

## ABSTRACT (ENG)

This thesis summarizes the results of a project dedicated to adaptive immune system of patients with partial DiGeorge syndrome caused by deletion of 22q11.2.

The introduction sets the DiGeorge syndrome into a broader context of international pathophysiological classification of primary immunodeficiencies and goes into detail describing its history, causes, clinical phenotype, therapeutic options and changes of the immune system.

The attached manuscripts illustrate the premature aging of the T cell population, but also impaired development of B cells with low class-switched memory and high naïve subpopulations, along with high serum levels of BAFF, a B cell survival factor. The surprising lack of T independent marginal zone-like (MZ-like) B cells is reflected in decreased natural anti- $\alpha$ -Gal antibodies. The faulty B cell maturation and imperfect germinal center response is not caused by a deficit of follicular helper T cells, which are in fact increased in DiGeorge syndrome patients, and in most cases doesn't lead to hypogammaglobulinaemia. Despite the high incidence of autoimmune disease, in particular thyroiditis and thrombocytopenia, and a trend towards hypergammaglobulinaemia in adolescence and adulthood, we saw normal proportion of regulatory T cells (Tregs) and normal expression of the transcription factor Helios, a marker of thymus-derived Tregs.

The outcome of this thesis project is an enrichment of our knowledge of the immune system dysregulation seen in patients with partial DiGeorge syndrome, the most common primary immunodeficiency with syndromic features, as obtained on its largest Czech cohort. The novel findings are correlated with clinical course of the disease and routinely available laboratory parameters, thus allowing for higher standard of care and monitoring for all patients.