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Redhead pigment boosts skin-cancer risk

'Ginger' mice more susceptible to melanoma even without ultraviolet radiation.

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BAS CZERWINSKI/EPA/ALAMY

People with red hair are more susceptible to skin cancer — but it may not all be the fault of the sun.

Fair-skinned, red-haired folks know — sometimes through painful experience — that they are more susceptible to the damaging effects of the Sun's ultraviolet (UV) rays, including sunburn, skin ageing and a higher risk of skin cancers. But a study published today in *Nature*[1] suggests that in mice, the pigment responsible for this colouring has a role in the development of melanoma.

"There is something about the redhead genetic background that is behaving in a carcinogenic fashion, independent of UV," says David Fisher, a cancer biologist at Massachusetts General Hospital in Boston, who led the study. "It means that shielding from UV would not be enough."

Compared to people with darker skin, those with fair, freckly skin and red hair produce a different form of the pigment melanin. This red–yellow form, called pheomelanin, is less effective at protecting the skin from UV damage than the darker form, eumelanin. The difference is caused by a mutation in the gene *MC1R*[2].

But for a number of years there have been hints that UV exposure alone might not account entirely for the risk of melanoma in redheads. Fisher and his team wanted to investigate the molecular backdrop for this increased risk.

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The researchers looked at how melanomas develop in mouse models of olive-skinned, ginger and albino colouring. The last group had the same genetic background as the dark-skinned mice but lacked the enzyme needed to synthesize melanin. The researchers also tweaked each group's genes to be more susceptible to developing benign moles, which Fisher says is a probable first step in the development of melanoma.

No sunlight needed

The researchers planned to expose the mice to UV light and monitor differences in melanoma development. But before they got to that part of the experiment, about half the ginger mice had developed melanomas. Fisher says that he and his team were shocked. "The first thing we needed to do was bring a UV meter into the animal room to be sure there wasn't some inadvertent UV being radiated out of the light bulbs or something," he says. "And it turned out there was not."

Nature Podcast

David Fisher talks to the *Nature* Podcast about the new study.

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The result suggested that the pigment itself was a cause of melanoma. The researchers suggest that the increased melanoma risk could have something to do with the pigment-production process, or a by-product of it, in melanin-containing cells called melanocytes.

Eugene Healy, a clinical dermatologist at the University of Southampton, UK, says that although the mechanism is interesting, it is probably a less common trigger of melanoma than UV radiation. Indeed, in the UK, 8 out of 10 cases of melanoma are due to UV exposure. In humans, most melanomas develop on skin that sees the sun. "You almost never see melanoma, for example, on the buttocks," says Healy.

To complicate the picture, one of Healy's own studies, published in 2010, suggested that pheomelanin was protective against the effects of UV radiation in another type of skin cell, the keratinocyte[3].

The sun-safety message does not change because of the latest results. "UV is very tightly and convincingly linked to the formation of most non-melanoma types of skin cancer," Fisher says. "One of the most important messages from this is to avoid an assumption that this takes UV off the hook." It is possible that UV exposure worsens the carcinogenic mechanism of the red pigment, he adds.

Healy is keen to avoid alarming people with fair complexions. "Whatever risk was there, was always there. But we don't see lots of spontaneous melanomas in redheads. We shouldn't be sending out a worrying message for them."

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