounds which inhibited desmoid tumor cellular growth by more than 50% but did not affect normal fibroblast proliferation. Two drugs were investigated in this study, and Dasatinib and FAK Inhibitor 14 treatments resulted in unique metabolomics profiles for the normal fibroblast and desmoid tumor cells, in addition to the T41A and S45F. The biochemical pathways that differentiated the cell lines were aminoacyl-tRNA biosynthesis in mitochondria and cytoplasm and signal transduction amino acid-dependent mTORC1 activation. This study provides preliminary understanding of the metabolic differences of paired normal and desmoid tumors cells, their response to desmoid tumor therapeutics, and new pathways to target for therapy.