Stem Cells and Their Dynamic Niche in Lung Repair and Regeneration

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Abstract

In the lung, alveolar type II cells (AT2) serve as facultative stem cells that slowly produce alveolar cells throughout the life time but dramatically expand to replace the lost epithelium after injury. How this process is orchestrated at the cellular level and what are the underlying mechanisms that modulate their cell fate and ensure efficient regeneration remain obscure. Here we used a 3D organoid co-culture of AT2 stem cells and immune cells to determine the functional impact of inflammatory niche on stem cell behaviors. Single cell RNA-sequencing on cells from co-cultures led us to dissect cell fate transitions from AT2 stem cells to alveolar type I (AT1) lineage, which is modulated by immune cells. In particular, we discovered a new regulatory mechanism that operates between interstitial macrophages and AT2 cells to induce AT1 differentiation. Our results reveal the differentiation trajectory of AT2 cells into AT1 cells and show that a transient inflammatory niche orchestrates lung repair via directly governing the cellular and molecular behavior of AT2 stem cells by priming stem cell activity and directing lineage differentiation and maturation. Importantly, our organoid coculture recapitulates the cellular response of alveolar regeneration during repair of injury.

Keywords: *Stem Cells, Niche, Regeneration*

Biography

Dr. Lee established her own research group at the Wellcome Trust - MRC Stem Cell Institute in 2016 and her group focuses on understanding cellular behaviour and regulatory networks of adult stem cells and niche cells. She is currently a Faculty member at the Department of Physiology, Development, and Neuroscience, University of Cambridge and was recently awarded with the Wellcome Trust Sir Henry Dale Fellowship and ERC starting grant.