

Coencapsulation of ISCs and MSCs Enhances Viability and Function of Both Cell Types for Improved Wound Healing

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Introduction: We previously demonstrated that insulin secreting cells (ISCs) accelerate healing of chronic wounds, and it is known that mesenchymal stem cells (MSCs) also accelerate wound healing. Here, we report that the combination of both cell types coencapsulated into a synthetic hydrogel dressing accelerates chronic wound healing 3x faster than control and 2x faster than each cell type delivered singly. Specifically, insulin released by ISCs activates the PI3/Akt pathway, which is vital to the function and survival of MSCs. MSCs in turn improve the viability and function of ISCs.

Materials and Methods: MSCs and/or rat islet tumor RIN-m cells were encapsulated into polyethylene glycol diacrylate hydrogel sheets and applied to 1 cm² full thickness excisional wounds on the dorsa of genetically diabetic male mice (BKS.Cg-m ^{+/+}Leprdb/J) in accordance with protocols approved by the Rutgers IACUC. Encapsulated cell viability was assessed using a LIVE/DEAD® Viability/Cytotoxicity Kit. Akt phosphorylation, insulin, VEGF, and TGF-β1 secretion were assessed by ELISA. Animals were sacrificed on postoperative day 14 and 28 and wound tissue was collected for histological and western blot analysis.

Results and Discussion: ISC:MSC combination groups had the highest levels of every secreted product and phosphorylated Akt, and closed wounds in 14 days (Fig 1), ISC-only or MSC-only groups closed wounds in 28 days, control groups closed wounds in 40 days. Further, ISC:MSC groups healed without intermediate scab or scar.

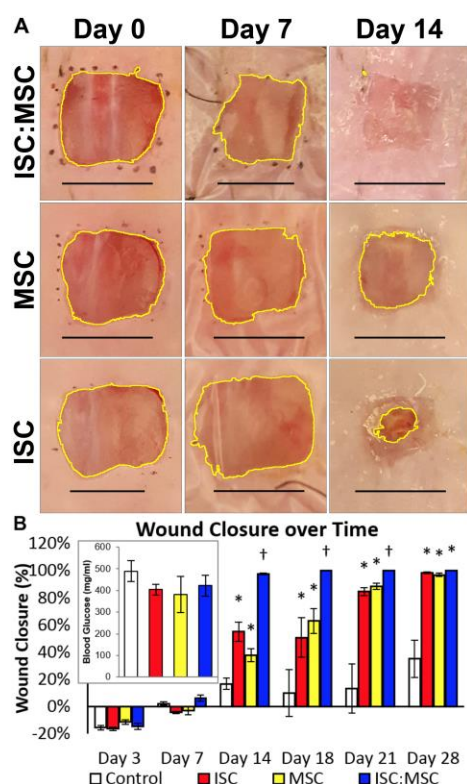


Figure 1. Progression of wound healing. **A.** Rows follow single animals. After Day 0, unhealed wounds are imaged through dressings. Day 14 ISC:MSC shows closed wounds with dried hydrogel residue. Images were uniformly adjusted for contrast, saturation, and brightness. Yellow outlines were automatically generated with the NIH ImageJ Wound Healing tool. **B.** Percent wound closure and glucose levels (inset). Asterisks indicate statistically significant increases ($p < 0.05$) compared to control; crosses represent significance compared to all other groups. Error bars show standard error of mean.

Conclusions: Combining MSCs with ISCs results in a more robust healing response than singly delivered cells, warranting further investigation of coencapsulation for MSC therapies.

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