Published Paper:

Nature Communications volume 14, Article number: 5995 (2023) Doi: 10.1038/s41467-023-41608-9

Tracing immune cells around biomaterials with spatial anchors during large-scale wound regeneration

Yang Yang[1,2], Yi Man[1*], Yili Qu[2*]

[1] Department of Oral Implantology & State Key Laboratory of Oral Diseases and National Clinical Research Center for Oral Diseases, West China Hospital of Stomatology, Sichuan University; Chengdu 610041, China.

[2] Department of Prosthodontics & State Key Laboratory of Oral Diseases and National Clinical Research Center for Oral Diseases, West China Hospital of Stomatology, Sichuan University; Chengdu 610041, China.

[*] Corresponding author. Email: manyi780203@126.com (Y.M.) & qqyili@126.com (Y.Q.)

ABSTRACT

Background and purpose: After severe skin damage, the resulting scar usually contains dense extracellular matrix (ECM) fibers devoid of the hair follicle, which lack sensation and endocrine function as well as the flexibility of normal skin. The immune system plays a varying role in driving scar fibrosis or hair follicle regeneration upon different environmental stimuli. Recently, tissue regeneration mediated by immunoregulatory biomaterials is emerging as a prospective strategy in tissue engineering. The biomaterials ' topographical properties, such as pattern and diameter, play important roles in influencing cell activities and manipulating the related immune response during wound regeneration. As a result, there is an urgent need to explore the immunoregulatory mechanisms stimulating hair follicle regeneration in skin repair.

Methods: Here we present a method for skin wound regeneration using biodegradable aligned ECM scaffolds with different diameters: A300 (319 ± 100 nm), A600 (588±132nm), and A1000 (1048 ± 130 nm). Currently, development in single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics (ST) has enabled the assessment of gene expression at spatial resolution, which has been applied to detect regional cellular communication. The large-scale wound healing model with implanted biomaterials provides an ideal method to understand and probe the role of the immune system in tissue regeneration.

Conclusions: We show that the implantation of A300 scaffolds accelerates wound coverage and enhances hair follicle neogenesis. Multimodal profiles highlight the potential role of regulatory T cells in mitigating tissue fibrous by suppressing excessive type 2 inflammation. We find that immunodeficient mice lacking mature T lymphocytes show the typical characteristic of tissue fibrous driven by type 2 macrophage inflammation, validating the potential therapeutic effect of the adaptive immune system activated by biomaterials. These findings contribute to our understanding of the coordination of immune systems in wound regeneration and facilitate the design of immunoregulatory biomaterials in the future.

KEYWORDS

Biomaterials, Skin regeneration, Immunoregulatory effects, Single-cell RNA sequencing, Spatial transcriptomics