MC1R protects skin from UVB-radiation-induced cutaneous photoaging

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Introduction
Melanocytes are cells that produce melanin, the pigment that protects skin from ultraviolet radiation (UVR)-induced damage. There are two forms of melanin: eumelanin and pheomelanin. People who produce mostly eumelanin have darker hair and skin, and eumelanin protects individuals from UVR damage. People who produce mostly pheomelanin have lighter hair and skin, and pheomelanin does not protect skin from UVR. The type of melanin produced is dependent on whether the melanocortin-1 receptor (MC1R) is activated by α-melanocortin-stimulating hormone (α-MSH). If MC1R is activated, eumelanin is produced. If MC1R is not activated or is blocked, pheomelanin is produced. Variations of the MC1R gene affect the protein activity. Therefore, polymorphisms in the MC1R gene are responsible for the differences in hair and skin color between individuals. The MC1R gene variants associated with red hair, fair skin, and poor tanning ability are linked with higher risk of skin diseases such as melanoma.

Photoaging is the premature aging of skin due to damage caused by UVR exposure. One mechanism by which UVR causes photoaging is increasing the production of matrix metalloproteinases (MMP). MMPs build up and collagen production decreases, many of the physical manifestations of photoaging appear, such as wrinkles.

Methods
Mice: Expose mice to 1000 J/m² of UVB every 3 days for a week.

Evaluate macroscopic skin lesions for degree of roughness and scales
Assay epidermal thickness for epidermal hyperplasia
RT-qPCR analysis for expression of MMP-1 and collagen fibers in skin

Keratinocytes:
Activate MC1R in cells by applying a treatment of α-MSH
Expose treated cells and control cells to 100 J/m² of UVB radiation 24 hours
Perform RT-qPCR and assay MMP-1 and collagen levels

Figure 1: Wild type control mice and MC1R null mice have visible differences in pigmentation. Both were exposed to UVB radiation to assess the role of MC1R in preventing skin lesions and maintaining dermal strength and elasticity.

Results
Figure 2: MC1R null mice have thicker epidermal layers than wild type mice in UVB-induced photoaging. Dorsal skin from red haired mice (Tyr-Mc1r+/+) and wild type (Tyr-Mc1r+/+) mice were isolated after 3 weeks of UV radiation for H&E staining and histogram estimate for epidermal thickness, an important indicator of photoaging.

Figure 3: Quantitative data calculating the epidermal thickness. The skin of the red haired mice is around twice as thick as that of the wild type mice, indicating epidermal hyperplasia.

Figure 4: MMP-1 is downregulated by α-MSH induced activation of MC1R in HaCaT keratinocytes. The level of MMP-1, whose high levels cause the degradation of dermal collagen with UVR-induced photoaging, in HaCaT cells was assayed with RT-qPCR as indicated in methods.

Discussion
The results showed that MC1R protects skin from UVB-induced photoaging. The keratinocyte control group expressed twice as much MMP-1 as the α-MSH treatment-activated MC1R HaCaT keratinocytes, indicating they underwent much more collagen degradation. The control group also expressed significantly lower levels of COL1A1, the gene responsible for making type 1 collagen, indicating less collagen production. In summary, in the presence of UVR, functional MC1R plays an essential role in gene regulation to prevent photoaging and to maintain skin strength and elasticity.

Conclusions
- MC1R plays a crucial role in protecting skin against UVB-induced photoaging
- MC1R functions to ameliorate UVR-induced epidermal thickening
- Functional MC1R results in lower levels of collagen-degrading MMP-1
- Functional MC1R accelerates expression of genes that maintain skin strength and elasticity

Acknowledgements
I would like to thank the members of the Cui lab for their help, especially Dr. Rutao Cui, for allowing me to work in his lab, and Dr. Bo Zhu, for being my mentor.

I would also like to thank the BU RISE program for this wonderful opportunity.