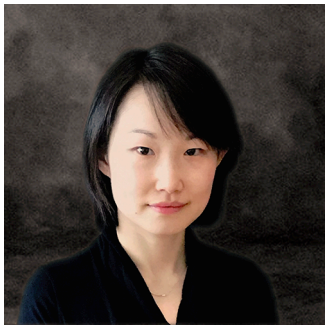
SickKids | PETER GILGAN CENTRE FOR RESEARCH AND LEARNING

# Models of Congenital Malformation and Disease

## Faculty Search Seminar




## Dr. Mu He

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# The molecular cell atlas of mammalian airway in development and disease state


The conducting airway for air passage forms a protective mucosal barrier and presents the primary target of various airway disorders. Previous studies utilizing single cell RNA sequencing (scRNAseq) have systematically characterized airway cell types in adults and lineage networks within the developed airway in normal and chronic inflammatory conditions. Whether the same programs for airway regeneration in adults are also operating during embryogenesis, however, remains an open question. To better understand how the airway developmental programs are established to support air breathing and the barrier functions in newborns, we constructed a single-cell atlas of the human and mouse developing airway. Our data reveal, hitherto unrecognized heterogeneity of cell states with distinct differentiation programs and immune features associated with the airway epithelium. Ciliated cells, one of the major cell types found in the airway epithelium, form motile cilia and generate efficient ciliary flow essential for mucus clearance. From our transcriptomic analysis, we identified gene modules associated with embryonic ciliated cells and postnatal ciliated cells, as well as a ciliated precursor state conserved in mice and humans. Furthermore, we identified a cell cluster exhibiting two sets of gene modules, the *Foxj1* associated cilia module and the *Gp2* associated secretory module. This cell state has not been observed in adult airway during homeostasis and regeneration. In parallel, we characterized a mouse mutant that shows altered epithelial cell landscape and multiple airway defects, including mucous cell hyperplasia and abnormal mucociliary clearance. Our data suggest that efficient mucociliary clearance depends on both ciliated cells and secretory cells. Our study illuminates unique programs for mammalian airway development and present a tractable mouse model for understanding the cellular processes required for airway differentiation and mucosal barrier function.


**Monday | January 20th | 2020 | 3 pm**

**PGCRL Event Room 1**

Hosts: Drs. Brian Ciruna & John Brumell

*Dr. Mu He is being interviewed for a Scientist position at the Research Institute*