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Proteomic Analysis Reveals Anti-Fibrotic Effects of Blue Light Photobiomodulation on Fibroblasts

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Background and Objectives: This study was aimed at determining the effects of blue light photobiomodulation on primary adult mouse dermal fibroblasts (AMDFs) and the associated signaling pathways.

Study Design/Materials and Methods: Cultured AMDFs from adult C57BL/6 mice were irradiated by blue light from a light-emitting diode (wavelength = 463 ± 50 nm; irradiance = 5 mW/cm^2; energy density = 4–8 J/cm^2). The cells were analyzed using mass spectrometry for proteomics/phosphoproteomics, AlamarBlue assay for mitochondrial activity, time-lapse video for cell migration, quantitative polymerase chain reaction for gene expression, and immunofluorescence for protein expression.

Results: Proteomic/phosphoproteomic analysis showed inhibition of extracellular signal-regulated kinases/mammalian target of rapamycin and casein kinase 2 pathways, cell motility-related networks, and multiple metabolic processes, including carbon metabolism, biosynthesis of amino acid, glycolysis/gluconeogenesis, and the pentose phosphate pathway. Functional analysis demonstrated inhibition of mitochondrial activities, cell migration, and mitosis. Expression of growth promoting insulin-like growth factor 1 and fibrosis-related genes, including transforming growth factor β1 (TGFβ1) and collagen type 1 α2 chain diminished. Protein expression of α-smooth muscle actin, an important regulator of myofibroblast functions, was also suppressed.

Conclusions: Low-level blue light exerted suppressive effects on AMDFs, including suppression of mitochondrial activity, metabolism, cell motility, proliferation, TGFβ1 levels, and collagen I production. Low-level blue light can be a potential treatment for the prevention and reduction of tissue fibrosis, such as hypertrophic scar and keloids. Lasers Surg. Med. © 2019 Wiley Periodicals, Inc.

Key words: blue light; fibrosis; photobiomodulation; low-level light therapy; fibroblast; proteomics; phosphoproteomics

INTRODUCTION

Photobiomodulation (PBM), also known as low-level light therapy (LLLT), employs low-power light source (usually below 500 mW) irradiation to induce biological effects [1]. Different from intense light treatment that heats the treated tissue, PBM is not mediated by a thermal effect on cells [1]. PBM, especially using a red light source, has also been shown to stimulate hepatocyte proliferation and metabolism [2,3], fibroblast proliferation, and wound healing [4]. On the other hand, red light PBM has been widely demonstrated to be beneficial for osteoarthritis [5], pain control [5], chemotherapy adverse effect management [6], and wound healing in animal models or human trials [7]. Although the underlying mechanisms of red light PBM are not well understood, it had been postulated that mitochondrial cytochrome c oxidase (COX) is activated due to its preferential absorption of red light [1], and the increased COX activity leads to increase of adenosine triphosphates (ATPs), cyclic adenosine monophosphates (cAMPs), mitochondrial membrane potential, nitric oxide (NO), and calcium ion concentration [1,8]. ATPs and cAMPs participate in G-protein-coupled receptor signaling pathways and activate the downstream cAMP-dependent

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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