Correlation of collagen formation related genes expression with the healing process of thermal injury to skin and subcutaneous tissue

Pengzhan Xu[1], Lexuan Bi[1,2], Yayun Wang[3], Xiaoli Zhang[2], Qingxin Shang[1] and Dong Wang[1,3,*]

[1]Institute of Regenerative Medicine, Binzhou Medical University, Yantai 264003, China
[2]School of Nursing, Binzhou Medical University, Yantai 264003, China
[3]Department of Histology and Embryology, Binzhou Medical University, Yantai 264003, China

The present study delineates the extracellular matrix (ECM) remodelling dynamics during thermal injury repair through integrated transcriptomic and histopathological analysis. The gene expression dataset GSE8056 was analysed via GEO2R, identifying 306 differentially expressed genes between early (0–3 days) and late (>7 days) healing phases, with significant enrichment in collagen-centric pathways (e.g., ECM-receptor interaction). Protein-protein interaction network analysis (STRING database; Cytoscape Cytohubba plugin) revealed 10 hub genes (COL1A1, COL1A2, COL3A1, COL4A1, COL5A1/2, COL6A1, COL11A1, COL12A1, and COL14A1) governing collagen assembly. In a rat thermal injury model, histopathology (haematoxylin-eosin staining, Masson's trichrome) demonstrated progressive tissue regeneration: acute epidermal necrosis (0d), inflammatory scab formation with nascent epidermis (3d), and collagen deposition increasing significantly by day 7 ($P < 0.05$). Immunohistochemistry validated stage-specific collagen isoform expression: COL1A1, COL1A2, and COL3A1 were elevated at both 3d and 7d, while COL4A1 peaked at 7d—aligning with basement membrane reconstruction during re-epithelialisation. Transcriptomic data corroborated upregulation of all four collagens in late-phase human wounds. These results establish collagen isoforms as temporal regulators of ECM remodelling; COL1A1, COL1A2, COL3A1 and COL4A1 can be used as target genes for clinical thermal injury wound repair intervention.

Keywords: Burn thermal damage, collagen fibre, collagen gene, skin, wound healing.

thermal injures include debridement, skin grafting, continuous dressing changes, and anti-infection therapies[4,5]. Studies have shown that 70% of patients with thermal injury will have tissue contracture, adhesion, hypertrophic scar and other complications during wound healing, which will seriously affect the normal life, mental health and social function of patients[6]. There is no recognised more effective treatment for the pathological scar of the wound caused by thermal injury except surgical excision[4–7].

The skin's structure consists of the epidermis and dermis, with subcutaneous tissue connecting the skin to underlying muscles and bones. Although the thin epidermis plays a minimal role in thermal responses[8], the dermis and subcutaneous tissue contain dense collagen and elastin networks crucial for wound healing and functional recovery[8,9]. Deep dermal wound healing is typically segmented into four sequential steps: haemostasis, inflammation, proliferation, and remodelling[10–12]. Signalling molecules significantly contribute to wound healing success by maintaining inflammation, stimulating angiogenesis, regulating fibroblast/keratinocyte secretions, proliferation and migration[13,14]. Fibroblasts are responsible for wound healing processes by releasing collagen, which forms a collagen-rich extracellular matrix (ECM)[15–18]. However, previous studies only used basic methods such as morphology to observe the changes in the internal key mechanism of the wound healing process and could not find effective intervention targets to formulate treatment plans for different repair stages of thermal injury so as to effectively reduce the adverse wound healing outcomes, such as hypertrophic scars.

Based on the pathophysiological process of skin thermal injury repair, we hypothesise that collagen expression in the injured area may undergo significant temporal changes post-injury. Previous global gene microarray