PHOTOBIOLOGY AND PHOTOPROTECTION

NRF2 OVEREXPRESSING SKIN-DERIVED PRECURSORS AGAINST UV-INDUCED DAMAGE IN A THREE-DIMENSIONAL MODEL

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Introduction: Skin photodamage involves ultraviolet (UV)-induced reactive oxygen species (ROS) overproduction and NF-E2-related factor 2 (Nrf2) inactivation. In our previous study, skin-derived precursors (SKPs) were shown to ameliorate a UV-induced damage in mice, probably via the Nrf2 activation and ROS scavenging.

Objective: To clarify the mechanism of SKPs against UV-induced damage in a three-dimensional (3D) skin model.

Materials and Methods: SKPs nrf2 gene was modified using lentiviral infection, and 3D skin models were reconstructed with keratinocytes and fibroblasts based on type I collagen. Subsequently, these models were divided into 6 groups: normal group, irradiated group, overexpressed group, control group, silenced group and negative control group. Before irradiation, respective SKPs were injected into the last four groups. Then, all groups except the normal group were exposed to UVA + UVB. Finally, the parameters were determined by the pathological and molecular-biological techniques.

Results: Normal 3D skin models looked like milky white analogs with a clear, well-arranged histopathological structure. After the skin was exposed to irradiation, it exhibited cell-swelling, disorganized structure, and developed a nuclear-concentration with many apoptotic cells. The expressions of cellular protective genes and Nrf2/HO-1/PI3K/Akt proteins remarkably decreased, which was accompanied by an increase in oxides and decrease in antioxidants ($P < 0.05$). However, these phenomena were reversed by nrf2-overexpressed SKPs. The 3D skin in the overexpressed group showed mild swelling, neatly-arranged cells, and few apoptotic cells. Cellular protective genes and Nrf2/HO-1/PI3K/Akt proteins were highly expressed, and the oxidative biomarkers were remarkably ameliorated ($P < 0.05$).

Conclusions: It is indicated that Nrf2 is crucial for protection of SKPs against UV-mediated damage through the activation of the Nrf2/HO-1/PI3K/Akt pathway.