SKIN CANCER

Novel mouse model reveals strategy to delay drug resistance in melanoma

Emergence of drug resistance in patients with *BRAF*-mutated melanoma is a major hurdle to the treatment success of targeted agents, such as vemurafenib. Martin McMahon, Darrin Stuart and colleagues have now developed a mouse model system that employs primary human cancer specimens to understand the consequences of drug resistance.

McMahon explains, “fragments of *BRAF*-mutated human melanomas were implanted into immunocompromised mice where they grew into large tumours, which were removed and serially propagated into additional mice.” Although the tumours initially regressed with vemurafenib treatment, the mice developed drug-resistant tumours after 100–200 days, as observed in human patients with melanoma. He continues, “thus, we provide a complementary model for understanding mechanisms of human drug sensitivity and resistance.”

The researchers showed that resistance to vemurafenib can be accompanied by tumour addiction to the drug, resulting in tumour shrinkage in response to drug cessation. Furthermore, “an intermittent drug-dosing regimen can be used to cause initial melanoma regression, but also to forestall the onset of drug resistance. Changing the dosing regimen of vemurafenib might allow patients to remain free of drug-resistant disease for a longer period of time.” The team plans to test whether intermittent dosing and the use of different agents during drug holidays will prevent drug resistance, enabling patient remission.

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