Researchers optimize lung stem cell engineering process

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The Center for Regenerative Medicine (CReM) at Boston University and Boston Medical Center has engineered two new categories of lung epithelial cells in vitro using pluripotent stem cells. Published in *Stem Cell Reports*, CReM researchers detailed their use of single cell RNA sequencing, a state-of-the-art technique they employed to generate the most comprehensive profile to date of air sack-like (alveolospheres) and airway-like (bronchospheres) cells derived from pluripotent stem cells. These profiles are new components associated with the Center's Open Source stem cell repository and can be used to create lung tissue in vitro enabling the testing of new drug treatments for a variety of lung diseases.

Diseases affecting the lung, including emphysema, cystic fibrosis, acute respiratory distress syndrome and pulmonary fibrosis, cause considerable morbidity and mortality in the US. However, there are not many treatment options available for those diseases, in part due to the limited availability of human lung cells for research.

Creating human lung epithelial cells in the lab has been a challenge, and lineage-specific reporters, which indicate each cell's specific type, are key to understanding lung epithelial stem cell development. In this study, the researchers used both murine and human pluripotent stem cell lines with airway secretory lineage reporters, which enables their tracking, purification and profiling. Mapping the expression profiles of all genes one cell at a time revealed unexpected heterogeneity in the stem cell-derived lung cells, and the research team at the CReM used this information to improve the airway cells engineered in the lab.

"With our collaborators, we were able to identify factors that we can use to more optimally generate patient-derived lung cells in vitro," said Katie McCauley, PhD, a post-doctoral fellow in the CReM and the study's first author.

CReM's pioneering research using induced pluripotent stem cells (iPSCs), which self-renew indefinitely as undifferentiated cells that become specific adult cell types, has helped create an inexhaustible source of disease- or patient-specific stem cells. Researchers use these cells to construct disease models in a lab and test potential treatments for a variety of diseases affecting the lungs. In 2014, the National Institutes of Health helped to fund the first of its kind lung stem cell repository, which provides researchers open (free) access to the different types of induced pluripotent lung cells to use in their laboratories.

"These findings help us stay true to our mission of Open Source sharing of datasets, cells, and protocols with our colleagues who are dedicated to applying these tools to one day help patients," said senior author Darrell Kotton, MD, the David C. Seldin Professor of Medicine at BU School of Medicine and Director of the CReM of Boston University and Boston Medical Center. "The global research community now has access to this information, which they can use to better understand these newly engineered cells and more quickly develop disease-specific cell line models that can be used to test new therapies and treatments for diseases."

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