408. Single-cell Sequencing Identifies Variability in Host Response Among Different Genera of Influenza Viruses
Beth Kristine. Thielen, MD, PhD; Jaime Christensen; Anna K. Strain, PhD; Steven Shen, MD, PhD; and Ryan Langlois, PhD; 1University of Minnesota, Minneapolis, Minnesota; 2Minnesota Department of Health, St. Paul, Minnesota
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Background. Seroprevalence and surveillance studies indicate that influenza C virus (ICV) infection is common among humans, and initial exposure occurs early in life. ICV often causes milder disease than influenza A and B viruses, but the mechanisms underlying differences in pathogenicity remain poorly understood.

Methods. To compare early events of infection in natural target sites, we cultured primary human tracheal/bronchial epithelial cells under air-liquid interface conditions to allow differentiation. We infected these cells with human strains of influenza A, B or C virus. Cells were infected at low MOI (0.1) to ensure populations of directly infected cells and uninfected neighboring cells. To compare the early immune response and cell tropism among these viruses, we performed single-cell RNA sequencing of mock- and influenza-infected cells. In parallel, we infected cells pretreated with interferon to mimic later rounds of infection after an early immune response is initiated.

Results. Infection of primary cells by all three viruses was confirmed by RT-qPCR of bulk cell lysates. As expected, prior exposure to interferon B results resulted in reduced levels of viral transcripts. At the single-cell level, we identified expression of genes associated with specific cell types, including basal, ciliated and secretory cells. We also identified expression of interferon stimulated genes, but these genes were not homogeneously expressed among all cell subpopulations and varied among cultures infected with different influenza viruses. We also found distinct differences in gene expression in cells previously exposed to interferon, suggesting that host environment varies over subsequent rounds of infection.

Conclusion. Single-cell sequencing is an important tool for studying the host response to influenza infection in complex cellular environments such as the respiratory tract, in which cells vary in their susceptibility to infection and antiviral response. Further analysis will characterize differences among directly infected vs. neighboring cells and correlate responses with pathogenicity.

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409. Using the Host Response to Reduce Unnecessary Antibiotic Use in Outpatient Acute Respiratory Infections
Robert Sambursky, MD and Annie Bell, MSN, APN; RPS Diagnostics, Sarasota, Florida
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Background. Acute respiratory tract infections (ARI) often resolve without antibiotics. Yet, antibiotics are prescribed in 60–98% of cases despite lack of confirmed bacterial etiology. Antigens, culture and molecular testing identify pathogens; however, do not differentiate colonization from invasive infection. Since antibiotics are often prescribed despite the low prevalence of confirmed bacterial infection in patients with ARI, we analyzed the impact of adding host response biomarkers to the clinical and microbiological evaluation of outpatients with ARI.

Methods. A secondary analysis was performed using data from two suspected ARI cohorts derived from two clinical studies. A clinical reference algorithm, which included bacterial culture, respiratory PCR panels for viral and atypical pathogens, procalcitonin, CBC, serology, and Myxovirus resistance protein A (MxA), was used to define infection based on pathogen detection plus host response and classify infections that may benefit from antibiotics. Antibiotics were considered “warranted” if patients exhibited a bacterial-specific host response, with or without bacterial pathogen detection, and a detected bacterial pathogen without a host response was deemed to be colonization and “at risk for antibiotics.” The percentage requiring antibiotics was calculated by dividing the number of patients with a host response for bacteria by the total number of patients at risk for receiving antibiotics (warranted + at risk). A Chi-square test was performed to determine the difference between patients likely to be treated with antibiotics, bacteria detected with or without host response and bacteria detected with a host response.

Results. Each dataset (Self, n = 205) and (Shapiro, n = 229) was analyzed separately and pooled (n = 445). Upon enrollment, 15% (Self) and 55% (Shapiro) were febrile. A pathogen was detected in 67% (Self) vs. 82% (Shapiro) subjects. Reduction in antibiotic prescription was calculated to be 35–44%. (P < 0.001–0.004), with host response was evaluated in addition to bacterial pathogen detection. Results presented in Table 1.

Conclusion. Host response may aid in differentiating viral infection and bacterial colonization from invasive bacterial infections requiring antibiotics.