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Photoprotective effect of SKPs on skin photodamage in Balb/c hairless mice

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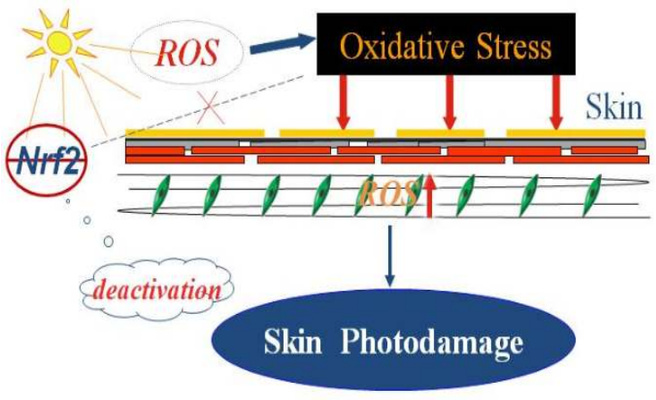
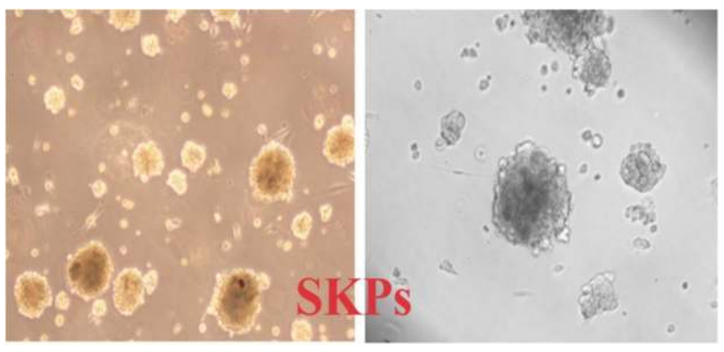
INTRODUCTION

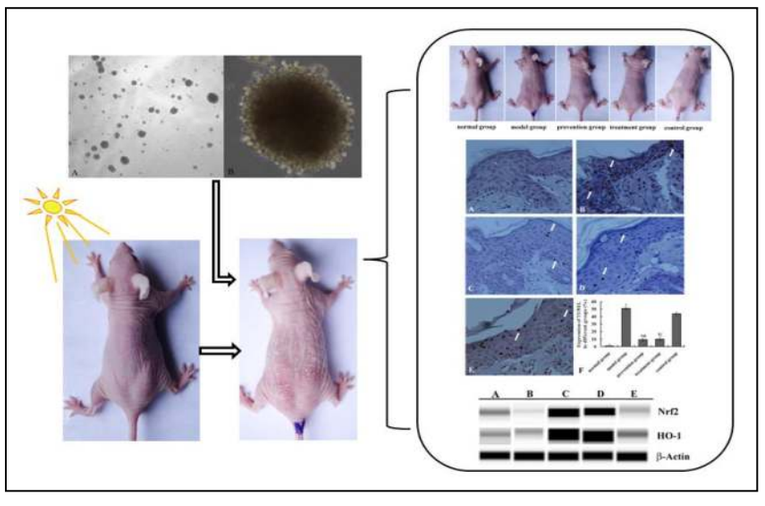
Skin photodamage a special damage in skin, is characterized by erythema, edema, dyspigmentation, sallowness, fine and coarse wrinkles, telangiectasia, and roughness . At present, it is considered that UV-induced reactive oxygen species (ROS) generation and NF-E2-related factor 2 (Nrf2) inactivation are involved in skin photodamage. The activation of the transcription factor Nrf2 plays a critical regulatory role in protecting cells against UV insult and reducing photo-oxidative damage.



Skin-derived precursor cells (SKPs), a population of dermal stem cells, are considered to be involved in wound repair and skin regeneration through the activation of Nrf2. Moreover, our previous in vitro study revealed that SKPs have a powerful ability to resist UV-induced apoptosis and DNA damage through the activation of Nrf2. However, no reports concentrate on the treatment of skin photodamage with SKPs. Therefore, it is hypothesized that SKPs may represent a promising strategy for skin photodamage.



GRAPHICAL ABSTRACT



OBJECTIVE

To investigate the photoprotective role of SKPs in UV-induced photodamaged mice.

METHODS

Mice were divided into five groups: normal group, model group, prevention group, treatment group and control group. The latter four groups were exposed to a two-week UVA+UVB irradiation. Mice in the prevention group received weekly SKPs injections for 2 weeks before irradiation, while those in the last two groups respectively received a two-time injection of SKPs and Hanks after irradiation. One week after final intervention, skin appearance, pathological alterations and oxidative indicators were evaluated by ELISA, immunohistochemical analysis and western blotting.

RESULTS

1. SKPs reversed mice photodamaged skin.

After irradiation, lesions appeared as erythema, edema, scales and wrinkles on mice dorsal skin; however, these were significantly ameliorated by subcutaneous SKP injection.

