

Criteria for the use of fibrin matrix in tissue engineering

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Fibrin (sealant) is an attractive biomatrix for tissue engineering for tissue engineering/regeneration because it consists of biologic components of the natural clotting cascade. When the two fibrin sealant components are mixed, coagulation occurs, and in the further course of the process, the activated factor XIII (FXIIIa) causes cross-linking of the fibrin monomers. Factor XIIIa also cross-links plasma-derived fibronectin to fibrin, which is important for cell adhesion via the RGD domain. Furthermore α_2 -antiplasmin and plasmin activator inhibitor 2 (PAI-2) which help to control subsequent fibrinolysis of the clot are also cross-linked to fibrin by FXIIIa.

Two different kinds of fibrin clots: white, non transparent "coarse clots" formed at an ionic strength and pH value within the physiological range, and transparent "fine clots" produced at a higher ionic strength and/or pH value. Fine clots are almost crystal clear and relatively brittle. The ionic strength of the fibrin sealant formulation can also affect the degree of cross-linking and cell toxicity. To a variable extent, sealant persistence in vivo can be controlled by adding an antifibrinolytic agent. Studies have demonstrated that aprotinin, a natural protease inhibitor, is superior to synthetic antifibrinolytic agents. While fibrin-based biomatrix has been used as a cellular scaffold during wound healing, the efficacy can be enhanced by including bioactive agents which promote specific cellular responses. Certain growth factors, i.e. basic fibroblast growth (bFGF), and vascular endothelial growth factor VEGF (only isoform 165) specifically bind to fibrin(ogen), so that fibrin biomatrix can be directly used for delivery. The combined use of keratinocytes and a fibrin matrix was first described in 1988 for skin regeneration.

Other cells including chondrocytes, human myofibroblasts, and osteoprogenitor cells, have also been successfully grown in fibrin gels. Moreover fibrin sealant has been used to deliver tracheal epithelial cells and preadipocytes. Fibrin serves as a unique binding site for the vascular endothelial cell surface receptor VE-cadherin. Fibrin-specific signaling through this receptor causes the vascular endothelial cells in injured blood vessels to migrate, proliferate, differentiate, and form new blood capillaries. The resulting neovascularization is prerequisite for successful tissue regeneration.