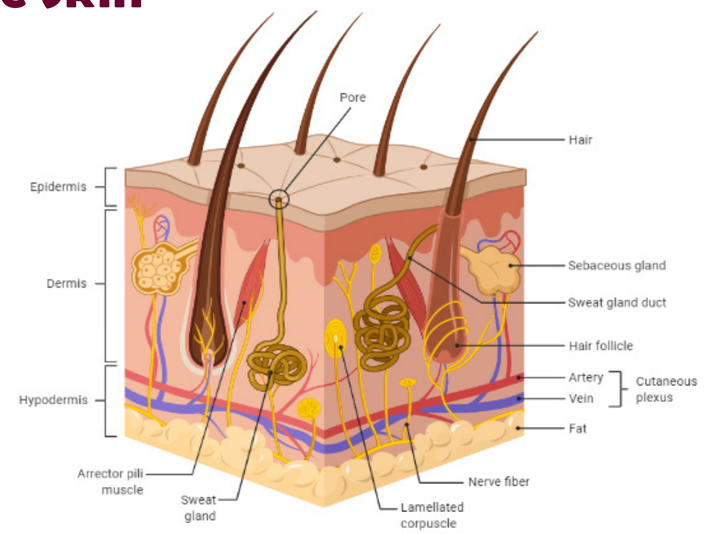
SCARLESS CUTANEOUS (SKIN) WOUND REPAIR

Promoting by Mesenchymal Stem Cell-Exosome therapy

The skin is frequently damaged as a result of acute and chronic wound such as extensive burns, trauma, or diabetic ulcers. Serious wound conditions not only result in unsightly appearance, but also can bring many complications to patients, that may danger to their lives.

The Skin



Skin is the external tissue barrier that acts as the first body protection line to block the entry of microbes and inflammatory particles into human bodies. Skin is composed of 3 layers: **epidermis, dermis, and subcutaneous layer (hypodermis)**.

Poor Wound Healing

Poor wound healing at the injury site, especially in an exposed site, is associated with *an unappealing esthetic appearance* in patients and also results in:

- **Bad Skin Barrier**
- **Tissue Infection & Necrosis**
- **Loss of Main Function in Extreme Cases**
- **Other Serious Local or Systemic Consequences**

REFERENCES

i). Hu, P.... & Chiarini, A. (2019). Mesenchymal stromal cells-exosomes: a promising cell-free therapeutic tool for wound healing and cutaneous regeneration. Burns & trauma, 7. ii) Qiu, H....& Wang, H. (2020). Prospective application of exosomes derived from adipose-derived stem cells in skin wound healing: A review. Journal of cosmetic dermatology, 19(3), 574-581. iii) Goodarzi, P.... & Arjmand, B. (2018). Mesenchymal stem cells-derived exosomes for wound regeneration. Cell Biology and Translational Medicine, Volume 4, 119-131.

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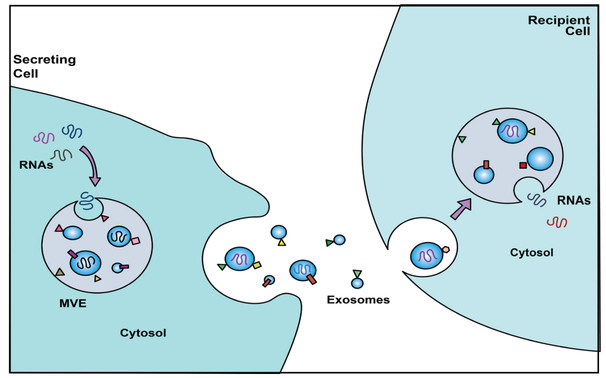
Mesenchymal stem cell-exosomes (MSC-Exos) are secreted by mesenchymal stem cells that carry various bioactive molecules, such as mRNA, miRNA, and proteins, and deliver to the recipient cells. MSC-exos act as the cell communicators by delivering messages to regulate cellular processes.

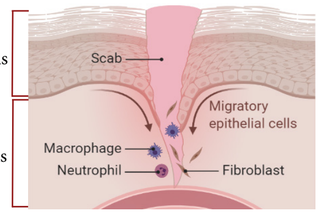
They have the following characteristics to promote wound healing:

- **Regenerative effect**
- **Immunomodulatory effect**
- **Anti-apoptotic effect**



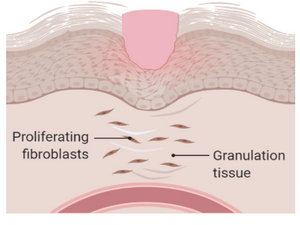
Stages of Wound Healing Process

STAGE 1: INFLAMMATION



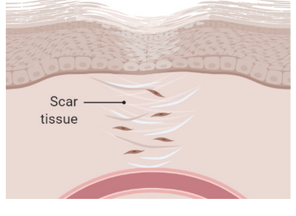
Inflammation is the earliest response to wound repair. It is characterized by **hyperemia, serous exudation, local redness and swelling**. A moderate inflammatory response helps to remove inflammatory factors, fight infection and remove cell debris, thus repairing damaged tissues.

STAGE 2: PROLIFERATION



In this stage, **angiogenesis** (blood capillary formation), **collagen deposition** (increase wound strength), **granulation tissue formation, re-epithelization** (formation of new skin tissues)**, and wound contraction** concur. Proliferation of fibroblasts is crucial for skin tissue repair and regeneration.

STAGE 3: REMODELING



Scar formation happens in this stage. Extracellular matrix (ECM) remodeling can last 2 weeks to >1 year. The key to **ECM reconstruction** is the synthesis and degradation of collagen. Insufficient or excessive ECM formation can cause the wound surface not to heal or scar formation.

How MSC-Exos Help in Cutaneous Wound Repair

- MSC-exos help in the **regulation of inflammatory factors** that plays an important role in skin tissue regeneration, and excessive production of cytokines may lead to tissue injury.
- MSC-exos can **drive the up-regulation of an anti-inflammatory cytokine**, e.g. IL-10, which plays a critical role in the control of cutaneous wound inflammtion and scar formation.
- MSC-exos **transport the bioactive molecules**, such as proteins and RNAs, into the receiving cells to **regulate their proliferation and migration**, by modulating the expression of growth factors and their related genes. It helps in the formation of granulation tissue and collagen that provide the structural support for wound repair.
- MSC-exos also promote the proliferation of skin cells.
- MSC-exos help in the regulation of ECM re-synthesis.
- MSC-exos accelerate the wound healing process by promoting the synthesis of type I collagen, type III collagen and elastin proteins in the early stage; while MSC-exos inhibit collagen synthesis in late stage to reduce scar formation.

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