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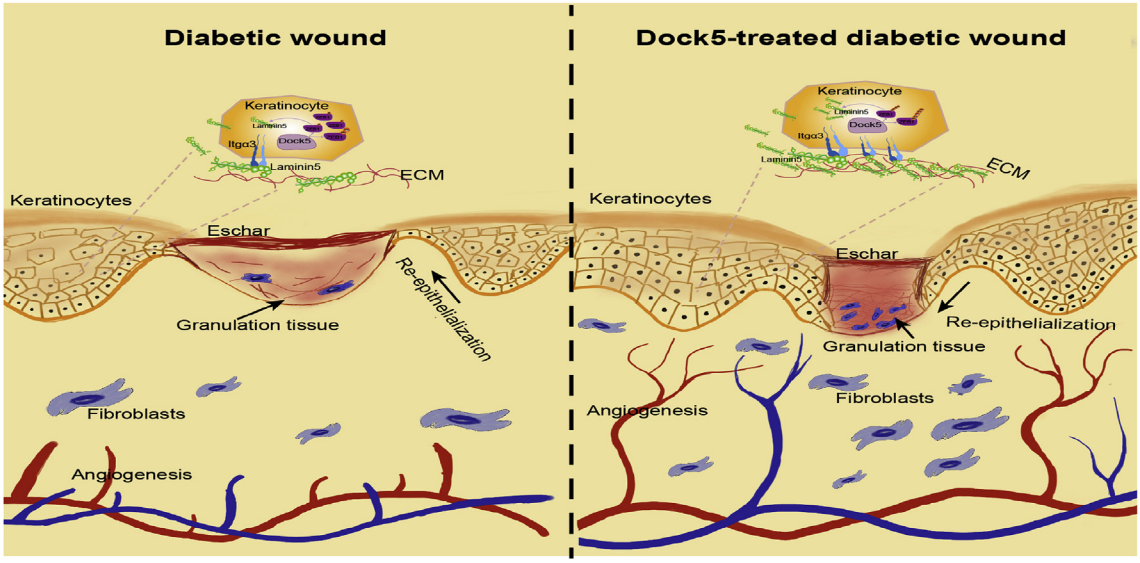
Dock5 activation facilitates diabetic wound healing

Cutaneous wound healing is a highly complex biological process composed of four relatively independent but overlapping phases: coagulation, inflammation, proliferation, and remodeling [1,2]. In the case of certain diseases, wound healing could get stuck in some phases, leading to the impairment of the whole process. For example, patients with diabetes tend to be bothered by diabetic foot ulcers (DFUs) [2]. Among these phases, the proliferative phase has attracted much attention within the field, which is characterized by re-epithelialization, neovascularization, and the formation of granulation tissue. Recently a research article published in *Diabetes* titled "Dedicator of cytokinesis 5 regulates keratinocyte function and promotes diabetic wound healing", Qu et al. addressed the potential role of dedicator cytokinesis 5 (Dock5) in this biological process. Through accelerating adhesion, migration and proliferation of keratinocytes during the proliferative phase, Dock5 promotes diabetic would healing [3].

It has been previously reported that Dock5, a member of the Dock superfamily, is associated with the protein-protein interaction process in several tissues [4]. In the aforementioned study, Qu et al. observed a dynamic increase of Dock5 expression level during the healing process, with its expression level reaching summit at the proliferative phase [3]. Using cultured keratinocytes, they demonstrated the regulatory role of Dock5 in cellular adhesion, migration, and proliferation *in vitro*. Further *in vivo* study showed that deletion of Dock5 led to impaired re-epithelialization, ECM remodeling, and granulation tissue formation. In terms of mechanism exploration, the authors found that the expression levels of one laminin-332 chain (LAMA3) and two integrin subunits (ITGA3 and ITGB4) were significantly changed after Dock5 deletion. Moreover, these three genes exhibited the same dynamic expression pattern as Dock5 during wound healing. Further studies illustrated that Dock5 regulates keratinocyte function and wound healing process through zinc finger E-Box binding homeobox 1 (ZEB1)/laminin-332/integrin signaling pathway, and that Dock5 directly decreases the half-life of the ZEB1 protein through increasing its ubiquitination and subsequently proteasomal degradation.

In addition, Qu et al. found that the expression levels of Dock5 in the skin samples of DFU patients and animal models are downregulated, and that restore of Dock5 expression in the wound edge of diabetic mice promotes wound healing. As such, the authors concluded that rescue of Dock5 expression may be explored as an effective therapeutic intervention for DFUs [3].

Taken together, in this study, Qu et al. demonstrated that the expression levels of Dock5 in the skin samples of DFU patients and animal models are decreased, and that restoration or activation of Dock5 in the wound edge of diabetic mice promotes wound healing. Currently, clinical treatment options for DFUs are still limited, therefore, new molecular targets are urgently needed within the field. Findings in this study identified Dock5 as a potential target for developing new treatments for DFUs, yet more investigation is required before clinical application.



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Summary scheme: Model depicting a pivotal role of Dock5 in diabetic wound healing. Dock5 activation facilitates keratinocyte adhesion, migration, and proliferation and improves re-epithelialization, granulation tissue formation, and extracellular matrix (ECM) deposition via ZEB1/laminin-332/integrin signaling.

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