

New study helps scientists understand melanoma development

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(Medical Xpress)—A new study by University of Kentucky researchers shows how a genetic defect in a specific hormonal pathway may make people more susceptible to developing melanoma, the deadliest type of skin cancer.

Fair-skinned people who tend to burn (rather than tan) from sun

exposure have a much higher risk for [melanoma](#) than darker-skinned people. On the surface, it appears that the amount of [melanin](#), the natural substance in the [skin](#) that determines pigment and acts as the skin's "natural sunscreen," would be the only determinant of melanoma risk. However, the truth is more complicated.

Published in *Molecular Cell*, the study looked at the role of the melanocortin1 receptor (MC1R), the receptor on melanocytes in the skin that gets called into action following ultraviolet exposure to help the skin lay down more UV-blocking melanin to protect itself. Fair-skinned people are more likely to inherit a defect in this receptor, and as a result, cannot make enough melanin to fully protect themselves from UV damage.

Since UV from sunlight or tanning beds is a major cause of melanoma, inherited problems in the MC1R means that the skin lacks natural protection by melanin, which acts as a biologic sunblock. This leads to more UV light chronically getting through to the sensitive layers of the epidermis, where it can contribute to cancer.

However, the UK study showed that MC1R defects contribute to melanoma development in ways other than [melanin production](#). Besides regulating the amount of melanin that gets made in the skin, MC1R also controls how well melanocytes can repair their DNA from UV damage. Having defects in MC1R signaling delays the body's ability to clear out existing DNA damage in the skin – leading to an increased potential for cancerous mutations.

"Knowing whether people have a specific genetic predisposition for melanoma could potentially save many lives", says Dr. John D'Orazio, Associate Professor and the Drury Pediatric Research Endowed Chair at UK's Markey Cancer Center. "If you happen to be born with a problem in this MC1R hormonal pathway, then you need to be extra careful with

respect to UV safety."

A good indication of a person's MC1R status is what happens to the skin after sun exposure.

"If you tan well, then your MC1R probably works well," D'Orazio said. "If you tend to burn, then you may have inherited a problem with your MC1R, and you probably should avoid purposeful UV exposure like tanning bed use or unprotected [sun exposure](#)."

D'Orazio and his research team found an important molecular link between MC1R signaling and DNA repair in their study. The team hopes to use this information to develop new melanoma-preventive treatments, like additives that can be included in sunblocks to ramp up the skin's ability to deal with UV damage.

Melanoma incidence has increased steadily over the past few decades – in the 1930s, an estimated one in every 1,500 Americans developed the diseases. Today, the odds are about one in every 60. Having a problem with the MC1R pathway raises a person's lifetime risk of melanoma about four-fold.

Provided by University of Kentucky

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