Lung Biology Research & Trainee Day
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Category: Staff/Tech/Other
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Title: Single cell transcriptomic profiling identifies molecular phenotypes of newborn human lung cells
Abstract: Rationale: While animal model studies have extensively defined mechanisms controlling cell diversity in the developing mammalian lung, the limited data available from late stage human lung development represents a significant knowledge gap. The NHLBI Molecular Atlas of Lung Development Program (LungMAP) seeks to fill this gap by creating a structural, cellular and molecular atlas of the human and mouse lung. Methods: Single cell RNA sequencing generated transcriptional profiles of 5500 cells obtained from two one-day old human lungs from the LungMAP Human Tissue Core Biorepository at the University of Rochester. Frozen single cell isolates were captured, and library preparation was completed on the Chromium 10X system. Data was analyzed in Seurat, and cellular annotation was performed using the ToppGene functional analysis tool. Single cell sequence data from 32000 postnatal day 1, 3, 7 and 10 mouse lung (n = 2 at each time point) cells generated by the LungMAP Research Center at Cincinnati Children's Hospital and Medical Center, using Dropseq platform, was integrated with the human data. In situ hybridization was used to confirm the spatial location of cellular phenotypes. Results: Transcriptional interrogation of donor newborn human lung cells identified distinct clusters representing multiple populations of epithelial, endothelial, fibroblasts, pericytes, smooth muscle, and immune cells and signature genes for each of these populations were identified. Computational integration of newborn human and postnatal mouse lung development cellular transcriptomes facilitated the identification of distinct cellular lineages among all the major cell types. Integration of the human and mouse cellular transcriptomes also demonstrated cell type-specific differences in developmental states of the newborn human lung cells. In particular, matrix fibroblasts could be separated into those representative of younger cells (n=393), or older cells (n=158). This is the first comprehensive molecular map of the cellular landscape of neonatal human lung, including biomarkers for cells at distinct states of development. Our results indicate that integrated single cell RNA profiling of human and mouse lung will help identify common and species-specific mechanisms of lung development and respiratory disease.