Whole Exome Sequencing and Integrated Genomic Analysis of 'Wild-Type' Desmoids Identifies Potential Drivers of Tumor Initiation

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Traditional methods for analyzing mutations which are associated with desmoid tumors have identified abnormalities in the *CTNNB1* gene in approximately 85% of tumors; this alteration causes activation of Wnt/b-catenin signaling which is oncogenic. The current study shows no clear differences in outcome or in gene expression in tumors with and without *CTNNB1*mutation. Based on this finding, we sought to examine whether tumors without *CTNNB1*mutation were associated with genetic events that could dysregulated Wnt/b-catenin signaling in other ways. Using whole-exome sequencing (a more sensitive method of detecting mutations than traditional sequencing modalities) mutations were actually identified in approximately 95% of tumors. In the remaining 5% of lesions, genetic events which have the potential to activate Wnt signaling (the signaling pathway dysregulated as a result of *CTNNB1* mutation) are universally identified. For example, in a few samples, spontaneous changes in the *APC* gene were found. These results support the hypothesis that alteration of a common pathway causes tumor formation in all patients with desmoid fibromatosis and that a better understanding of this pathway may lead to new treatments for the disease.