P118 | Early distinct immune responses in COVID-19 vaccine-breakthrough versus non-vaccinated patients

C. Holetschek[1,2], M. Goekkaya[1,2], D. Luschkova[1], P. Eder[1], D. Rauer[1,2], C. Römmele[3], G. Gorochov[4,5], C. Traidl-Hoffmann[1,2], A. Neumann[1,2]

[1]University of Augsburg, Environmental Medicine, Medical Faculty, 86156 Augsburg, Germany; [2]Helmholtz Center Munich, Institute of Environmental Medicine, 85764 Munich, Germany; [3]Uniklinikum Augsburg, Medizinische Klinik III, 86156 Augsburg, Germany; [4]University Hospitals Pitié Salptrière, Department of Immunology, 75013 Paris, France; [5]Sorbonne Université, Centre d Immunologie et Maladies Infectieuses (CIMI), 75013 Paris, France

Background: COVID-19 patients show a versatile range of severity from asymptomatic to critical conditions requiring hospitalization. SARS-CoV-2 vaccination reduces the probability for severe disease. However, the correlates of immune protection against severe disease still need to be clarified as a function of vaccination status. We investigated multiple dimensions of the immune response, including single-cell proteomics, in vaccine-breakthrough (VB) versus non-vaccinated (NV) patients, early after becoming SC2 positive, in correlation with severity.

Materials and Methods: Patients (N=270) were recruited at their first SC2 positive test or early after, and four samples were taken within the first month. Serum cytokine levels were measured by ultra-sensitive ELISA (Simoa, Quanterix). PBMCs were analyzed by singe-cell intra-cellular-staining (ICS) cytometry, Elispot, and single-cell CyTOF, before/after stimulation with Spike and Nucleocapsid peptide pools.

Results: In NV, two cytokine combinations accurately (>95%) predicted either symptom severity, mainly by type-I-interferon and IL-17, or risk of hospitalization, by the ratio of type-I-interferon to inflammatory cytokine levels.

This is different for NV and VB infections in non-hospitalized patients. The cytokine profile in VB was significantly skewed to that of asymptomatic NV.

Asymptomatics show a significantly higher frequency of Th1-related cytokine expression and a higher level of poly-functional CD4 T-cells expressing multiple cytokines.

VB asymptomatic patients exhibit an early significantly higher antibody response against the Spike antigen, in combination with a significantly stronger Spike-specific CD4 and CD8 T-cell response.

Interestingly, antibody response and Th2-related CD4 expression were not higher in NV asymptomatic patients.

Conclusions: COVID-19 severity can be accurately predicted in NV and VB as early as seven days post symptoms, which is important for guiding personalized treatment. Lower disease severity in VB is associated with a different cytokine profile than in NV patients, in correlation with SC2-specific T-cell response, which is important for guiding future vaccine development.

A potent anti-nucleocapsid CD4 Th1 response, associated with lower viral loads and lower inflammatory cytokine levels, characterizes the

asymptomatic disease course. More severe patients have less potent SC2-specific T-cell response, higher viral loads, and higher levels of inflammatory cytokines, apparently produced by monocytes rather than particular T-cells.

Keywords: SARS-CoV-2, Prediction, Inflammatory Cytokines, Type-I Interferon, Single Cell Analysis