REGENERATIVE APPROACHES FOR EPIDERMOLYSIS BULLOSA: TISSUE ENGINEERING AND GENE THERAPY

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Introduction: Epidermolysis bullosa (EB) is a group of rare genetic disorders characterized by skin fragility and blister formation. The current management of EB is mainly symptomatic, with no definitive cure. Recent advancements in tissue engineering and cell therapy have provided promising alternatives: gene-edited keratinocyte transplantation, fibroblast therapy, mesenchymal stem cell (MSC) transplantation, revertant mosaicism-based therapy (RMBT), and induced pluripotent stem cell (iPSC)-based therapy.
Materials and Methods: A literature review of recent preclinical and clinical studies was conducted. The focus was on therapeutic efficacy, safety, and clinical feasibility.
Results: Gene-edited keratinocyte transplantation has shown long-term epidermal regeneration and reduced blister formation, particularly in EB junctional and dystrophic subtypes. These transplants, created through *ex vivo* gene correction, have demonstrated engraftment success rates exceeding 80%, with no major immune rejection reported. Fibroblast therapy improves collagen production and enhances dermal stability, though it doesn't address the genetic cause of EB. MSC therapy demonstrates immunomodulatory effects, promoting tissue repair. Clinical trials report improvements in patient-reported pain and skin elasticity. RMBT utilizes naturally corrected keratinocytes, offering a genetically stable and patient-specific treatment option. iPSC-based therapy presents a novel strategy by reprogramming patient-derived fibroblasts into pluripotent cells, genetically corrected using CRISPR-Cas9 and differentiated into keratinocytes, facilitating autologous grafts with long-term stability. Vyjuvek, the first FDA-approved topical gene therapy for dystrophic EB, delivers functional COL7A1 via a herpes simplex virus (HSV-1) vector, significantly improving wound healing in patients with dystrophic EB. Despite these advances, challenges such as immune compatibility, tumorigenicity, and cost remain key barriers to widespread implementation.
Conclusion: Cellular therapies represent a significant advancement in the management of EB, with gene-edited keratinocytes and iPSC-based approaches holding the most potential for long-term disease correction. Fibroblast and MSC therapies provide supportive benefits in wound healing and inflammation control. Further clinical trials and optimization of these strategies are required to enhance accessibility and long-term safety.
Keywords: Epidermolysis bullosa, gene therapy, cell therapy, keratinocyte transplantation, MSC, iPSC, Vyjuvek.