Toward Development of a Preventive Strategy for UV-induced Sunburn and DNA Damage Based on Utilizing Selective MC1R Agonists

Julia Kiernan[1], Natalie Hone[1], Renny Starner[1], Viki Swope[1], Zalfa Abdel-Malek[1]
[1]Department of Dermatology; University of Cincinnati College of Medicine

Introduction

The *melanocortin-1 receptor* (*MC1R*) is an important regulator of human pigmentation and a melanoma susceptibility gene. The MC1R expressed on melanocytes regulates the tanning response and repair of DNA damage induced by solar ultraviolet radiation (UV). Developing small peptide analogs of the physiological MC1R agonist α-melanocyte stimulating hormone (α-MSH) that are highly selective for this receptor should provide photoprotection by minimizing the short-term (sunburn) and long-term (skin cancer) effects of sun exposure.

Hypothesis

The highly selective α-MSH analogs, the tetrapeptide LK467 and the tripeptide LK 514, are effective in reducing the induction and enhancing the repair of UV-induced DNA photoproducts.

Aim

To measure the effects of LK 467 and LK514 on cyclobutane pyrimidine dimers (CPD), the major form of DNA photoproducts induced by UV, in human epidermis and melanocytes.

Methods

Human skin (neonatal foreskins) explants were dissected to include control untreated, analog-treated (5 daily treatments), UV-exposed, analog-treated (daily treatments 3 days prior to, and 2 days post UV) and UV-exposed groups. The skin sections were fixed 2 h and 48 h post UV, and immunostained for CPD. Sections were examined by fluorescence microscopy. Photographs were acquired for image analysis using Image J software to quantify CPD in the total epidermis and in melanocytes that were co-stained for the melanocytic marker TRP-1.

Results

Treatment with 1 nM LK 467 resulted in statistically significant reduction in CPD 48 h post UV in the epidermis and in melanocytes, without altering the induction of CPD immediately after UV. However, treatment with 1 µM LK 514 did not have any effect on either induction or repair of CPD.

Conclusions

LK 467 at 1 nM enhances CPD repair in melanocytes and keratinocytes of human epidermis. LK 514 at 1 µM had no effect on CPD in the epidermis, including melanocytes.

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