ABSTRACT (ENG)

The modern approach to studies of monogenic inborn errors of immunity, driven by unprecedented advances of genetic tools, opens vast undiscovered areas of immune system components and functions. In particular, the diseases with striking clinical phenotypes with normal or near normal baseline immunophenotype, such as disorders of innate and intrinsic immunity with susceptibility to single pathogen, provide a unique window into the host-pathogen interactions. This thesis covers various novel aspects of immunopathology, genetics and clinical facets behind some such diseases, namely chronic mucocutaneous candidiasis due to hypermorphic (gain-of-function, GOF) *STAT1* mutations, which hamper Th17-associated immune activities, and Mendelian susceptibility to mycobacterial diseases (MSMD) due to impairment of IL-12, IL-23/IFNγ signalling pathway. Moreover, it contributes to the mounting evidence that IL-6 signalling is non-redundant in anti-staphylococcal immunity. Finally, it explores the novel Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) as a single pathogen-driven life-threatening immunopathology, which most likely develops due to individual, yet unknown, genetic predisposition. The findings presented in this thesis were in several cases translated directly into the patients' clinical management, for example the use of JAK inhibitors in STAT1 GOF patients and the use of newly developed STAT phosphoflow protocol for dose adjustments, the recommendations on vaccination against SARS-CoV-2 in STAT1 GOF patients, the prophylaxis and treatment with IFNγ in patients with AD partial IFNγR1 deficiency, individualized therapeutic recommendation for a patient with unique combined impairment of IFNγ and NOD2 signalling, or the identification of severity predictors in PIMS-TS and its recommended management strategies.