Abstract (lay version) of project

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

While some aspects of individual desmoid tumors are shared between patients, each tumor has unique molecular and clinical characteristics. This means that selecting the right therapies for future patients with desmoid tumors requires a special type of map. This map, which we call a "dependency map," would enable a clinician in the future to know therapy(ies) to prescribe based on the genetic characterization of that individual patient's tumor. In our project, we aim to produce freely available foundational resources and develop a pilot version of a desmoid tumor dependency map that the entire scientific community can use. We will first test a large number (>6,000) of existing drugs that might be repurposed for desmoid tumors. But, we hypothesize that the most promising future drugs for desmoid tumors likely don't yet exist. So, in our project we will focus on using new genetic tools, including a special type of molecular "scissors" called CRISPR/Cas9 to disable every gene in the genome in a systematic fashion and look for evidence of desmoid tumor cell killing in the laboratory. These experiments will prioritize the best targets to ensure drug companies know which targets to work on for desmoid tumors and ensure they include desmoid tumors in future drug discovery programs that might be focused otherwise on other tumor types. At the end of our project, we will complete (1) an inventory of nearly 20 desmoid tumor laboratory models that will be fully genomically characterized and available at a third-party distributor for all scientists to access, and (2) an initial prioritization of existing drugs and drug targets for desmoid tumors. This effort will help us understand what size and scale of a full Desmoid Tumor Dependency Map will ultimately be needed until we can make accurate dependency predictions for each patient.