Translational Immunology

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Balancing immunity: Autoimmunity, immunosuppression, Infection and Vaccination

The translational immunology lab focuses on human immunology. We are interested in antigen-specific immune responses in the context vaccinations and autoimmune disease.

Evolution of the humoral immune response following repeated seasonal influenza vaccination

Viruses mutate and thereby evade the host immunity. If this happens at a high rate, as in influenza, such ‘escape’ is a major challenge for vaccine design. An influenza vaccine protecting us from all potentially occurring viral variants remains the holy grail of influenza vaccine research. The current influenza vaccination strategy of yearly vaccination with adapted strains aims to counteract viral escape. To better understand the factors influencing vaccine responses in healthy and immunosuppressed individuals, we study the immune responses following influenza vaccination in these subjects. In the setting of seasonal influenza vaccination, we found that in immunosuppressed subjects (i.e. HIV infection) the response profiles (i.e. a multidimensional vector that includes time and antigen specificity) are similar to those in healthy, whereas the magnitude of the response is dampened (Berger C T. Human Vaccine Immunother, 2015). In a follow-up study on healthy subjects we could show that the vaccine response to the influenza vaccine is moreover strongly affected by the previous vaccination history. We found evidence that the vaccine response can become skewed, rendering the subject prone to viral escape (Bigler, M.B. et al. (in preparation)). We are currently expanding these findings in a prospective clinical study of repeated annual influenza vaccination over three consecutive seasons from 2018–2021. We investigate the evolution of the B cell responses by immunophenotyping and B cell receptor sequencing, and by defining the antibody functions and cross-reactivity. Specifically, we aim to dissect whether adaptations in the vaccine formulation recruit new naïve B cells to the overall influenza response (i.e. broaden the response) or mainly boost/adapt the preexisting immunity (i.e. skew the response). Using a systems approach, this data may allow formulating predictions based on the pre-vaccination profile and repertoire. This may help identifying (i) who is in need for yearly vaccination, and (ii) which antigenic difference between subsequent vaccinations induce diversification of the vaccine response. Ultimately, we aim to apply this towards more personalized rather than one-size-fits-all vaccination strategies, to reduce the risk of vaccine failure.

The immunological targets in autoimmune vasculitis

Autoimmune diseases occur when the immune system attacks self-proteins. Understanding the target of the immune response in autoimmune disease may enable developing therapies interfering with the cause of immunopathogenesis directly. Target identification moreover allows developing tools to measure autoimmunity. Clinically relevant autoantibodies have been described in various autoimmune disease. Immunological biomarkers in predominantly T cell-mediated autoimmune diseases have not yet been established for clinical use. Giant cell arteritis (GCA) is a T cell-mediated, inflammatory disease of unknown etiology. GCA exclusively affects the large arteries. Disease manifests as an inflammatory syndrome and ischemic symptoms resulting from stenosis of inflamed arteries. There is strong evidence that T cells play an important role in disease induction and/or maintenance. The pathogenesis remains, however, unknown. One of the goals of our lab is to unravel the events leading to disease and more specifically the immunological target of the T cells. We study this within the framework

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Autoimmunity . T cell . TCR . Vaccines . Antibodies . Human Immunology
of a prospective single-center GCA cohort at the university hospital Basel that we are running with the rheumatology clinic. All patients seen at our institution with clinical suspicion of GCA are enrolled. The cohort-data entails a comprehensive set of clinical, routine laboratory, pathological (biopsy), and vascular diagnostic (ultrasound duplex studies and PET studies) information, as well as the longitudinal biobanking of blood and serum samples. This cohort is a precious source to address translational research questions (e.g. Kistner A et al., Rheumatology 2017; Berger CT et al., Rheumatology 2018; Berger CT et al., Annals of the Rheumatic Diseases 2019).

The main current focus is to analyze the inflammatory infiltrate in the artery biopsies of GCA patients. We use next-generation sequencing of the TCRαβ repertoire to identify the expansion of dominant T cell clones in biopsies from patients. Using the collected information on the TCR repertoire, we then aim to identify the target of the expanded T cell clones. To do so, we established a workflow to transfect the identified TCRαβ of expanded T cells into TCRαβ-deficient Jurkat. The thereby generated set of transfected TCRαβ-Jurkat cells is used as reporter cell lines to screen against putative targets of the transfected TCR. For this antigen discovery studies we use an unsupervised (‘MHC class II ligandome of artery tissue’) and a supervised (viral antigen) screening approach (Bigler MB et al., Arthritis and Rheumatology 2018). Identifying the source of the antigen that T cells recognize in GCA will inform on the potential disease-causing processes. This may pave the way for novel approaches (i) to prevent GCA by identifying subjects at risk, and (ii) to develop immune-therapies aimed at improving antigen-specific tolerance.

**Selected Publications**


**Connection to Clinical Practice**

**PD Dr. Thomas Daikeler and Prof. Dr. Christoph Hess**

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**The Swiss Giant Cell Arteritis Cohort**

Giant cell arteritis (GCA) is the most prevalent of the primary vasculitis syndromes with an increasing disease incidence. Patients typically present with constitutional symptoms, headache, and a systemic inflammatory syndrome. To date therapy of GCA is based largely on steroids, and guided by parameters reflecting disease activity only partially, as indicated by recent imaging-studies. Furthermore, intensity and duration of steroid therapy remain a matter of debate, and no consensus exists in defining remission. Both GCA itself and the steroid based therapy are associated with significant morbidity. Improving diagnostic accuracy and monitoring of disease activity thus would be of great importance. To study these clinical problems, we established in 2011 a prospective interdisciplinary cohort of patients with GCA at the University Hospital Basel. Since 2020, we co-lead a Swiss Cohort for GCA that involves all University Hospitals in Switzerland. In the Relevant clinical data, laboratory parameters, serum and peripheral blood mononuclear cells from all patients are collected at longitudinal time-points. Vascular disease activity is assessed using new technologies such as color-coded duplex ultrasound and positron emission tomography. Thereby we aim at integrating clinical data, imaging studies, and extended immunological and histomorphological assessments for a more detailed understanding of the immunopathogenesis of GCA. This may help to (i) further develop precise, ideally non-invasive, tools to diagnose and monitor disease activity, and (ii) generate strategies towards interfering with specific pathways associated with disease activity and/or complications.