

**Augmenting endogenous Wnt signaling improves skin wound healing.**

**Journal:** PLoS One

**Publication Year:** 2013

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**PubMed link:** 24204695

**Funding Grants:** Enhancing healing via Wnt-protein mediated activation of endogenous stem cells

**Public Summary:**

We work with a protein called Wnt, which is a potent stem cell activator. Wnt signaling is required for both the development and maintenance of the skin, yet whether it is important for skin wound repair was not clear. We used a genetic strain of mice to visualize the distribution of Wnt responsive cells, and found that the pattern of Wnt responsiveness varies with the hair cycle, and that it also correlates with wound healing potential. We used a biochemical approach that we developed to show that topical application of reconstituted Wnt3a protein results in better skin wound healing. Given the importance of Wnt signaling in the maintenance and repair of skin, liposomal Wnt3a may have widespread application in clinical practice.

**Scientific Abstract:**

Wnt signaling is required for both the development and homeostasis of the skin, yet its contribution to skin wound repair remains controversial. By employing Axin2(LacZ/+) reporter mice we evaluated the spatial and temporal distribution patterns of Wnt responsive cells, and found that the pattern of Wnt responsiveness varies with the hair cycle, and correlates with wound healing potential. Using Axin2(LacZ/LacZ) mice and an ear wound model, we demonstrate that amplified Wnt signaling leads to improved healing. Utilizing a biochemical approach that mimics the amplified Wnt response of Axin2(LacZ/LacZ) mice, we show that topical application of liposomal Wnt3a to a non-healing wound enhances endogenous Wnt signaling, and results in better skin wound healing. Given the importance of Wnt signaling in the maintenance and repair of skin, liposomal Wnt3a may have widespread application in clinical practice.

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