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3D-bioengineered human amniotic membrane scaffold for improvement of wound healing in diabetic rats

In the tissue engineering context, attention to the biological scaffolds due to the safety, efficacy, and bio-mimicity was discussed. Among the natural scaffolds, human amniotic membrane (HAM) has shown to be promising and has been used for wound and reconstructive aims since the early twentieth century. While the use of the HAM in clinical intervention seems to be advantageous, there are some issues that should be addressed. Particularly, with regard to tissue regeneration process, applying the intact HAM is more problematic, due to the high density of the texture which limits cell penetration and migration to the site. Definitely, a micro-porous three-dimensional (3D) scaffold is more suitable for cells penetration, migration, and homing, which enables cell functionality and improves their participation in tissue regeneration.

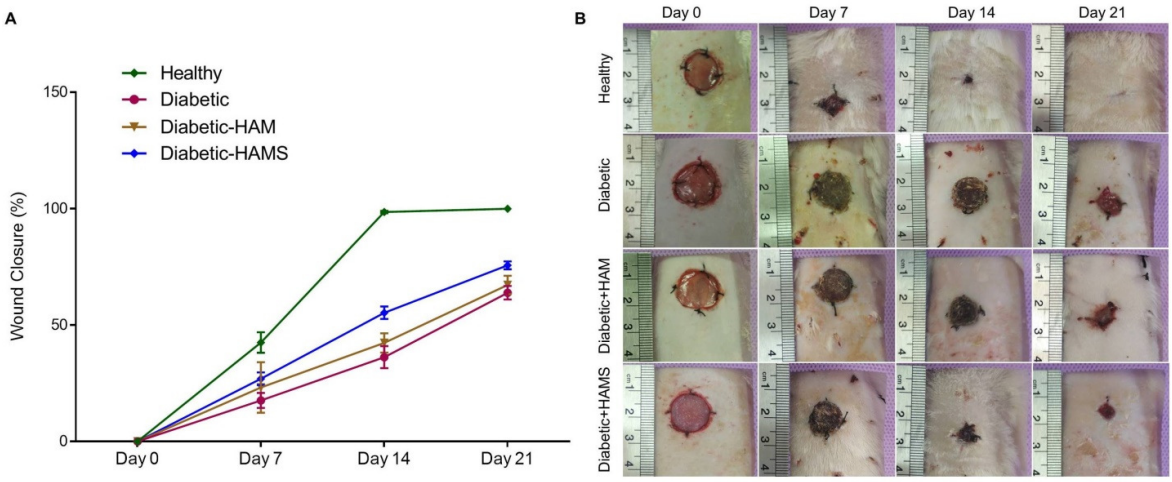
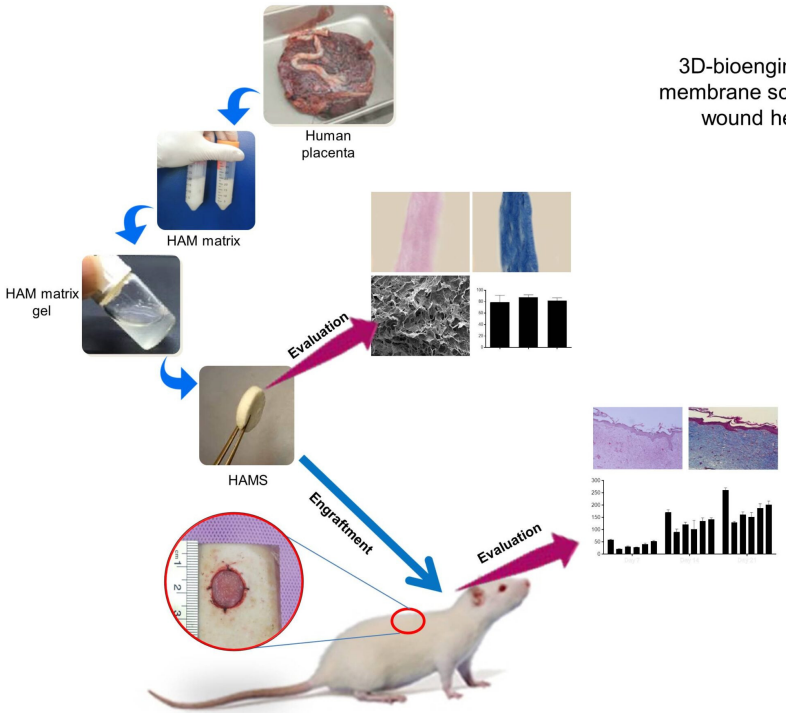


Fig. 1. (A) Wound closure rate which expressed as percent of initial wound area 7, 14 and 21 days after wound infliction. (B) Representative images of wound healing in treated and untreated groups.

In this study, the impact of 3D-bioengineered human amniotic membrane-derived extracellular matrix scaffold (HAMS) in wound healing carried out on streptozotocin-induced diabetic rats. The results demonstrated that the HAMS engraftment improved the quality of the restored tissue with respect to both intact HAM engraftment and spontaneous healing. As shown in Figure 1A, the wound closure rate was higher for the HAMS engrafted rats compared to the HAM engrafted ones and diabetic groups from days 7 to 21. Furthermore, histological, molecular and biomechanical analyses supported the clinical observations. Histological analysis of the skin revealed significantly increased cellularity (including numerical density of epidermal basal cells and fibroblasts, as well the length density of blood vessels), the numbers of proliferating cells and the amount of collagen deposition in the wounds of the rats engrafted with HAMS at days 7, 14 and 21 compared to those other diabetic rats. Furthermore, in Diabtic-HAMS group, the transcripts for genes contributing to regeneration (*Tgf-β, bFgf and Vegf*) upregulated more than those of Diabetic-HAM group, when compared to diabetic ones. HAMS also regulated the inflammatory response by mediating anti-inflammatory cytokines such as *Tnf-α* and *Il-1β*, and as well cell density of neutrophil and macrophage cells.



Graphical abstract

Overall, under in vivo conditions, we were able to show that the HAMS engraftment had more impact on diabetic delayed wound healing process compared to traditional use of intact HAM. It is therefore suggested that the bioengineered 3D micro-porous HAMS is more suitable for cells adhesion, penetration, and migration for contributing to wounded tissue regeneration.

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