

ADIPOSE-DERIVED STROMAL CELLS PROMOTE SURVIVAL OF ENDOTHELIAL CELLS AND KERATINOCYTES IN WOUND HEALING MODEL

Kellen A. Knowles, Dmitry Traktuev, and (Keith L. March), Center For Regenerative Medicine, Roudebush VA Medical Center, Indianapolis, Indiana 46202

Burn wounds are a significant medical challenge today. Current treatment includes the use of skin grafts or wound healing scaffolds to protect the wound and promote healing. However, pre-existing conditions and factors such as smoking can compromise normal healing thru decreased growth factor production, prolonged inflammation, tissue hypoxia, reduced cellular migration and ECM deposition, and impaired revascularization, making the wound more susceptible to infection.

Adult pluripotent cells have been proposed as a therapy for multiple disorders because they have been shown to decrease inflammation and promote host tissue preservation and angiogenesis. Adipose-derived stromal cells (ASC) are a population of mesenchymal, pluripotent cells derived from adipose tissue. Compared to bone marrow derived MSC, ASC can be easily obtained thru minimally invasive procedures. It has been shown in previous studies that ASC improved wound closure in normal and diabetic mice and stimulated proliferation of human dermal fibroblasts, increasing the epithelialization of cutaneous wounds.

The next challenge is to find a clinically relevant cell-delivery method. In light of this, we propose the use of current clinical wound healing scaffolds as a delivery vehicle for ASC in combination with endothelial cell (EC) and keratinocytes. We hypothesize that that ASC will promote keratinocyte and EC survival (both are used clinically), thus promoting epithelialization and neovascularization of graft. The use of ASC, EPC and keratinocytes in combination with wound healing scaffolds currently used by physicians, such as Integra is a novel combination and will provide a faster transition to clinic if it is found to be efficacious.

Our lab has shown that ASC promote survival of EC on Integra and support the formation of vascular-like cord structures. Factors secreted by ASC promote keratinocytes ingrowth in a wound closure assay. Keratinocytes also showed increased survival when cultured with ASC.