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## **BRAF T1796A Mutations Are Absent in Desmoplastic Melanoma**

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### **Background:**

Desmoplastic melanoma is an uncommon variant of cutaneous melanoma that mimics soft tissue sarcoma both clinically and morphologically. An activating thymine adenine missense mutation at nucleotide 1796 (T1796A) of the BRAF oncogene has been identified in a high proportion of conventional cutaneous melanomas, but its frequency in the desmoplastic subtype is not known.

### **Design:**

We tested 57 conventional vertical growth phase melanomas and 12 desmoplastic melanomas for the BRAF T1796A mutation using a newly developed, mutation-specific primer extension technology (Mutector® assay). The assay is designed to detect rare BRAF alleles with the T1796A mutation in a background of wildtype alleles (as few as 1 mutant in 100 wild type are detected routinely). Only in the presence of a mutant allele does primer extension occur with the incorporation of biotinylated nucleotides. Wild-type alleles cause incorporation of a di-deoxy nucleotide and terminalation of extension. Biotinylated primers are then detected colorimetrically, and reported as an optical density with a spectrophotometer. The ME180 cell line (wild-type BRAF) and the HTB72 melanoma cell line (homozygous for BRAF T1796A) served as controls. A mutation is defined as  $OD(\text{sample})/OD(\text{negative control}) > 2$ .

### **Results:**

Using the Mutector® assay, BRAF mutations were detected in 23/57 conventional melanomas and 0/12 desmoplastic melanomas ( $p=0.0006$ ) with appropriate positive and negative controls.

### **Summary of Clinicopathologic Features and BRAF Status for Desmoplastic and Non-desmoplastic Melanomas**

Melanoma type	Site	Patients (n)	Mean age (yrs)	Caucasian (%)	Male : Female	Mean depth of invasion (mm)	BRAF mutation n (%)
Desmoplastic	Head and neck	11					0 (0)
	Trunk	1					0 (0)
	Total	12	54	100	6 : 6	14.1	0 (0) **
Non-desmoplastic	Head and neck	20					5 (25)
	Trunk	17					7 (41)
	Extremity	17					11 (65)
	Acral	3					0 (0)
	Total	57	59	91	30 : 27	3.1	23 (40)**

\*\*  $p = 0.0006$ , Fishers exact 2-tailed test

### **Conclusions:**

In contrast to conventional cutaneous melanomas, the desmoplastic variant does not harbor the highly prevalent T1796A activating mutation of BRAF. Mutations elsewhere in the BRAF gene constitute a small minority of the reported BRAF mutations found in various tumor types, including melanoma. It is, therefore, unlikely that other activating mutations in BRAF will be found in desmoplastic melanoma. Distinct genetic alterations may underlie well recognized clinical and morphologic differences among melanoma subtypes. Accordingly, patients with melanoma should not be regarded as a uniform group as new therapeutic strategies are developed that target specific genetic alterations.