

# Immuno- deficiency



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## Primary Immunodeficiency

Primary immunodeficiencies (PID) are a rapidly evolving group of genetically determined diseases of the immune system associated with susceptibility to infection and/or autoimmunity. To date, more than 300 different PID have been characterized.

Deficiency of the recombination activating genes (RAG) is associated with PID affecting number and function of both T and B lymphocytes. RAG-PID associated clinical phenotypes range from pediatric severe combined immunodeficiency (SCID) to adult-onset RAG-associated granulomas and autoimmune disease. While complete loss-of-function mutations lead to RAG-dependent SCID, so-called hypomorphic RAG mutations are associated with the late-onset RAG-associated diseases.

The mechanisms involved in autoimmunity and immune-dysregulation due to hypomorphic RAG-mutations are poorly defined. Autoimmunity and immune-dysregulation are also associated with RAG-independent PID, implying that PID and autoimmunity are fundamentally linked.

One main focus of the lab is to analyze in murine models how gradual RAG dysfunction impacts on immunity to infectious pathogens and at the same time to the formation of autoimmunity. This may help identifying mechanisms involved in the generation of autoimmunity in general.

## Connection to Clinical Practice

### Mike Recher, Christoph Hess

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### Molecular mechanisms in and personalized treatment of patients with primary immunodeficiency

Patients with suspected immunodeficiency or immune dysregulations are clinically evaluated in the Immunodeficiency Clinic of the Medical Outpatient Unit of the Basel University Hospital. If needed, patients are treated with supplementation of immunoglobulins and if available treatment specific immunologic treatment.

Since 2015, patients with the diagnosis of primary (genetically determined) immunodeficiency are included into a prospective cohort. Following informed consent, a standardized documentation of the physical status of the patient is combined with analysis of a standardized set of immunological lab data. In addition, the immuno-metabolism of sorted T and B lymphocytes is assessed in a collaboration with the Immunobiology Lab of Christoph Hess. Whole exome sequencing is performed and analyzed in a collaboration with Alexander Navarini, Dermatology, University Hospital Zurich. This allows us to prospectively study the disease course but also to determine the molecular mechanism of disease and to treat the patients in a personalized manner taking into account the molecular mechanism of disease.

Currently, more than 70 patients have been included into the prospective cohort. Identified specific PID-entities include CTLA-4 deficiency, BAFFR mutations and SP110 deficiency.

## Selected Publications

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