MicroRNA in Skin Regeneration

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MicroRNAs (miRNAs) have emerged as pivotal regulators of cellular processes, including fibroblast senescence, which is a critical factor in skin regeneration and wound healing.

Fibroblast senescence is characterized by a decline in cellular function and an increase in pro-inflammatory cytokine secretion, contributing to chronic wounds and impaired healing.

This literature review focuses on specific miRNAs that target fibroblast senescence, elucidating their mechanisms and potential therapeutic applications.

One of the most studied miRNAs in the context of fibroblast senescence is miR-29a.

Research by Yuan et al. demonstrated that miR-29a significantly inhibits fibroblast proliferation, migration, and collagen deposition following skin thermal injury.

This miRNA promotes the repair of denatured dermis by modulating the TGF-β2/Smad3 signaling pathway, which is crucial for fibroblast activation and extracellular matrix remodeling Yuan et al. (2021).

Additionally, exosomes derived from miR-29a-modified adipose-derived mesenchymal stem cells (ADSCs) have been shown to reduce excessive scar formation, further highlighting the role of miR-29a in regulating fibroblast behavior and senescence (Fang et al., 2016). Another important miRNA is miR-93-3p, which has been implicated in promoting wound healing by downregulating apoptotic peptidase activating factor 1 (APAF1) in fibroblasts.

Shen et al. found that exosomal miR-93-3p secreted by bone marrow mesenchymal stem cells enhances fibroblast survival and function, thereby mitigating the effects of cellular senescence (Shen et al., 2021). This suggests that miR-93-3p may serve as a therapeutic target to rejuvenate senescent fibroblasts and improve skin regeneration.
Moreover, miR-372-3p and miR-371a-3p have been identified as having anti-senescence effects in fibroblasts.

Casado-Díaz et al. noted that these miRNAs, when enriched in extracellular vesicles, can potentially treat skin ulcers associated with aging and other diseases (Casado-Díaz et al., 2020).

Their ability to modulate senescence pathways indicates a promising avenue for enhancing fibroblast function in regenerative medicine.

The role of exosomal miRNAs in fibroblast senescence is further supported by findings from Kim et al., who reported that senescent dermal fibroblasts release more exosomes than their proliferating counterparts.

These exosomes are part of the senescence-associated secretory phenotype (SASP), which can exacerbate aging and impair tissue regeneration (Kim et al., 2021).
Thus, targeting the miRNAs within these exosomes could provide a novel strategy to counteract the detrimental effects of senescence in fibroblasts.

In addition to these specific miRNAs, the broader context of miRNA modulation in fibroblast senescence is underscored by the work of Nanić et al., who explored the potential of cell micro-transplantation to enhance skin wound healing.

Their findings suggest that manipulating miRNA expression in fibroblasts can improve their regenerative capabilities, particularly in the context of aging and chronic wounds (Nanić et al., 2022). In conclusion, miRNAs such as miR-29a, miR-93-3p, and miR-372-3p play significant roles in targeting fibroblast senescence and enhancing skin regeneration.

The therapeutic potential of these miRNAs, particularly through the use of exosomes derived from stem cells, offers a promising strategy for improving wound healing outcomes in aging and pathological conditions.

Future research should focus on elucidating the precise mechanisms by which these miRNAs regulate fibroblast function and exploring their clinical applications in regenerative medicine.

Micro RNA and Fibroblast senescence

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