

# 恭賀陳志強醫師論文 刊登Cell期刊





Volume 161, Issue 2, 9 April 2015, Pages 277-290

Article

# Organ-Level Quorum Sensing Directs Regeneration in Hair Stem Cell Populations

Chih-Chiang Chen<sup>1, 2, 3</sup>, Lei Wang<sup>4</sup>, Maksim V. Plikus<sup>5, 6, 7</sup>, Ting Xin Jiang<sup>1</sup>, Philip J. Murray<sup>8</sup>, Raul Ramos<sup>5, 6, 7</sup>, Christian F. Guerrero-Juarez<sup>5, 6, 7</sup>, Michael W. Hughes<sup>9</sup>, Oscar K. Lee<sup>10</sup>, Songtao Shi<sup>11</sup>, Randall B. Widelitz<sup>1</sup>, Arthur D. Lander<sup>5, 7, 12</sup>, Cheng Ming Chuong<sup>1, 3, 13,</sup>

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doi:10.1016/j.cell.2015.02.016

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#### A Collective Path toward Regeneration

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# Highlights

- · Quorum sensing underlies collective regenerative behavior in a hair follicle population
- Sensing occurs via injury → CCL2 → macrophage → TNF-α → hair regeneration pathway
- · Coupling molecular diffusion and cell mobility achieves a long signaling length scale
- · Stem cell social behavior can be exploited to enhance the reliability of regeneration

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## Summary

Coordinated organ behavior is crucial for an effective response to environmental stimuli. By studying regeneration of hair follicles in response to patterned hair plucking, we demonstrate that organ-level quorum sensing allows coordinated responses to skin injury. Plucking hair at different densities leads to a regeneration of up to five times more neighboring, unplucked resting hairs, indicating activation of a collective decision-making process. Through data modeling, the range of the quorum signal was estimated to be on the order of 1 mm, greater than expected for a diffusible molecular cue. Molecular and genetic analysis uncovered a two-step mechanism, where release of CCL2 from injured hairs leads to recruitment of TNF-α-secreting macrophages, which accumulate and signal to both plucked and unplucked follicles. By coupling immune response with regeneration, this mechanism allows skin to respond predictively to distress, disregarding mild injury, while meeting stronger injury with full-scale cooperative activation of stem cells.

## Graphical Abstract

