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Umbilical Cord Mesenchymal Stem Cell-Derived Exosomes Ameliorate HaCaT Cell Photo-Aging

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Abstract

Umbilical cord mesenchymal stem cells (UCMSCs) have been identified as a potentially ideal cell type for use in regenerative therapeutic contexts owing to their excellent paracrine secretory abilities and other desirable properties. Previous work has shown that stem cell-derived exosomes can effectively reduce skin aging, but few studies have specifically focused on the role of UCMSC-derived exosomes in this context. In this study, we isolated exosomes derived from UCMSCs grown in a three-dimensional culture system and explored their ability to modulate the photo-aging of HaCaT keratinocytes. Cell viability and proliferation were assessed using CCK8 assay, whereas wound healing and transwell assays were used to assess cell migratory capabilities. UVB irradiation (60 mJ/cm^2) was used to induce photo-aging of HaCaT cells. TUNEL and SA-β-Gal staining were used to explore HaCaT cell apoptosis and senescence, respectively, whereas real-time quantitative PCR was used to assess the expression of relevant genes at the mRNA level. We found that UCMSC-derived exosomes were able to enhance normal HaCaT cell proliferation and migration while also inhibiting UVB-induced damage to these cells. These exosomes also reduced HaCaT cell apoptosis and senescence, increasing collagen type I expression and reducing matrix metalloproteinase (MMP1) expression in photo-aged HaCaT cells. Together, these findings indicate that UCMSC-derived exosomes have the potential to be used therapeutically to suppress skin aging.

Keywords: umbilical cord mesenchymal stem cells, exosomes, photo aging, keratinocytes

Introduction

The aging of skin occurs owing to a confluence of exogenous and endogenous aging process, with chronological- and photo-aging being primary drivers of these process.[1] Intrinsic chronological aging at present is inevitable and results from genetic and physiological processes, whereas extrinsic aging leads to the development of morphological changes such as reduced skin elasticity, increased skin roughness, and the development of wrinkles. This process is characterized by reductions in basal collagen type IV and collagen type VII levels in the skin as a consequence of environmental exposure to pollution, smoke, or ultraviolet (UV) radiation.[2] UV radiation derived from sunlight exposure is the primary driver of photo-aging, with UVA (320–400 nm), UVB (280–320 nm), and UVC (200–280 nm) forms of radiation all contributing to this process.[3] As UVB and UVC radiation can easily penetrate the atmosphere of the Earth, they are the primary drivers of epidermal damage and associated skin damage.

UVB rays are important for facilitating antimicrobial peptide production and vitamin D absorption, but as they are more energetic than UVA rays they are better able to induce DNA damage in epidermal cells.[4] UVA radiation can, in contrast, penetrate to deeper layers of the dermis and cause photo-aging over extended periods of exposure. The keratinocytes composing of the epidermis serve as a barrier that prevents environmental pathogens and irritants from entering into the body. These cells are organized in the form of a stratified squamous epithelium, with keratinocyte stratum corneum formation being important for protecting against extrinsic damage.[5] Absorption of light by

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