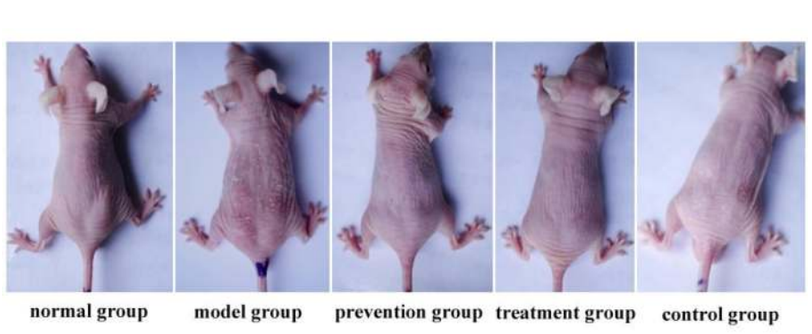


Fig. 1. Skin visual manifestation and scores of hairless mice in different groups. Visual changes in the skin of the hairless mice in the different groups (normal group, model group, prevention group, treatment group, and control group) after the 2-week irradiation period or SKP/HANKs injection.

2. SKPs alleviated UV-induced skin histopathological changes.

Hyperkeratosis, acanthosis, and spongiosis in the epidermis, as well as dermal papillae edema and inflammatory cell infiltration, were observed in both model and control groups; however, these conditions could be resolved with SKPs.

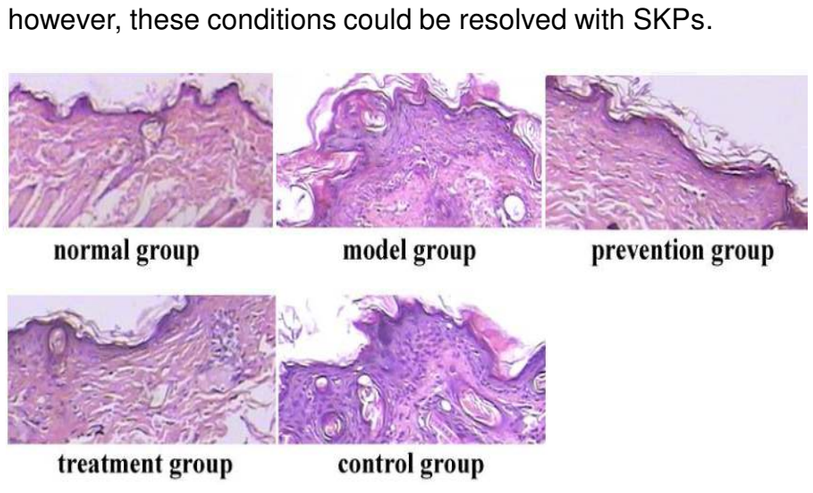


Fig. 2. Figure 4. SKP treatment improved UV-induced skin histopathological alterations. Skin sections from different groups were stained with H&E (× 100).

3. SKP treatment reduced UV-induced cutaneous apoptosis.

TUNEL-positive cells in the normal group were scarce; but UV irradiation remarkably enhanced the appearance of TUNEL-positive cells in the model group and control group. This phenomenon, however, was reversed with SKP injection.

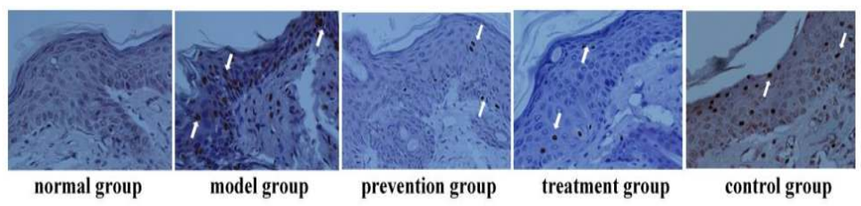


Fig.3. Effects of SKPs on UV-induced apoptosis in skin by TUNEL staining. Immunohistochemical analysis of TUNEL-positive (TUNEL+) cell expression in five groups (magnification × 400).

4. SKPs ameliorated photo-oxidative stress in mice skin.

UV irradiation, on the one hand, lowered the activities Nrf2, HO-1, GPX, SOD, CAT and GSH; on the other, enhanced the levels of ROS, MDA, and H2O2. On the contrary, SKPs injection overthrew these phenomena, whereas Hanks worked ineffectively.

5. SKPs upregulated Nrf2 and HO-1 expressions in mice photodamaged skin.

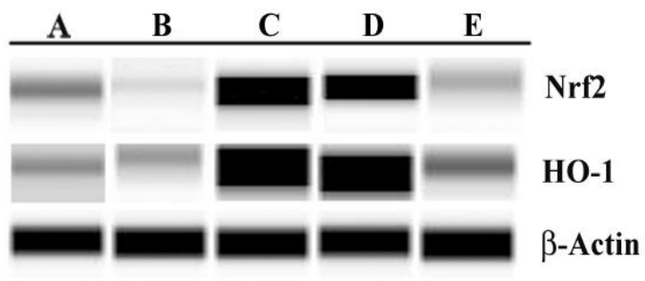


Fig.4. Western blot analysis in SKPs for Nrf2 and HO-1 expression. A, normal group; B, model group; C, prevention group; D, treatment group; E, control group.

CONCLUSIONS

Our study firstly uncovered the protection of SKPs against UV-induced damage in the skin of hairless mice. It is suggested that SKPs have the potential to control photodamage through the activation of Nrf2 and its associated pathway, and by scavenging ROS and preventing OS. Future in vitro studies to further clarify the photoprotective role of SKPs are warranted.

ACKNOWLEDGEMENTS

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