Abstract ID: 93530

Student: Hodl Isabel

Area of Research: Immunology, microbiome research and respiratory diseases

PhD Programme: DS Bone Muscle and Joint (BMJ)

Semester: 6

Altered cellular immune response to vaccination against SARS-CoV-2 in patients with B-cell depleting therapy

Isabel Hodl; Clarissa Sallegger; Patrick Forstner; Nazanin Sareban; Martina Moritz; Barbara Dreo; Eduard Schulz; Angelika Lackner; Barbara Kleinhappl; Stefan Hatzl; Florentine Moazedi-Fürst; Thomas Seifert-Held; Bettina Heschl; Michael Khalil; Christian Enzinger; Hildegard Greinix; Martin H. Stradner; Ivo Steinmetz; Peter Schlenke; Johannes Fessler

Background: B-cell depleting therapies result in diminished humoral immunity following vaccination against COVID-19, but our understanding on the impact on cellular immune responses is limited. Here, we performed a detailed analysis of cellular immunity following mRNA vaccination in patients receiving B-cell depleting therapy. Methods: We analyzed T-cell responses in autoimmune patients treated with B-cell depleting therapy and healthy controls after receiving two mRNA vaccinations against COVID-19. We isolated PBMCs and stimulated them with a peptide pool covering the spike protein in vitro. Reactive T-cells were determined by IFN? ELISpot assay and staining for effector cytokines by flow cytometry. Anti-SARS-CoV-2 spike receptor-binding domain antibody assays were performed to elucidate B-cell responses. To complement our cellular analysis, we performed immunophenotyping for T- and B-cell subsets. Results: In this work, we show that SARS-CoV-2 vaccination using mRNA vaccines elicits cellular T-cell responses in patients under B-cell depleting therapy. Some facets of this immune response, including TNF? production of CD4+ T-cells and GzmB production of CD8+ T-cells, however, are distinctly diminished in these patients. Consequently, it appears that the finely coordinated process of T-cell activation with a uniform involvement of CD4+ and CD8+ T-cells as seen in HCs is disturbed in autoimmune patients. In addition, we observed that immune cell composition does impact cellular immune responses as well as sustainability of anti-spike antibody titers, a fact that also holds true for healthy individuals. Conclusion: Our data suggest disturbed cellular immunity following mRNA vaccination in patients treated with B-cell depleting therapy. Immune cell composition may be an important determinant for vaccination efficacy.