Improving Wound Healing Using α-gal: Antibody Stimulated Macrophage Directed Wound Healing

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INTRODUCTION: Macrophages are the crucial mediator of the wound healing response. Attracted by foreign bodies and inflammatory chemokines, they modulate the immune response and coordinate the transition to healing by the release of a variety of cytokines and growth factors. The α-gal epitope (Galα1-3Galβ1-4GlcNAc-R (α-gal) is abundantly synthesized on glycolipids and glycoproteins of non-primate mammals and New World monkeys by the glycosylation enzyme alpha1,3galactosyltransferase (alpha1,3GT)[1]. In humans, this epitope is absent because the α-1,3GT gene was inactivated in ancestral Old World primates[1]. Instead, humans produce the anti-Gal antibody (anti-gal), which specifically interacts with α-gal epitopes (primarily in the digestive tract) and which constitute approximately 1% of circulating immunoglobulins[2]. We hypothesized that direct application of α-gal into wounds would be a safe and novel method to stimulate macrophages on a limited basis and thus promote wound healing.

MATERIALS AND METHODS: Because wild type mice naturally express α-gal and thus do not express anti-gal, we used α-1,3galactosyltrasferase knockout mice (α-1,3GT KO mice), which were stimulated to produce anti-gal at titers comparable to humans. Bilateral 6 mm dorsal full-thickness splinted skin wounds were created and the mice were then treated with a one-time dose of α-gal nanoparticles directly into the wound. At post-op day 3, 6, and 9, two mice from each group were euthanized and the wounds were harvested for analysis.

Results: On post-op day 3, mice treated with α-gal containing nanoparticles demonstrated an increased rate of keratinization (average keratinocyte migration of 225.7 μm versus 143.1 μm, a 57.7% increased rate of healing; p value .23) By 6 days post-op, mice treated with α-gal containing nanoparticles demonstrated an even more significantly increased rate of keratinization (average keratinocyte migration of 2376 μm versus 986.4 μm, a 141% increased rate of healing p value .0002, with 3/4 experimental wounds demonstrating complete re-epithelialization versus only 1/4 controls). There were no systemic or local adverse effects seen in α-gal treated mice. All wounds were healed in both groups by day 9.

Conclusion: One-time application α-gal nanoparticles stimulated a significantly enhanced the wound healing response. This promising approach may be translated to human application, as a simple and natural means to enhance wound healing in both normal and pathologic conditions.

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