BTS/BALR/AUK-BLF Early Career Investigator Symposium

T1 THE LOCAL AND SYSTEMIC RESPONSE TO SARS-COV-2 INFECTION IN CHILDREN AND ADULTS

¹KB Worlock, ^{1,2}M Yoshida, ³RGH Lindeboom, ³N Huang, ⁴CR Butler, ³N Kumasaka, ³C Dominguez Conde, ³L Mamanova, ³L Bolt, ³L Richardson, ³K Polanski, ^{3,5}E Madisson, ¹JL Barnes, ¹J Allen-Hyttinen, ⁶E Kilich, ⁴BC Jones, ⁶A de Wilton, ³A Wilbrey-Clark, ³W Sungnak, ³JP Pett, ³E Prigmore, ^{1,6}H Yung, ^{1,6}P Mehta, ⁷A Saleh, ⁷A Saigal, ⁷V Chu, ⁶JM Cohen, ⁷C Cane, ⁷A Iordanidou, ⁴S Shibuya, ⁸A-K Reuschl, ⁹AC Argento, ⁹RG Wunderink, ⁹SB Smith, ⁹TA Poor, ⁹CA Gao, ⁸JE Dematte, ⁹NU SCRIPT Study Investigators, ¹⁰G Reynolds, ¹⁰M Haniffa, ¹¹GS Bowyer, ^{11,12}M Coates, ¹¹MR Clatworthy, ¹³FJ Calero-Nieto, ¹³B Göttgens, ⁴C O'Callaghan, ⁴NJ Sebire, ⁸C Jolly, ⁴P de Coppi, ⁴CM Smith, ⁹AV Misharin, ^{1,6}SM Janes, ^{3,14}SA Teichmann, ³KB Meyer, ^{1,6}MZ Nikolić. ¹UCL Respiratory, Division of Medicine, University College London, London, UK; ²Division of Respiratory Diseases, Department of Internal Medicine, Jikei University School of Medicine, Tokyo, Japan; ³Wellcome Sanger Institute, Cambridge, UK; ⁴NIHR Great Ormond Street BRC and UCL Institute of Child Health, London, UK; ⁵European Molecular Biology Laboratory - European Bioinformatics Institute, Cambridge, UK; ⁶University College London Hospitals NHS Foundation Trust, London, UK; ⁷Royal Free Hospital NHS Foundation Trust, London, UK; ⁸UCL Division of Infection and Immunity, University College London, London, UK; ⁹Division of Pulmonary and Critical Care Medicine, Northwestern University Feinberg School of Medicine, Chicago, USA; ¹⁰Biosciences Institute, Newcastle University, Newcastle upon Tyne, UK; ¹¹Department of Medicine, University of Cambridge, Cambridge, UK; ¹²Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; ¹³Wellcome - MRC Cambridge Stem Cell Institute, University of Cambridge, Cambridge, UK; ¹⁴Department of Physics/Cavendish Laboratory, University of Cambridge, Cambridge, UK

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Introduction and Objectives Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the current coronavirus disease 2019 (COVID-19) pandemic. Whilst a substantial proportion of adults infected with SARS-CoV-2 progress to develop severe disease, children rarely manifest respiratory complications. However, the underlying mechanism behind this disparity remains largely unknown. Understanding the differences in the local and systemic response to SARS-CoV-2 infection at single cell resolution between children and adults may offer key clues about the pathogenesis of SARS-CoV-2 infection, providing guidance for future therapies and treatments.

Methods To address this we generated a healthy reference multi-omics single cell data set from children (n=30) from infancy to adulthood (n=11). Here we profiled triple matched samples: nasal and tracheal brushings and PBMCs for single cell analysis, where we tracked the developmental changes for 59 airway and 45 blood cell populations at both

transcriptomic and proteomic level. These were then contrasted with equivalent data from paediatric and adult COVID-19+ patients collected across a range of disease severities (total n=32), enabling age and disease-specific variances to be analysed at single cell level.

Results Striking differences within the paediatric and adult immune responses in COVID-19 were observed, including an overall weaker interferon-response signature, with fewer interferon-stimulated immune cell subpopulations within children infected by SARS-CoV-2 compared to adults. In peripheral blood, a greater proportion of naïve cell populations was observed with disease, with the response in adults primarily dominated by the adaptive immune system. In the airway epithelium, we found the highest viral load in goblet and ciliated cells in infected adults and most notably, described a novel inflammatory epithelial cell population, enriched within our COVID-19 patients, representing a transitional regenerative state between secretory and ciliated cells. Through the integration of matched blood and airway samples we were able to investigate the dynamics between local and systemic response to COVID-19, finding marked differences.

Conclusions Overall, this largest paediatric single cell COVID-19 study to date showed significant differences in response to SARS-CoV-2 between children and adults, reflecting the changes of the immune landscape over developmental time, which in children are dominated by naïve and innate responses.

T2 CLUSTER ANALYSIS OF TRANSCRIPTOMIC DATASETS TO IDENTIFY ENDOTYPES OF IDIOPATHIC PULMONARY FIBROSIS

^{1,2}LM Kraven, ²AR Taylor, ^{3,4}PL Molyneux, ^{3,4,5}TM Maher, ²AJ Yeo, ²WA Fahy, ^{3,4}RG Jenkins, ^{1,6}LV Wain. ¹Department of Health Sciences, University of Leicester, Leicester, UK; ²Research and Development, GlaxoSmithKline, Stevenage, UK; ³Royal Brompton Hospital, London, UK; ⁴National Heart and Lung Institute, Imperial College, London, UK; ⁵Keck School of Medicine, University of Southern California, Los Angeles, California, USA; ⁶National Institute for Health Research, Leicester Respiratory Biomedical Research Centre, Glenfield Hospital, Leicester, UK

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Rationale Considerable clinical heterogeneity in Idiopathic Pulmonary Fibrosis (IPF) suggests the existence of multiple disease endotypes. Identifying these endotypes could allow for

Abstract T1 Figure 1