TISSUE ENGINEERING AND THE MYOFIBROBLASTS

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Myofibroblasts are cells that are present during wound healing and numerous fibrous pathologies. They are known to contract and secrete new extracellular matrix but the complete role of these cells as well as their interactions with other cells are still not well understood. The use of a tissue engineering approach allows placing cells in a very similar context found in vivo with the presence of major elements as fibroblasts (Fb), myofibroblasts (Myo), keratinocytes (K), microvascular endothelial cells (MVEC) and/or matrix. Various methods of tissue engineering reconstruction can been performed, the method of E. Bell being the most famous where cells were seeded in a collagen gel. In our lab, we have developed a new method allowing to reconstruct tissue very similar than original one, stimulating the cells to create their own matrix similarly than they do in vivo. Dermal cells (with or without MVEC) were allowed to grow in the presence of ascorbate. These cells formed manipulatable sheets that were then superimposed and left to adhere. Human K can then be seeded before elevating the tissue construct to the air-liquid interface to form a fully differentiated epidermis.

Thickness of the mesenchymal tissue is a good reflection of the balance of the production and degradation of the matrix and has allowed us to understand some of the phenomena involved during formation of the hypertrophic scars (Hscar). The thickness of dermis was increased when K isolated from Hsc were used in comparison with K from normal biopsies. Collagen, MMP and cell growth variation can explain the fibrotic response of Fb depending on K origin. We thus can conclude on a possible role of K during Hsc formation, secreting factors enhancing fibrosis. Capillary formation has been analyzed depending on Fb origin. When MVEC were seeded with Fb, they organized in a capillary-like network that was morphologically different depending on Fb origin. When mesenchymal cells were isolated from normal wound or Hsc, a significant increase in capillary-like structure number and length was observed in comparison with network organized in presence of Fb from normal skin. We hypothesize that Fb from wounds and Hsc could play a more important role on neovascularization than expected.

The interaction of keratinocytes, endothelial cells and fibroblasts are vital during the development of normal and pathological scars. The use of a tissue engineering approach can help to understand pathogenesis of Hsc and other fibrosis.

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