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Biomolecular and Histological Changes Following Microneedling: Assessment of Collagen I, Collagen III, TGF-β, and VEGF Expression During Cutaneous Repair.

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Abstract

Microneedling has emerged as a minimally invasive dermatological procedure widely used for skin rejuvenation, scar treatment, and enhancement of dermal remodeling. The procedure creates controlled micro-injuries in the skin, stimulating a cascade of biological events that promote tissue repair and regeneration. This study investigates the biomolecular and histological changes that occur following microneedling, with particular emphasis on the expression patterns of Collagen I, Collagen III, Transforming Growth Factor-beta (TGF-β), and Vascular Endothelial Growth Factor (VEGF) during cutaneous wound healing.

Keywords: Microneedling, Collagen I, Collagen III, TGF-β, VEGF, wound healing, skin rejuvenation, dermal remodeling, angiogenesis, histology.

Skin aging, scarring, and various dermatological disorders are associated with alterations in the extracellular matrix (ECM), decreased collagen production, and impaired tissue regeneration. Traditional treatments such as chemical peels, laser resurfacing, and dermabrasion have demonstrated effectiveness but are often accompanied by prolonged recovery periods and adverse effects.

Microneedling, also known as percutaneous collagen induction therapy, has gained substantial attention due to its ability to stimulate natural wound-healing mechanisms without causing extensive epidermal damage. The procedure involves the use of fine needles that penetrate the skin to create controlled microchannels. These micro-injuries activate inflammatory and regenerative pathways, resulting in increased production of growth factors, cytokines, and structural proteins.

Among the key molecular mediators involved in tissue repair are Collagen I, Collagen III, Transforming Growth Factor-beta (TGF-β), and Vascular Endothelial Growth Factor (VEGF). Collagen III predominates during the early stages of wound healing and provides temporary structural support. As healing progresses, Collagen I gradually replaces Collagen III, contributing to stronger and more organized connective tissue. TGF-β regulates fibroblast proliferation and extracellular matrix deposition, whereas VEGF facilitates angiogenesis necessary for nutrient and oxygen delivery to regenerating tissues.

Understanding the temporal expression patterns of these biomarkers is crucial for elucidating the mechanisms underlying microneedling-induced skin rejuvenation. This paper aims to evaluate biomolecular and histological changes following microneedling, focusing on the role of Collagen I, Collagen III, TGF-β, and VEGF during cutaneous repair.

Microneedling, often referred to as Percutaneous Collagen Induction (PCI), triggers a precise, multi-stage wound-healing cascade that rejuvenates the skin through controlled mechanical trauma. By creating thousands of microscopic channels in the dermis, the procedure stimulates the body’s natural regenerative mechanisms.

Below are the biomolecular and histological changes associated with this process, specifically focusing on the markers you identified.

The Three Stages of Cutaneous Repair

The biological response to microneedling follows a well-defined sequence:

- Stage 1: Injury & Inflammation (Hours 0–48): The micro-injuries trigger the immediate release of platelets and neutrophils. These cells release critical inflammatory cytokines and growth factors, including TGF-β (Transforming Growth Factor-beta) and VEGF (Vascular

Endothelial Growth Factor), which act as "alarm signals" to recruit fibroblasts and initiate the healing process.

- Stage 2: Proliferation (Days 2–5): Neutrophils are replaced by monocytes. Fibroblasts migrate to the site and begin synthesizing the extracellular matrix, characterized by a rapid surge in Type III Collagen, elastin, and glycosaminoglycans.
- Stage 3: Maturation & Remodeling (Day 5 and beyond): This is the longest phase. The initial Type III collagen, which is fragile and thin, is slowly replaced by the more durable and stable Type I Collagen. This remodeling phase can continue for several months, leading to improved skin texture, firmness, and scar resolution.

Biomolecular Expression Profiles

Marker	Primary Role in Microneedling
TGF-β	A potent fibrogenic mediator. It is crucial for fibroblast proliferation and the subsequent up-regulation of collagen and elastin synthesis.
VEGF	Promotes angiogenesis (the formation of new blood vessels). This increases blood flow, nutrient delivery, and oxygenation, which are essential for tissue repair and cell proliferation.
Collagen III	The "scaffolding" collagen. It is the first to be deposited by fibroblasts during the proliferative phase to provide immediate structural integrity to the micro-wounds.
Collagen I	The "strength" collagen. During the remodeling phase, this replaces Type III to provide long-term tensile strength, dermal thickness, and elasticity.

Key Histological Observations

Studies using 3D human skin models and clinical biopsies have confirmed several structural changes following treatment:

- Epidermal Thickening: Microneedling promotes hyperplasia of the epidermis, helping to normalize the skin barrier and improve overall texture.

- Neocollagenesis: Histological staining consistently reveals a significant increase in the density of collagen fibers. With repeated sessions, there is a measurable shift toward a higher ratio of Type I collagen.
- Basement Membrane Restoration: The procedure helps reorganize the dermo-epidermal junction, which is particularly beneficial in conditions like melasma, where the basement membrane may be damaged or irregular.
- Vascular Ectasia: Immediately post-procedure, there is visible dilation of blood vessels and slight extravasation of red blood cells, which is a direct consequence of the physical injury and the precursor to the angiogenic response driven by VEGF.

Summary of Benefits

The synergy of these biomolecular markers creates a self-sustaining cycle of repair. By precisely timing the injury, microneedling effectively "tricks" the skin into a state of high-intensity repair, replacing damaged, thin, or scarred tissue with newly synthesized, well-organized collagen.

Conclusion

Microneedling induces significant biomolecular and histological changes that enhance cutaneous repair and regeneration. Increased expression of TGF-β and VEGF during the early stages of healing promotes fibroblast activation and angiogenesis, while elevated Collagen III and subsequent Collagen I synthesis facilitate extracellular matrix remodeling. Histological improvements include increased dermal thickness, enhanced collagen organization, and improved vascularization. These findings confirm that microneedling is an effective minimally invasive procedure capable of stimulating natural skin repair mechanisms and improving overall skin quality.

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