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Rapid review

Is there more than one road to melanoma?

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Context Sunlight is the main environmental cause of most cutaneous melanomas. Exposure to intense bursts of ultraviolet radiation, especially in childhood, starts the transformation of benign melanocytes into a malignant phenotype. Paradoxically, outdoor workers have a decreased risk of melanoma compared with indoor workers, suggesting that chronic sunlight exposure can have a protective effect. Further, some melanomas form on sun-exposed regions; others do not. Although some melanomas arise from pre-existing melanocytic naevi (moles), many arise de novo. These observations suggest that melanoma arises from multiple pathways, with initiating and promoting factors differing for each.

Starting point Janet Maldonado and colleagues recently studied the distribution of *BRAF* gene mutations in 115 patients with invasive primary melanomas (*J Natl Cancer Inst* 2003; **95:** 1878-80). These researchers found that *BRAF* mutations were statistically significantly more common in melanomas occurring on intermittently sun-exposed skin than elsewhere. By contrast, *BRAF* mutations in melanomas on chronically sun-damaged skin were rare. These findings strongly suggest that distinct genetic pathways lead to melanoma.

Where next? The study of gene-environment interactions is clearly the next arena for epidemiological research into melanoma. The recent identification of polymorphisms in the melanocortin-1 receptor could open up an avenue of investigation into a molecular distinction between those individuals whose melanomas arise on chronic sun-exposed skin from those in whom tumours will develop on sun-protected skin or from melanocytic naevi. If a dual pathway for melanoma is supported by other investigations, public-health messages can be tailored to the population at risk.

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