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Evaluating CD47 blockade as a potential immunotherapy for desmoid-type fibromatosis.

Abstract:
Desmoid-type fibromatosis (DTF) is a rare, low-grade, soft-tissue tumor affecting the extremities and the trunk. As DTF does not progress after diagnosis in most cases, no specific initial treatment is recommended. However, a minority of patients develops progressive DTF with debilitating and life-threatening complications. In these cases, therapies include chemotherapy, surgery, radiation, or targeted therapy. Immunotherapy either targets immune checkpoints, thereby increasing the efficiency of the adaptive immune system, or don't-eat-me signals, thereby enhancing the phagocytosis of tumor cells through the innate immune system. Though immunotherapy has significantly increased survival in a variety of cancers, it has not been explored in DTF yet. Therefore, we propose to investigate whether immunotherapy, more specifically blocking CD47 as a don't-eat-me-signal, as a potential therapy for DTF. To this end, we will first determine through ATAC Seq if CD47 and immune checkpoint regulatory proteins such as PDL1 are differentially regulated in DTF. Then, we will use a unique adaptive transfer model to explore whether CD47 blockade eliminates ectopic human DTF grafts under the kidney capsule of immunocompromised mice. These results will not only expand knowledge how don't-eat-me-signals and immune checkpoints are regulated in DTF but will also explore CD47 blockade as a new therapy for DTF.