

This abstract was submitted to the DTRF Research Workshop in September, 2018.

Gene expression profiling of desmoid tumors

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Desmoid tumors are proliferations of relatively benign appearing fibroblasts. Despite their histologic bland appearance, a significant subset of these tumors recurs aggressively and requires often debilitating surgery. Currently there are no molecular markers that predict the behavior of desmoid tumors.

We performed gene expression profiling of 70 archival desmoid tumor specimens to address several clinical issues of management of desmoid tumors: 1) to identify markers that could distinguish desmoid tumors that can be followed by “watchful waiting” at the time of their initial biopsy from tumors that require aggressive surgical therapy; 2) to identify markers that could be used in surgical pathology practice to distinguish scars from recurrent desmoid tumors; 3) to identify biological processes that may account for differences in clinical outcomes between patients with mesenteric vs. extremity location and between patients carrying different mutations in *CTNNB1* (T41A, S45F, S45P). We have also used our gene expression dataset to characterize immune cell infiltration in desmoid tumors. For the validation of gene expression results, we constructed new tissue microarrays composed of 92 archival desmoid tumor specimens.

We identified significantly differentially expressed genes between scars and recurrent desmoid tumors and between primary desmoid tumors carrying different mutations in gene encoding beta-catenin. We did not find significant differences in comparison of primary desmoid tumors that did and did not progress, and between tumors in mesenteric vs. extremity location. Deconvolution of immune cell signatures in desmoid tumors did not yield significant results.

We performed validation of selected findings from gene expression profiling by immunohistochemistry. For this purpose, we focused on genes implicated in Wnt signaling that may be differentially expressed scars and recurrent tumors, and between desmoid tumors carrying different mutations in *CTNNB1*. Unfortunately the available antibodies for NKD1, LCK, STK4, STK24, EGFR and ETS1 did not produce interpretable results on FFPE sections.

We have sampled multiple regions from primary/recurrent tumors to explore the molecular heterogeneity of desmoid tumors. We performed gene expression and DNA copy number profiling of 9 different regions from 2 patients and 7 regions from a third patient. RNA-seq results indicated molecular heterogeneity in these patients as reflected by differences in *CTNNB1* mutations between different areas of the tumors and differences in gene expression profiles between different regions of a single tumor specimen. The analysis of copy number changes in these specimens also indicated intra-tumor heterogeneity. These findings indicate significant molecular complexity within desmoid tumors.