Allogeneic mesenchymal stem cells in trilayered artificial skin: incorporated or injected? A GMP preclinical study

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INTRODUCTION

The treatment of skin ulcers, such as the chronic ones diabetic patients suffer, are a medical challenge that still needs to be addressed and skin substitutes represent a promising alternative treatment for this. Most of the skin substitutes are single-layered or bilayered, thus there is a lack of full thickness trilayered artificial skin substitutes, which would emulate skin function better.

OBJECTIVE

To develop and evaluate the efficacy and safety of a trilaminar artificial skin model composed of mesenchymal stem cells in the basal layer, fibroblasts within the dermis, and keratinocytes on the surface, using a fibrin–hyaluronic acid matrix as a scaffold.

METHODS

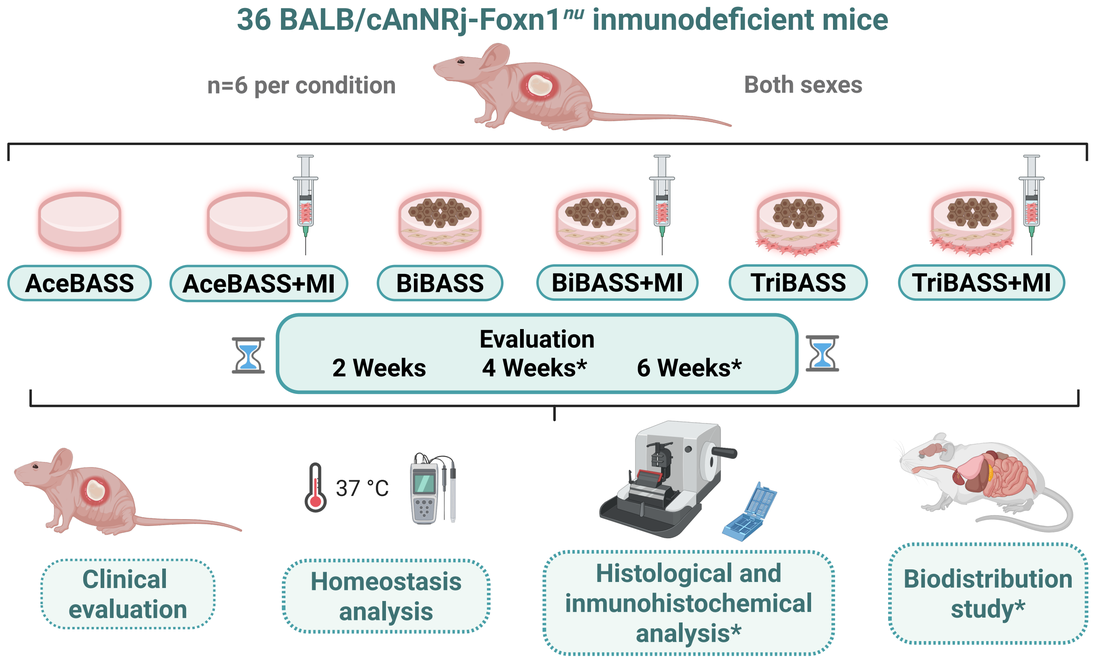


Figure 1. Experimental design: BALB/cAnNRj-Foxn1^{nu} mice (n = 6 per condition, both sexes) received AceBASS, BiBASS, or TriBASS ± MI and were evaluated at 2–6 weeks by clinical, homeostasis, histological/immunohistochemical, and biodistribution analyses.
(AceBASS, acellular; BiBASS, bilayered; TriBASS, trilayered; MI, mesenchymal injection).

RESULTS

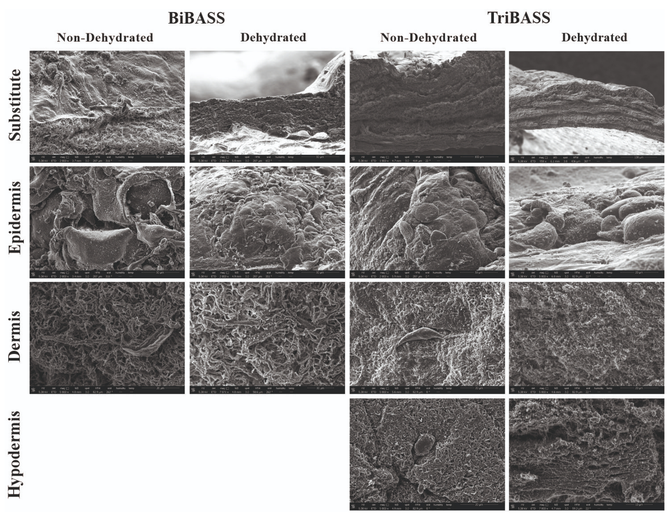


Figure 2. SEM images illustrate morphology and cellular organization in non-dehydrated and dehydrated constructs



Figure 3. Clinical evaluation at week 6. Representative images show improved wound closure following treatment with bioengineered skin substitutes, with the most favorable outcomes observed for TriBASS. Baseline wounds were comparable across groups.

