CHINESE-AMERICAN LUNG ASSOCIATION

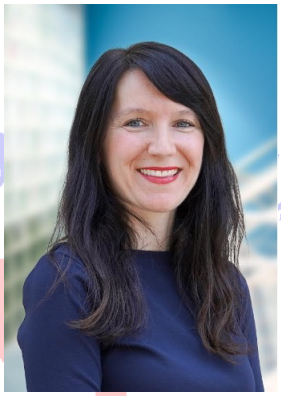
CALA Happy Friday Seminar

April 8th, 2022

Time: EST 10:30 am; PST: 7:30 am; Beijing time: 10:30pm

Zoom: 849 9682 9273 (Password: 654321)

Dissecting alveolar patterning and maintenance at single-cell resolution



Astrid Gillich, PhD
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Bio: Dr. Gillich completed her undergraduate studies in Biotechnology at the University of Natural Resources and Life Sciences in Vienna and her PhD in Stem Cell Biology at the University of Cambridge. As a graduate student with Azim Surani she studied mechanisms of epigenetic reprogramming in the mammalian germ line. Dr. Gillich then joined the lab of Mark Krasnow in the Department of Biochemistry at Stanford University as a postdoctoral researcher where she investigated mechanisms of alveolar formation in the lung. She is now a Principal Investigator at Calico Life Sciences in San Francisco. Her lab aims to understand the cellular and molecular programs governing the patterning, maintenance and repair of the lung, and what goes wrong with these programs as our lungs age and in age-associated diseases.

Abstract: In mammalian lungs gas exchange occurs in thin-walled air sacs called alveoli, which are surrounded by a dense mesh of capillaries. Defects in patterning, maintenance or repair of alveoli lead to diseases that compromise gas exchange, including chronic diseases such as bronchopulmonary dysplasia, pulmonary fibrosis and chronic obstructive pulmonary disease, as well as the acute respiratory distress syndromes accompanying severe alveolar injury or virus-induced damage, as in Covid-19. Despite the tremendous disease burden and the urgent need for therapies, the mechanisms that establish and maintain the pattern and architecture of alveoli are not well understood. Here we use mosaic genetic labeling, single-cell RNA-sequencing and high-resolution deep imaging to elucidate the three-dimensional structure and cellular composition of alveoli. We show that an alveolus in the mouse lung is composed of only 10-15 cells of seven different types, each with a remarkable, distinctive structure. Two of them are intermingled capillary cell types with complex ‘swiss cheese’ morphologies and distinct functions. One cell type that we name the ‘aerocyte’ is specialized for gas exchange and unique to the lung. The other cell type, termed ‘general capillary’, is specialized to regulate vasomotor tone and functions as a progenitor cell in capillary maintenance and repair. By mapping alveolar development at single-cell resolution at a defined position in the lung, we find that alveoli form surprisingly early by budding of epithelial cells out from the airway stalk between enwrapping smooth muscle cells that rearrange into a ring of myofibroblasts at the alveolar entrance. Our analysis suggests a novel mechanism of alveolar formation and provides the foundation for investigations of the structure, function and maintenance of the gas exchange surface in health, disease, aging and evolution.