Abstract (lay version) of project

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Single cell-derived clonal analysis of desmoid tumors to investigate tumor-stroma interactions

Tumor cells, which carry a mutation in their DNA,interact with the surrounding normal, non-mutant, "stromal" cells where the tumor arises. This interaction is of great clinical importance because it controls tumor progression and treatment response. Disrupting tumor-stromal interactions provides new avenues for targeted therapy as is now recognized in other cancers, such as breast and lung cancers. In desmoid tumors (DTs), it is difficult to distinguish the tumor cells from the normal cells because both populations are made of the same family of mesenchymal fibroblastic cells. In the past year, we analyzed several DT samples and found that the non-mutant population makes up an unexpectedly high percentage of the total tumor mass. We also developed a method to establish cell cultures from single cells, which allowed us to isolate the mutant DT cell populations and normal non-mutant cells from a heterogeneous mixture of cells originating from DT patient samples. We identified some key differences on the cell surface between the two groups that allowed us to improve the speed and sensitivity of our isolation methods. We hypothesize that the mutant cells interact with the normal cells, and that this interaction is important to maintain cell growth. In the past year, we identified a number of potential molecules as candidates for such cell-cell interaction. We tested one such factor, and we were successful at controlling the growth of DT cell populations by controlling its activity. We will test more secreted factors that mediate this two-way crosstalk. We will also study the role of direct cell-cell contact between DT cells and normal cells in modulating the neoplastic phenotype. Drugs that can disrupt tumor-stromal interactions will be tested on cell cultures from DT patients. This work will enhance our knowledge of DT biology, and identify novel treatment approaches for DTs.