Abstract 14060: Syndesomes: Novel Therapeutics for Chronic Ulcers and Peripheral Ischemia

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Abstract

Introduction: Peripheral arterial disease patients often suffer from ischemia and chronic non-healing ulcers. Our previous studies showed a dramatic reduction in syndecan-4 protein in the muscle of obese diabetic mice. Reduction of syndecan-4 (co-receptor for FGF-2) suggests a resistance to FGF-2 stimulation in diseased state. Here, we demonstrate a novel strategy to address the problem by delivering the missing syndecan-4 and FGF-2 in a liposomal formulation.

Hypothesis: Delivering the missing syndecan-4 would improve the therapeutic potential of FGF-2 for treating both ischemia and wounds in a diseased state.

Methods: Treatments were microencapsulated in a 4% alginate as microspheres or discs. An ob/ob mouse model with 10 weeks of high fat diet was used to recapitulate the diseased condition. Ischemia was created in mice through femoral artery ligation and alginate microspheres were placed at the incision site. Blood perfusion in the feet was monitored using laser speckle contrast imaging. Excisional wound model was used to examine if the therapy could improve wound healing in diseased model.

Results: We found that syndesomes (S4PL) with FGF-2 significantly increased blood perfusion at day 7 and 14 compared to FGF-2 alone (Fig. 1A). Immunostaining confirmed that there was increased endothelial vascularization (Fig. 1B) and reduced inflammation in both thigh and calf muscles. S4PL + FGF-2 significantly increased wound closure compared to all other groups in the excisional wound model. (Fig. 1C) Immunostaining for cytokeratin showed significant re-epithelialization in S4PL + FGF-2. Finally, we found dramatically reduced inflammatory response in both S4PL and S4PL + FGF-2 groups when immunostained for M1 macrophage (CD86). (Fig. 1D)

Conclusions: The studies support that restoring the diseased tissue to its native state by delivery of missing co-receptors with the growth factors may be an appealing therapeutic strategy to treat ischemia and non-healing ulcers.
Key Words:
Peripheral artery disease (PAD)
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