Abstract

Current treatment options for acute and chronic wounds fail to promote adequate tissue regeneration, and instead lead to permanent scarring and loss of function. In the skin, repair following injury involves a cascade of events that includes clotting, inflammation, wound closure via cell proliferation and migration, and re-vascularization. Commonly, the process culminates with scarring, and regeneration of normal skin components, including hair follicles and adipose tissue, fails to occur. While many tissue engineering strategies for wound treatment have focused on the use of scaffolds for delivering cells to facilitate wound closure, few approaches have targeted the immune response, despite substantial evidence that excessive immune-mediated inflammation is detrimental to achieving regenerative outcome from endogenous skin progenitor cells. Macrophages are essential regulators of this process, and are involved in both advancing inflammation and promoting tissue repair in skin and beyond. In recent work, we demonstrated that the provisional extracellular matrix protein fibrin and its precursor fibrinogen can differentially regulate a critical event in macrophages – their inflammatory activation. In this project, we propose to leverage these interactions and develop new fibrin(ogen)-based adhesive hydrogels to modulate the immune and thus regenerative response after skin wounding. In Aim 1, we will utilize a recently popularized injury model for wound-induced hair neogenesis (WIHN), in which new hair follicles and sebaceous glands regenerate in large acute and burn skin wounds. This model provides a platform for studying how to modulate wound healing to promote more complete skin regeneration, and will be used to examine how adhesive hydrogels control macrophage inflammatory activation and the healing response. In Aim 2, we will further establish the translational potential of this approach by investigating the effects of the engineered hydrogels on the function of primary human macrophages. The long term goal of the proposed work is to develop improved strategies for treatment of acute and chronic skin wounds.