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Photobiomodulation of blue light irradiation on human keratinocytes, fibroblasts, and endothelial cells involved in wound healing and angiogenesis

Autor: Jingbo Shao
Institut / Klinik: Chirurgische Klinik
Doktorvater: Priv.-Doz. Dr. P. Téoule

Background: Blue light irradiation (BLI) has been widely reported to induce photobiomodulation (PBM) across different cell types. Based on the experimental basis reported, we further investigate its effects on cell types involved in wound healing and angiogenesis, with various light doses at continuous irradiation mode.
Methods: In terms of short-term (from 0 to 2 h) irradiation , cellular responses of immortalized human keratinocytes (HaCaTs), normal human dermal fibroblasts (NHDFs), and human umbilical vein endothelial cells (HUVECs) after light treatment at 450 nm were analyzed by kinetic assays on cell viability, proliferation, ATP quantification, migration assay, and apoptosis assay. The level of gene expression and potential mechanisms of photobiomodulation were analyzed by transcriptomic and bioinformatic analyses. Additionally, cellular responses after long-term irradiation, which was over 2 h, and sequential light treatments with irradiance at 23 and 10 mW/cm^2 were investigated by XTT and ATP. Moreover, more influencing factors were assessed by comparison of cell viability after altering cell culture conditions, including medium irradiation, medium refreshment, and the existence of phenol red.
Results: A biphasic effect was observed on HaCaTs, NHDFs, and HUVECs. 4.5 J/cm^2 irradiation stimulated cell viability, proliferation, and migration. mRNA sequencing indicated involvement of transforming growth factor beta (TGF-β), ErbB, and vascular endothelial growth factor (VEGF) pathways after the low-fuence irradiation. High-fluence (18 J/cm^2) irradiation inhibited these cellular activities by downregulating DNA replication, the cell cycle, and mismatch repair pathways. The biological effect of 4.5 J/cm^2 were further verified to stimulate cell lines after 2 h irradiation at an irradiance of 23 mW/cm^2 by XTT and ATP quantification. However, after extending the corresponding irradiation time up to 5 h, cell viability decreased continuously. Irradiation only on medium could induce changes in cell viability, and medium refreshment after irradiation could eliminate the changes in cell viability. No significant difference was observed in cell viability after irradiation on phenol red and phenol red-free medium.
Conclusions: (1) HaCaTs, NHDFs, and HUVECs exhibited a dose-dependent pattern after BLI. Meanwhile, cell-type-specific responses followed by BLI were obvious. These findings broaden the view of PBM following BL irradiation of these three cell types, thereby promoting their potential application in wound healing and angiogenesis. Our data on low-fluence BLI at 450 nm indicates clinical potential for a novel modality in wound therapy. (2) Overexposure under BLI not only led to severe inhibitions on cell growth but also ended up with cytotoxicity after longer time of irradiation. (3) The interaction between photons and components of the medium (riboflavin) potentially caused photosensitization, which resulted in the generation of reactive oxygen species (ROS) and influenced cellular responses.