RESPONSE OF CONNECTIVE TISSUE CELLS TO INJURY-GROWTH CONTROL AND CONNECTIVE TISSUE METABOLISM

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The response of connective tissue cells in tissues that are injured ranges from cell death on the one extreme to DNA synthesis, cell proliferation, increased protein synthesis and formation of new connective tissue matrix constituents on the other.

At least two examples of this response to injury can be seen in the process of wound repair and during the genesis of the lesions of atherosclerosis. During the process of wound healing, fibroblast proliferation occurs both concomitantly and following an inflammatory response that includes the participation of thrombocytes, polymorphonuclear neutrophilic leukocytes and monocytes. Factors important in the stimulus of the proliferative response of the fibroblasts are presumed to derive from constituents released from thrombocytes during the process of blood coagulation and subsequently to be dependent upon the ability of the monocytes to modulate into macrophages, debride the wounds and release factors important in the stimulation of DNA synthesis and protein synthesis. The types of collagen that are formed during the process of wound repair and maturation may also be related to factors released from platelets and monocytes, since early in the process there appears to be an increased relative amount of Type III to Type I collagen.

In similar fashion, the process of atherogenesis has been shown to be the result of proliferation of arterial smooth muscle cells within the intima of the artery wall. One major hypothesis concerning the etiology and pathogenesis of the lesions of atherosclerosis relates to those risk factors that lead to "injury" of the endothelium leading to focal sites of endothelial cell desquamation, resulting in the local adherence of thrombocytes followed by subsequent aggregation and release of factors contained within the platelets. At least one of these factors has been shown to be a relatively low molecular weight, basic protein that will specifically result in smooth muscle proliferation and in increased protein synthesis in cell culture.

Cell culture studies of fibroblasts, smooth muscle cells, as well as other cell types such as 3T3 cells and glial cells, have demonstrated that the principal component of whole blood serum responsible for the proliferation of these cells in culture is a factor derived from platelet aggregation and release that occurs during the process of serum formation. A series of correlative in vivo - in vitro studies have shown that this platelet factor is not only the principal mitogen present in serum responsible for cell growth and protein synthesis in culture, but appears to be important in stimulating the process of cell proliferation in vivo as well.

The role of fibroblasts, smooth muscle cells and other connective tissue cells in responding to these different forms of injury and potentially in other disease processes like rheumatoid arthritis, in terms of cell proliferation, connective tissue matrix formation and degradation will be discussed in terms of potential means of regulating these connective tissue cell functions.

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