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Engineering fibrin nanoparticles to enhance the rate of wound closure

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At fresh wounds the inability of certain patients to quickly stop woozing blood and begin the stages of wound healing is a major concern, especially in hemophilia, diabetes and Von Willebrand disease (VWD). The Centre for Disease Control (USA) reports that delayed blood clotting is responsible for 18.9% of blood based coagulation deaths in 2010. FDA-approved commercial blood clotting agents use >500 times the physiological concentrations of fibrinogen and thrombin to thwart blood loss, but the ensuing wound tissue remodeling events are negatively impacted. Our research objectives are to synthesize stable pre-polymerized fibrin nanoparticles that enable fibrin nanoparticle integration and stabilize fibrin scaffold, which thereby improve cell migration and tissue epithelialization by providing appropriate scaffold mechanics and porosity. To that end, we have synthesized Fibrin Nanoparticles (FBN) using a two-phase microfluidic fibrin droplet generator. We hypothesize that macroscopic fibrin geometries created using FBN networks will be better suited for wound healing therapies than commercially available bulk fibrin gels and will enhance cell migration. Traction force microscopy experiments quantitatively demonstrate that FBN can engage fibroblast cell adhesion and support cellular contractile forces similar to collagen functionalized substrates. Additionally, the results show that FBNs coupled with keratinocyte growth factor enhance human dermal fibroblast migration in a 3D wound assay mimic and also on in vivo mice dermal wounds. FBNs are patented and are currently being testing as a carrier for other tissue growth factors and antimicrobial agents, for enhanced wound healing rates on compromised tissues.

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