Researchers discover why redheads are more prone to melanoma

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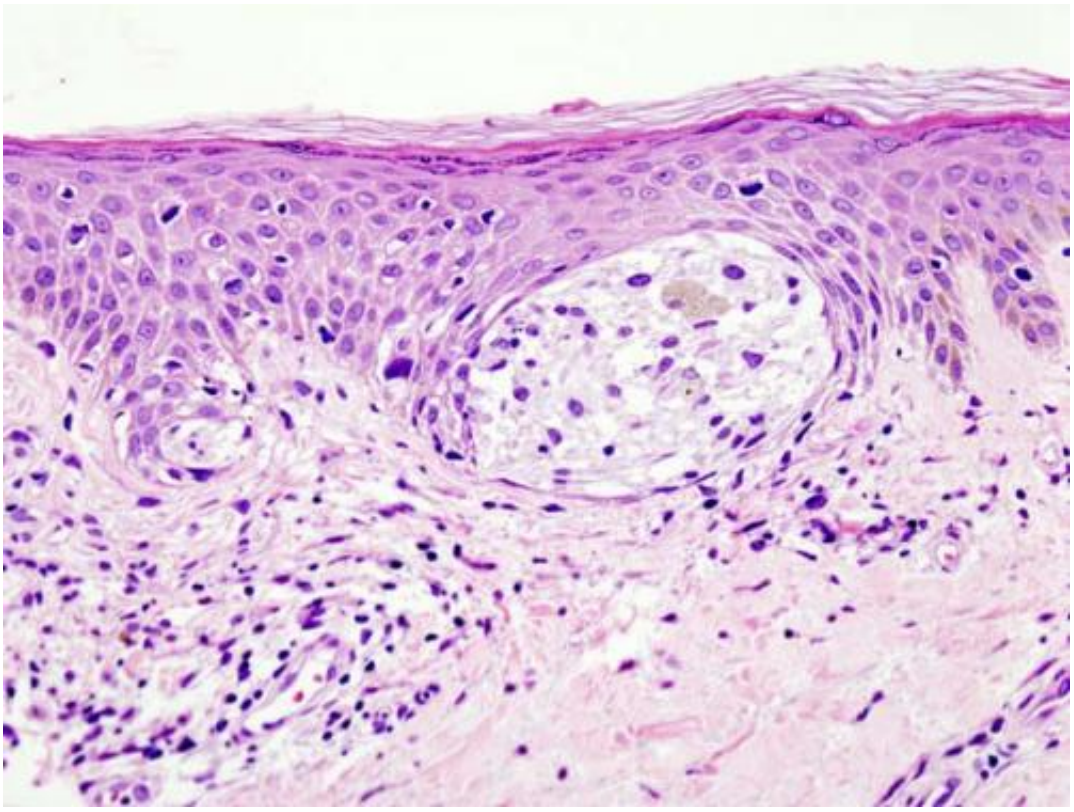

Melanoma in skin biopsy with H&E stain—this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

Red-haired people are known for pale skin, freckles, poor tanning ability and unfortunately, an increased risk for developing skin cancer. Research has shown that they have variants in Melanocortin 1 Receptor (MC1R), a protein crucial for pigmentation in humans, but how this

translates to increased risk for cancer and whether that risk can be reversed has remained an active area of investigation—until now.

For the first time, researchers from Boston University School of Medicine (BUSM) have shown that there is a way to reduce cancer risk in redheads. These findings appear in the journal *Nature*. Specifically they proved that MC1R, the protein involved in pigmentation, is affected by a special modification process called palmitoylation that is critical for its function. By enhancing palmitoylation in the variant MC1R proteins of redheads cancer risk can be reduced.

Making up one to two percent of the world's population, redheads carry variants of MC1R which are responsible for their characteristic features but also increases risk of skin cancers, the most dangerous of which is melanoma, a major public health concern with more than 3 million active cases in 2015. Much public health work has emphasized prevention by reducing sun exposure, particularly to DNA-damaging UV rays, but redheads bear a higher burden of disease making alternative risk reductions strategies an area of active interest.

"Up until now our understanding of the molecular biology of melanomagenesis (developing melanoma cancer) lacks explanations for how MC1R is affected by UV radiation, why redheads are more prone to melanoma, and whether the activity of red hair color variants could be restored for therapeutic benefit," explained corresponding author Rutao Cui, MD, PhD, professor of pharmacology and experimental therapeutics and professor of dermatology at BUSM.

In an experimental model, the researchers used a small molecule which could increase palmitoylation of MC1R named palmostatin B, and then exposed the model to UV light. The control group, without palmostatin B treatment, was also exposed to the UV light and showed a significant higher rate of developing melanoma. "These result suggest

pharmacological activation of palmitoylation prevents melanoma skin cancer in this particular model," said Cui.

According to the authors this study represents the first comprehensive analysis that stimulating palmitoylation can be used as a strategy to prevent disease. "We hope our study allows for the development of a pharmacological prevention strategy for red-headed people to protect their skin and let them enjoy the sun like other people.

More information: Shuyang Chen et al. Palmitoylation-dependent activation of MC1R prevents melanomagenesis, *Nature* (2017). DOI: 10.1038/nature23887

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