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## Why red-haired individuals are so prone to developing melanoma?

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Variants in the melanocortin-1-receptor (MC1R) gene, encoding a trimeric G protein-coupled receptor activated by  $\alpha$ -melanocyte-stimulating hormone ( $\alpha$ -MSH) are frequently associated with red or blonde hair, fair skin, freckling and skin sensitivity to ultraviolet (UV) light and several (RHC-variants) also associate with increased melanoma risk. However, not all of these associations have been attributed to phenotype, suggesting that some variants affect melanoma risk independent of phenotype. We have introduced MC1R loss-of-function mutations into the albino mice with complete absence of melanin and found that MC1R loss-of-function mutations augment UV-induced melanoma development in vivo, independent of their effects on pigmentation. For the additional roles of MC1R in melanoma development beyond pigmentation, MC1R controls UVB-induced G1-like cell cycle arrest and subsequent onset of premature senescence in melanocytes, abrogation of which contributes to melanoma development. Mechanistically, wt-MC1R stabilized PTEN against proteolytic degradation under UV exposure, resulting in inhibition of AKT phosphorylation and activation after UV exposure. These results provided a key insight into why red haired people are more likely to get melanoma and will potentially lead to the development of novel strategies and identification of therapeutic targets for melanoma toward developing targeted therapies in preventing and treating red-haired population suffering from melanoma.

### Biography

Rutao Cui is a Professor, Vice Chair of Pharmacology and Experiment Therapeutics, Professor of Dermatology and Director of Melanoma Biology, Boston University, USA. His studies were regarded as pioneer work in the research community and have been highlighted by various journals including Nature and Science and NIH Director, Dr. Francis Collins in his blog and also have been reported in different news including CBS news.

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