Syndesome-Based Alginate Dressings for Enhanced Wound Healing in a Diabetic Mice Model

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Statement of Purpose: Incidence of chronic non-healing wounds has significantly increased over the last decade due to a rising epidemic in type-II diabetes and peripheral arterial disease (PAD). PAD has a prevalence of 12-20% in population aged 65 and older in the US[1] and type-2 diabetes affects around 347 million people worldwide. Previous research has attempted to use growth factor proteins or genes to enhance the healing of cutaneous wounds but have achieved only limited success in healing chronic or recurring wounds in the long-term. Our previous work[2,3] has demonstrated a significant reduction of syndecan-4 protein (co-receptor for FGF-2) in diabetic mice. Furthermore, co-delivery of syndesomes (syndecan-4 proteoliposomes) with FGF-2 enhanced angiogenesis in diabetic mice. In this study, we tested the efficacy of a novel alginate wound dressing that delivered FGF-2 in combination with syndesomes in mice with diabetes, obesity and hyperlipidemia.

Methods: To recapitulate the human disease state, we used Ob/Ob mice and fed them a high fat diet for 15 weeks. We utilized a splinted, excisional wound model[4] and implanted 2% sodium alginate disks containing treatments into the wound, which were fabricated using a custom made high throughput mold. The treatments used included the following: PBS (control), FGF-2, syndesomes (S4PL), and syndesomes with FGF-2. We monitored the perfusion of the wounds over time using laser speckle imaging. After 14 days, mice were sacrificed and tissues harvested for histological processing.

Results: At day 14, wounds treated with syndesomes (S4PL) and FGF-2 healed the wound significantly more than FGF-2, S4PL and control groups (Fig. 1A, B). Histological analysis demonstrated increased re-epithelialization of the wounds treated with S4PL with FGF-2 in comparison to the other groups (Fig. 1C, D). Laser speckle imaging of wound at day 7 also showed increased perfusion in the S4PL with FGF-2 group compared to all other groups. (Data not shown) Furthermore, immunostaining for the M1 macrophage marker (CD86) showed significantly reduced inflammatory macrophages in both S4PL+FGF-2 and S4PL groups (Fig. 1E, F). Staining for an M2 macrophage marker (CD163) revealed enhanced levels when the syndesomes were delivered, compared to control and FGF groups (Fig. 1 G, H).

Conclusions: Taken together, our studies support that syndesomes significantly enhance FGF-2 activity in wound healing in diabetic mice. Thus, syndesome-containing alginate wound dressings may be useful in treating chronic wounds and restoring growth factor activity in disease states.

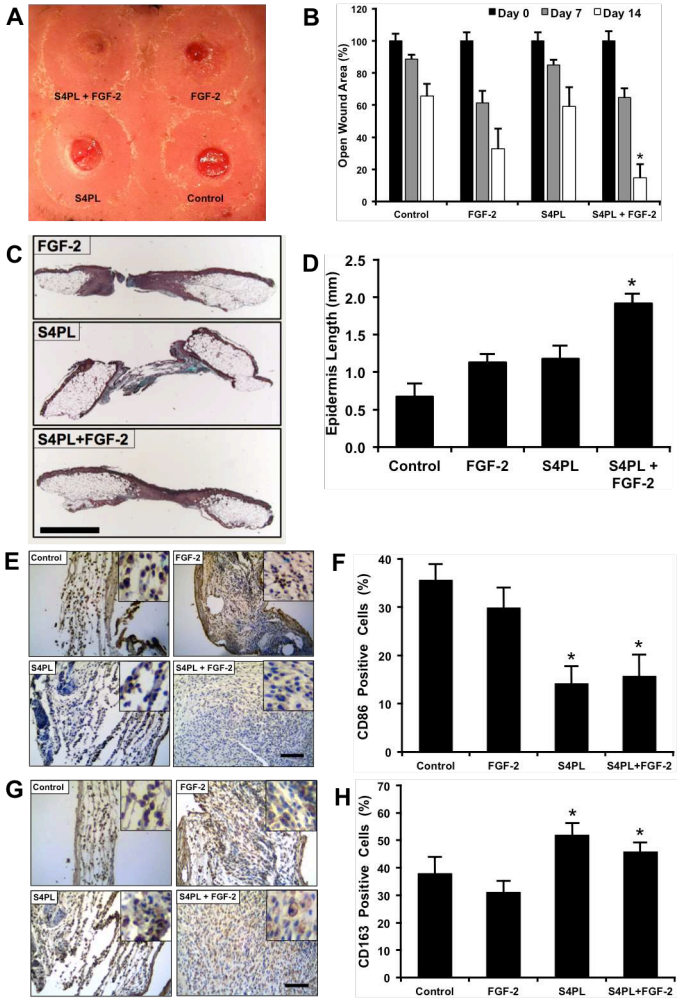

Figure 1. (**A**) Macroscopic image of the dorsal wound surface at day 14 with various treatments. (**B**) Quantification of open wound area macroscopically at days 0, 7 and 14. (**C, D**) H&E stained wound sections at day 14 and quantification of re-epithelialization. Bar – 1mm. * $p<0.05$ versus all other groups (n=10). (**E, F**) Immunostaining of the wound sections with M1 macrophage marker (CD86) and quantification of CD86 positive cells. Bar – 250μm. (**G, H**) Immunostaining for M2 macrophages marker (CD163) and quantification of CD163 positive cells. Bar – 250μm. *$p<0.05$ versus control and FGF-2 groups (n=10).

References:
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