

CYTOKINE PROFILE IN PATIENTS WITH PRIMARY ANTIBODY DEFICIENCY IN RESPONSE TO SARS-COV-2 ANTIGEN

Zane Lucāne¹, Sindija Papirte¹, Gita Gersone¹, Dagnija Straupmane², Baiba Šlisere², Baiba Vilne³, Linda Gailīte¹, Pēteris Tretjakovs¹, Natalja Kurjāne¹

¹Rīga Stradiņš University

²Pauls Stradins Clinical University Hospital

³Bioinformatics Laboratory, Rīga Stradiņš University

Objectives. An increased COVID-19 related morbidity and mortality has been reported in patients with primary antibody deficiencies. Immunization may therefore be particularly important in these patients. Specific cytokine signatures have been shown to be related to vaccine immunogenicity. Our aim was to investigate the cytokine profile that characterize the immune response to SARS-CoV-2 antigen *in vitro* in patients with primary antibody deficiency.

Materials and Methods. Study included 38 subjects: 31 patients with primary antibody deficiency and 7 healthy controls. We reviewed patient's clinical records to collect demographic and clinical data. QuantiFERON tubes were used for blood collection and sample incubation with SARS-CoV-2 spike-specific antigens or negative control for further analysis of IFN- γ production using an ELISA and IL-1 β , IL-4, IL-6, IL-10, IL-15, IL-17A, IL-21, TNF- α and TGF- β detection using xMAP technology.

Results. Of the 38 individuals (31.6% men; mean age 42.26, SD = 13.1), 28 patients and 7 controls had completed the vaccination regimen with a median time 164 (IQR = 114) days after vaccination. Overall, we found statistically significant increase in levels of INF- γ ($p < 0.001$), IL-10 ($p = 0.002$), IL-15 ($p = 0.008$), IL-17A ($p = 0.028$), IL-1 β ($p = 0.044$), but not IL-21 ($p = 0.756$), IL-4 ($p = 0.133$), IL-6 ($p = 0.795$), TNF- α ($p = 0.019$) and change in TGF- β ($p = 0.003$) levels following the SARS-CoV-2 antigen stimulation. The only statistically significant difference between the patient and control groups was observed in the change in TGF- β levels after stimulation with SARS-CoV-2 antigen ($p = 0.04$): TGF- β levels decreased by 167 pg/mL (median, IQR = 392) in the patient group and increased by 245 pg/mL (median, IQR = 724) in the control group. Differences in cytokine profiles were observed when comparing patient groups by comorbidities.

Conclusions. Patients with primary antibody deficiency show as rapid increase in both pro-inflammatory and antiinflammatory cytokine levels, following *in vitro* stimulation with SARS-CoV-2 antigen, however, cytokine profiles differ from those of healthy controls and between different comorbidities.