Regulatory T cells enhance tissue healing in mouse model

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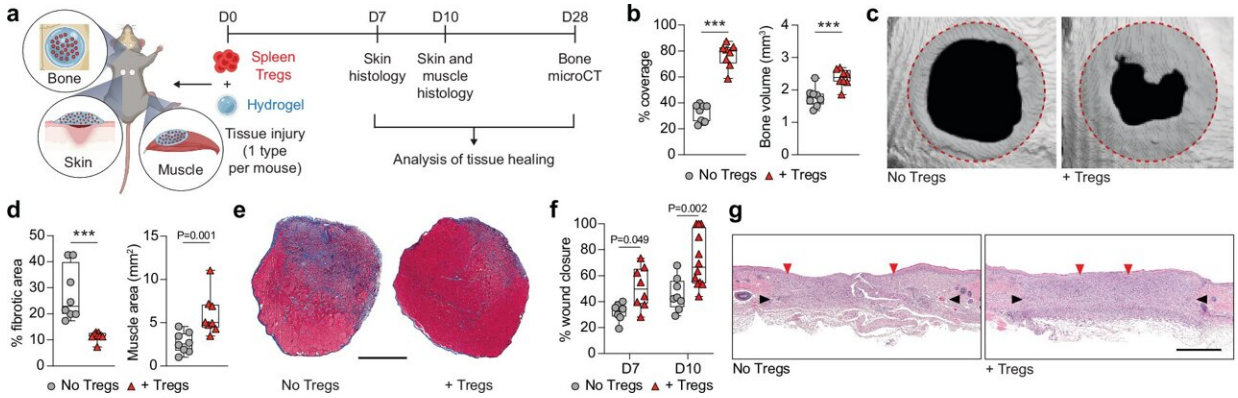

Local delivery of exogenous Tregs promotes healing of injured mouse tissues. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-51353-2

Investigators are constantly aiming to identify new therapeutic approaches for regenerative medicine. Recent strategies have focused on harnessing the power of the body's own tissue healing and repair mechanisms, including anti-inflammatory signaling molecules and immune cells.

Collaborating with Professor Shizuo Akira from IFReC, a research team led by Associate Professor Mikaël Martino from Monash University, who also held a cross-appointment position at Osaka University, recently published a significant advancement in regenerative medicine in *Nature*

Communications.

In the article, the researchers describe a potential new method involving administering regulatory T cells (Tregs) to enhance tissue healing.

Following tissue injury, certain immune cells initiate a pro-inflammatory response. To prevent chronic inflammation and further damage or disease, there must be a transition to an anti-inflammatory response to complete the healing process.

Although scientists have previously attempted to support regenerative medicine by modulating a patient's own immune cells, recent developments have seen researchers testing the effects of delivering specific cell types that can regulate both the immune system and tissue healing.

"We began exploring administering Tregs for regenerative medicine purposes because they can directly impact other immune cell types called monocytes and macrophages," says Mikaël Martino, lead author of the study. "Additionally, Tregs can secrete signaling molecules that support tissue healing. Despite their strong potential, few studies have explored using Tregs for such applications."

In this study, the team used a mouse model to simultaneously examine bone regeneration, muscle regeneration, and skin repair, ensuring the injuries were severe enough that therapeutic intervention was necessary. Using a cell delivery method called fibrin hydrogel, they then locally delivered Tregs to the injured areas.

"Compared with those administered fibrin hydrogel without Tregs, mice given Tregs showed enhanced bone volume and coverage over injured cranial areas, higher amounts of muscle tissue and larger muscle fiber size, and faster skin wound closure," explains Shizuo Akira, a senior

author of the study.

Further mechanistic investigation indicated that the administered Tregs take on an injury-specific phenotype once in the damaged area. In doing so, the Tregs display increased expression levels of genes related to immunomodulation and tissue healing.

Additional experiments demonstrated that the Tregs can cause the monocytes and macrophages in these tissues to switch to an anti-inflammatory state, specifically by secreting signaling molecules such as interleukin-10 (IL-10).

"Interestingly, we observed that when the gene encoding IL-10 is knocked out of the Tregs, their pro-healing effects are lost," says Martino. "This finding indicates the key role of IL-10 in how these Tregs support tissue repair and regeneration."

Overall, this study provides evidence of the strong potential of using Tregs as a cell-based therapy for regenerative medicine. These data will help develop innovative treatment methods that can promote tissue healing.

More information: Bhavana Nayer et al, Local administration of regulatory T cells promotes tissue healing, *Nature Communications* (2024). DOI: 10.1038/s41467-024-51353-2

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