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Understanding the S45F and T41A mutations in desmoid tumors- What is their significance?

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Ultimately, invasion and recurrence of desmoid tumor can be attributed to abnormal protein production which is in turn driven by regulatory gene mutations. The most commonly over-produced protein in desmoid tumors is □-Catenin, a protein that is important in transmitting growth signals in both normal and abnormal cells such as those that comprise desmoid tumors. There are only a small number of genetic mutations in *CTNNB1,* the gene which, when mutated, is responsible for B-Catenin over-production in desmoid tumors. Working with a large number of banked desmoid tumors retrieved from patients of known clinical outcome, it was possible to identify that one of the *CTNNB1* gene mutations, termed S45F, correlated with significantly increased rates of desmoid recurrence. This finding has now been confirmed in multiple studies world-wide.

In trying to determine why the S45F mutation appeared to be important as a possible driver of desmoid recurrence, we examined how different mutations of the *CTNNB1* gene might lead to different desmoid responses to therapies such as traditional chemotherapy (doxorubicin), radiation, and targeted therapies. It was possible to demonstrate that sensitivity versus resistance to some of these anti-desmoid therapies correlated strongly with the *CTNNB1* S45F gene mutational status. A possible implication of these studies, supported exclusively and extensi vely by the Desmoid Tumor Research Foundation, is that perhaps those patients whose desmoid tumors bear the S45F mutation should be considered for alternative multi-disciplinary therapies in addition to standard of care treatments.