

GENETICS

**MELANOMA—GRIN
AND TRAPP IT**

The genetic mutation rate in melanoma is much higher than in other solid tumors and hence, identifying recurring genetic alterations is crucial to generate targeted approaches to treat this disease. To this end, Yardena Samuels and her collaborators sequenced enriched exonic sequences (exome) of 14 DNA samples from metastatic melanoma and compared them with matched normal DNA to rule out those mutations that were not tumor specific.

Of all the mutations found, the researchers searched for those that occurred in two or more of the 14 samples. They found 10 mutated genes, including *BRAF*, which is commonly mutated in melanoma. One of the 10 genes, *TRAPP*—encoding for the transformation/transcription domain-associated protein—was found to be recurrently mutated in additional samples of melanoma. Knocking down *TRAPP* with short-hairpin RNA, induced cell death in melanoma cells that had mutations in *TRAPP*, showing that mutations in this gene are important for the survival of melanoma cells.

In a second analysis of the sequenced exome, the researchers identified 16 genes with more mutations than would be expected according to the general mutation rate in melanoma. From those 16 genes, *GRIN2A* was found to be mutated in six of the 14 samples. *GRIN2A* encodes a glutamate receptor subunit, so this finding could confirm a previously observed link between the glutamate pathway and cancer.

These results provide new clues about the biology of melanoma and new targets that may lead us to potential strategies to treat melanoma. “We plan to follow-up on our genetic data ... Clearly further genetic understanding is required and we therefore aim to perform additional exome captures as well as whole-genome sequencing to further decipher the melanoma genetic landscape”, concludes Samuels.

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Original article Wei, X. *et al.* Exome sequencing identifies *GRIN2A* as frequently mutated in melanoma. *Nat. Genet.* 43, 442–446 (2011)