Immuno-deficiency

Primary Immunodeficiency

Primary immunodeficiencies (PID), also known as inborn errors of immunity (IEI), are a rapidly evolving group of genetically determined human diseases associated with susceptibility to infection, autoimmunity/autoinflammation and/or lymphoproliferation. To date more than 450 different PID entities have been elucidated.
The main current basic immunology focus of the research lab is to characterise the role of a yet poorly studied transcription factor in the generation and maintenance of human memory T lymphocytes. This is done by analysing functional consequences of T cell intrinsic over- expression vs. knock-out of the transcription factor complemented by a detailed clinical immunology assessment of patients carrying homozygous loss of function mutations in the gene encoding the transcription factor.
The aim is to molecularly define a non-redundant role for this transcription factor in the generation of human T cell memory and to characterise drugable targets to potentially restore immunity in patients carrying loss of function mutations in the gene encoding this transcription factor.

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Selected Publications

Légeret C, Meyer BJ, Rovina A, Deigendesch N, Berger CT, Daikeler T, Heijnen I, Burstein E, Köhler H and Recher M (2020). JAK inhibition in a patient with X-linked reticulate pigmentary disorder J Clin Immunol. in press.

Delmonte OM, Baldin F, Ovchinsky N, Marquardsen F, Recher M, Notarangelo LD, and Kosinski SM (2020). Novel Missense Mutation in SP110 Associated with Combined Immunodeficiency and Advanced Liver Disease Without VOD. J Clin Immunol 40, 236–239.

Burgener AV, Bantug GR, Meyer BJ, Higgins R, Ghosh A, Bignucolo O, Ma EH, Loeliger J, Unterstab G, Geigges M, *et al.* (2019). SDHA gain-of-function engages inflammatory mitochondrial retrograde signaling via KEAP1-Nrf2. Nat Immunol 20, 1311–1321.

Marquardsen FA, Baldin F, Wunderer F, Al-Herz W, Mikhael R, Lefranc G, Baz Z, Rezaee F, Hanna R, Kfir-Erenfeld S, *et al.* (2017). Detection of Sp110 by Flow Cytometry and Application to Screening Patients for Veno-occlusive Disease with Immunodeficiency. J Clin Immunol 37, 707–714.

Navarini AA, Hruz P, Berger CT, Hou TZ, Schwab C, Gabrysch A, Higgins R, Frede N, Padberg Sgier BC, Kampe O, *et al.* (2017). Vedolizumab as a successful treatment of CTLA-4- associated autoimmune enterocolitis. J Allergy Clin Immunol 139, 1043–1046 e1045.

Connection to Clinical Practice

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Molecular dissection and personalised treatment of patients with primary immunodeficiency

Patients with suspected immunodeficiency or immune dysregulation are clinically evaluated in the Immunodeficiency Clinic of the Medical Outpatient Unit of the Basel University Hospital. Patients are treated with immunoglobulin supplementation and, if available, specific immuno-active compounds.

Since 2015, patients with the diagnosis of primary (genetically determined) immunodeficiency are included into a prospective research cohort. Following informed consent, a standardised documentation of the physical status of the patient is combined with analysis of clinically validated and/or research based immunological lab data and next generation immune-gene sequencing. This allows us to prospectively study the disease course but also to determine the molecular mechanism of disease and at best to treat the patients in a targeted, personalised manner.

Currently, more than 225 patients have been included into the prospective cohort and selected patients are further molecularly characterised in the research lab. Novel disease causing immune gene variants have been identified in CTLA-4, SP110, SDHA, SAMHD1, Ligase 4 and many others. Novel targeted personalised treatment strategies have been or are currently clinically evaluated in patients with disease causing mutations in CTLA-4, SDHA, POLA1, SAMHD1 and others.