Role of Integrin Signaling Pathways Driving the Collective Migration of Human Keratinocytes

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Chronic wounds are a major and growing healthcare issue in American society. In chronic wounds, decreased rates of keratinocyte migration and proliferation cause wounds to heal abnormally. There are many factors driving the decreased rate of keratinocyte migration in chronic wounds, including the concentration of epidermal growth factor (EGF) released into the wound and the relative stiffness of the wound [1,10]. Previous studies have found that cellular signaling integrins such as β1, and downstream cell signaling proteins such as focal adhesion kinase (FAK), ERK, and pSTAT3 influence the response to EGF , and may be a factor behind the decreased rates of proliferation and migration in chronic wounds. This research was aimed to test the effect of such cellular signaling integrins on wound closure. HaCaT Keratinocytes were seeded onto polyacrylamide (PAA) gels of different stiffnesses (30 and 100kPA), and treated with varying amounts of EGF. The cells were then analyzed for β1 and FAK, using western blot and immunostaining techniques. As predicted, increased expression of β1, FAK, and downstream signaling proteins was directly correlated with increased concentrations of EGF and increased gel stiffness. Unexpectedly, inhibiting FAK caused cell size (a critical factor in reepithelialization) to significantly decrease rather than increase. These results suggest that β1, FAK, and downstream signaling proteins are important components of wound closure, but that further investigation must be occur in order to determine the underlying reasons behind the effects of such integrins on wound reepithelialization observed in this research.