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Title: "Progress Towards a Desmoid Tumor Dependency Map"

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Abstract:

The success of cancer precision medicine is predicated on the ability to interpret the molecular information of a given tumor with regards to its underlying dependencies. While learning from the patient experience is critical to this goal, an insufficient number and diversity of cancer therapies are currently in use to fully realize this goal solely from clinical information. A complementary approach is the use of large-scale, systematic laboratory efforts to grow cellular models from tumors and map their dependencies. To pilot this for Desmoid tumors, we are creating a Desmoid Tumor Dependency Map as a resource to be shared with the scientific community. We have demonstrated the success of empowering patients in the United States to directly donate their living tissue for the generation of cellular models. We have created novel long term desmoid cell lines that are being deposited at ATCC. We have used the first several lines to complete screening of the Broad Institute's Drug Repurposing library of 6,725 compounds and are in the process of completing technically challenging "all in one" subgenome CRISPR/Cas9 screens focused on 3,000 genes that had previously been observed as dependencies in the Cancer Dependency Map. We are now scaling up the creation of long-term models via systematic screening of culture conditions. To enable this, we have developed a multiplexed genomic monitoring solution to track tumor cell content across conditions and passages. We are also piloting imaging-based methods to utilize early, heterogeneous desmoid tumor tissues for target validation. In aggregate, these activities will soon produce cell models, drug screening data and CRISPR/Cas9 dependency data that the entire DTRF community can freely utilize to power future discoveries.