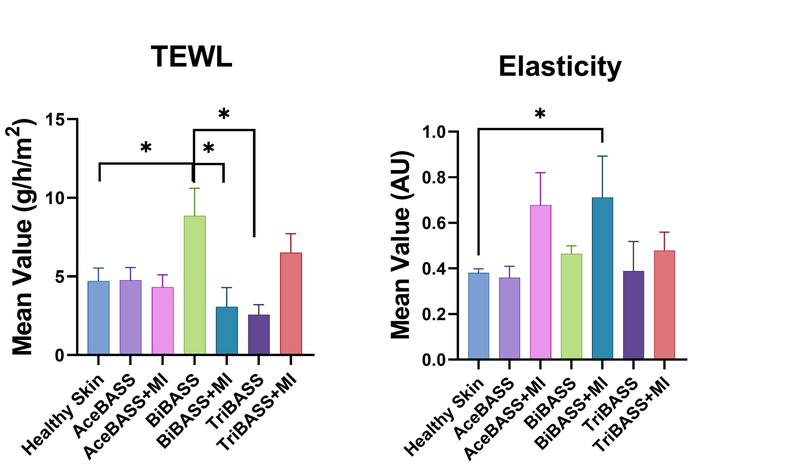


Figure 4. Skin function at week 6. Transepidermal Water Loss (TEWL) and elasticity measurements indicate restoration of skin homeostasis, with TriBASS showing values closest to healthy skin.

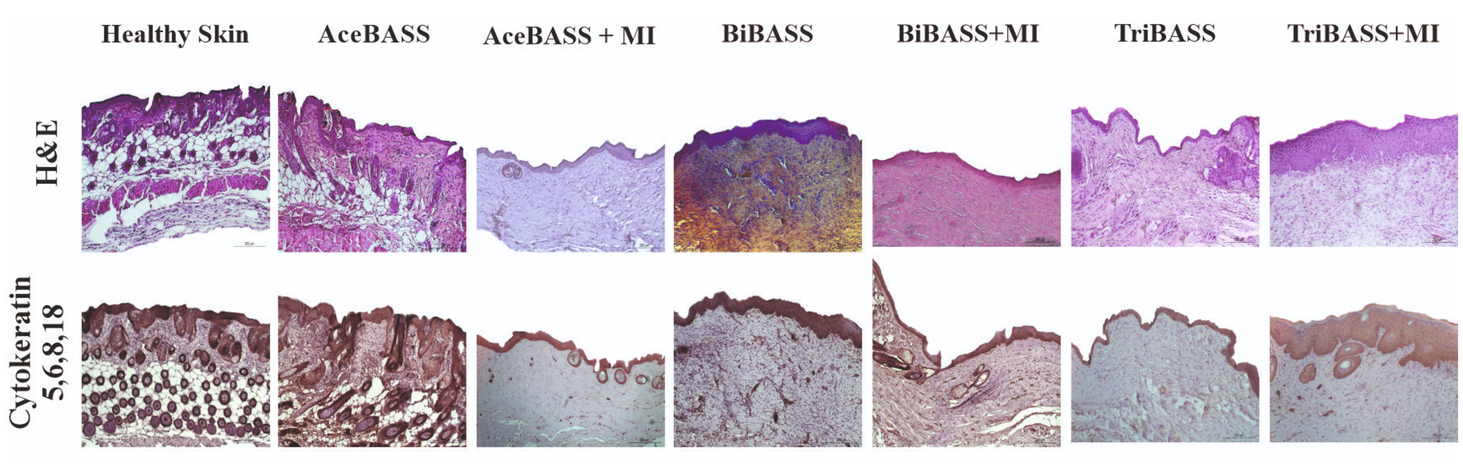


Figure 5. Histological and immunohistochemical analysis at week 6. H&E staining shows improved skin architecture with a well-defined epidermal and dermal organization in TriBASS compared to AceBASS and BiBASS. Cytokeratin (CK 5, 6, 8, 18) expression confirms the presence of a differentiated epidermis, with TriBASS displaying a pattern closer to healthy skin. No additional histological improvement was observed with mesenchymal injection (MI).

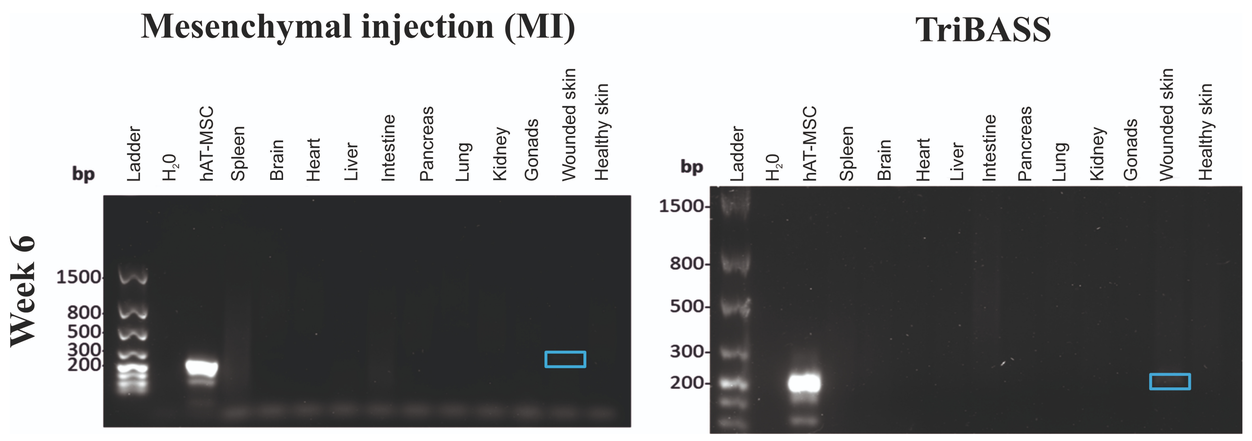


Figure 6. PCR analysis at week 6 shows no detectable presence of mesenchymal stem cells (MSCs) in major organs following mesenchymal injection (MI) or TriBASS treatment. Signal is restricted to the wound site (blue box), indicating absence of systemic biodistribution

CONCLUSION

TriBASS enables structurally organized and functionally competent skin regeneration without systemic MSC biodistribution. Mesenchymal injection (MI) provides no additional benefit.

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