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Friend or Foe: Inflammation in tissue regeneration and diseases

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Abstract

Tissue regeneration is a multi-step process mediated by diverse cellular hierarchies and states that are also implicated in tissue dysfunction and pathogenesis. Tissue injury instigates an inflammatory response by modulating immune system in the wound sites, which is essential for restoration of tissue homeostasis. However, signalling between stem cells and immune system is poorly understood. Alveolar type 2 (AT2) cells function as stem cells by self-renewing and differentiating into alveolar type 1 (AT1) cells that are essential for gas-exchange in the lung. However, how AT2 cells are activated from the quiescence and which trajectory they follow to differentiate into AT1 cells remain unknown. Here, we leveraged single-cell RNA sequencing in combination with in vivo lineage tracing and organoid models to finely map the trajectories of alveolar lineage cells during injury repair and lung regeneration. We identified how injury remodels immune system and inflammatory niches driven my macrophage dynamics orchestrate tissue regeneration during injury repair in the lungs. We also identified a distinct AT2-lineage population, Damage-Associated Transient Progenitors (DATPs), that arises during alveolar regeneration. Further, we found that chronic inflammation prevents AT1 differentiation, leading to aberrant accumulation of DATPs and impaired alveolar regeneration in chronic human lung diseases.

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