Scientific Abstract of Project

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"Using genome-scale CRISPR screening to create a Desmoid Tumor Dependency Map"

The success of cancer precision medicine is contingent on the ability to determine an optimal therapeutic strategy given the molecular classification of a patient's tumor. While desmoid tumors are relatively homogenous at the genomic level, we do not yet know to what extent this homogeneity induces dependency on a limited or an expansive number of cellular targets for survival and whether such targets are shared with other common cancers. Here, we hypothesize that desmoid tumors have a finite number of cellular dependencies and that a fraction of these are shared with other common cancers with active b-catenin signaling. We propose creating a pilot version of an experimental map of such dependencies in a manner that can be fully integrated with data emerging from common cancers to provide sufficient statistical power to prioritize dependencies driven by b-catenin mutations in desmoid tumors. To do this, we will perform genome-wide CRISPR/Cas9 viability screens and test over 6,100 existing therapeutics that have been developed for any human disease for evidence of desmoid tumor cell killing, with all data going into the public domain pre-publication to serve the entire desmoid tumor research community. This resource project will yield a reference map to nominate high priority targets for drug discovery, and may support the inclusion of desmoid tumors as inclusion criteria for ongoing clinical studies.