Lung Biology Research & Trainee Day
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Title: Mapping Pediatric and Adult Lung During a Pandemic
Abstract: Understanding the susceptibilities and resilience of the human respiratory tract and immune system has never been more urgent than in the years of the SARS-CoV2 pandemic. In this last 18 months, the members of the Lung Molecular Atlas Program human tissue core at the University of Rochester have been very active in both local and cross-consortia activities. We have grown the Biorepository for Investigation of Diseases of the Lung (BRINDL) by over 104 cases, 67 25 years of age as we took on the task of building a repository of COVID-19+ lung tissue. To date, we have banked tissue and cells from more than 12 individuals who died of COVID-19 pneumonia and 14 with a history of SARS-CoV-2 infection within 6 months who died of unrelated causes. BRINDL also contains 14 comparable aged donors with no evidence of SARS-CoV-2 infection. We have confirmed and ruled-out SARS-CoV-2 infection history by nucleocapsid PCR on lower airway swabs, tissue immunostaining and ELISA for SARS-CoV2 S-protein antibody in each case. Nucleocapsid PCR remained positive, with increasing cycles for detection, until approximately 40 days after symptom onset. One case remained PCR and immunohistochemistry positive for viral RNA and protein at 119 days after infection. In this case PCR was confirmed positive for only one of two nucleocapsid RNA. Plasma/lung homogenate anti-SARS-CoV2 spike protein trimer antibody was positive as early at 7-9 days after reported symptom onset and persisted up to approximately 150 days, although antibody was not detectable in two at 22-28 days and six out of ten between 42 and 180 days after infection. Tissue immunostaining for nucleocapsid protein was positive in 18 out of 22 cases in which it has been tested to date. The pattern of viral protein detection varies widely between cases and is particularly diffuse in a 14-year-old who had recovered from symptomatic COVID illness. Viral protein has been detected in airway epithelium but also in submucosal gland epithelium and scattered in alveolar cells. Routine histology identifies organizing diffuse alveolar disease with hyaline membranes in those succumbing rapidly to COVID-19 pneumonia with severe acute neutrophilic and lymphocytic infiltration while longer survivors demonstrate areas of organized thromboses and fibrosis. In addition to local repository work, LungMAP samples have been published in snRNAseq and sn ATACseq datasets and analyses including three publications addressing age and cell related expression of SARS-CoV2 receptors and cell entry mechanisms. We also have contributed to standardizing lung cell nomenclature, cell and structural ontologies as well as identification of RNA and protein biomarkers of up to xx cell types in a Cell Cards publication and in a cross-consortium Common Coordinates Framework interactive structure-cell-gene-protein tools.