Molecular and Immune-Mechanism of Keloid Development

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Keloids are problematic scars characterized by excessive fibroblast proliferation and collagen deposition that extend beyond the original wound and often recur after treatment. To identify clinically actionable biomarkers and therapeutic targets, we conducted immune profiling on both blood and lesional tissue from a hospital-based cohort (104 keloid patients, 512 healthy controls, 100 patients with other scar or inflammatory skin conditions). Flow cytometry and single-cell RNA sequencing revealed a significant depletion of cytotoxic $CD8^+$ T lymphocytes (CTLs) in peripheral blood and within keloid margins. In the scar tissue, residual CTLs displayed high expression of the inhibitory NKG2A/CD94 receptor complex, which corresponded with elevated serum levels of soluble HLA-E (sHLA-E). Quantitative assays demonstrated that sHLA-E distinguished keloid patients with 83.7% sensitivity and 92.2% specificity, showing minimal cross-reactivity in hypertrophic scars or unrelated dermatologic diseases.

We then assessed response to combined intralesional triamcinolone and 5-fluorouracil therapy in a treatment subgroup. Patients with favorable outcomes exhibited pronounced reductions in sHLA-E post-treatment, whereas incomplete suppression of sHLA-E was linked to higher recurrence rates on follow-up. These results implicate the NKG2A/CD94 - sHLA-E axis in immune evasion within keloid pathology and position sHLA-E as both a diagnostic marker for keloid risk and a prognostic indicator of treatment efficacy. Incorporating sHLA-E monitoring into clinical practice could enable personalized strategies to prevent keloid formation and recurrence.

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