

UiO FOCIS CoE Symposium

- in collaboration with KG Jebsen Centre for Cancer Immunotherapy

Title: Immune Repertoires in Health and Disease

Date: Wednesday, May 29, Auditorium 1 (Grønt), Rikshospitalet

Time: 14:00-16:00, refreshments will be served from 13:45

Program

- 14:00-15:00 **George Georgiou**, University of Texas at Austin
The Human Serological Antibody Repertoire in Health and Disease
- 15:00-15:30 **Victor Greiff**, Department of Immunology, University of Oslo
Deciphering the complexity of B-and T-cell repertoires
- 15:30-16:00 **Ida Lindeman**, Department of Immunology, University of Oslo
Simultaneous transcriptional characterisation and clonal inference of autoreactive plasma cells in coeliac disease

We are looking forward to your attendance!



George Georgiou

Department of Chemical Engineering
University of Texas at Austin, USA



The Human Serological Antibody Repertoire in Health and Disease

A diverse ensemble of antibody proteins (immunoglobulins) circulates in all physiological fluids and plays a central role in protection against disease. Remarkably, more than 100 years after the discovery of antibodies, the number of distinct monoclonal antibodies that comprise the polyclonal response to an antigen, the amino acid sequences of these antibodies, their relative amounts, binding properties and functions, have remained elusive. We have developed a suite of technologies that capitalize on high mass accuracy LC-MS/MS proteomics, microfluidics and bioinformatics tools for the molecular-level deconvolution of the identities, relative amounts and functions of antibodies in human blood and also for the delineation of the relationships between antibody production and the relevant B cell immunological mechanisms. This presentation will briefly outline what we have learned about the serological antibody repertoire in response to vaccination or infection. The serum repertoire in the elderly and early in life will also be discussed.

Biography

George Georgiou is a Professor at the University of Texas, Austin. He received his B.Sc. from the University of Manchester, U.K. and Ph.D. from Cornell. His research is focused on understanding the serological antibody repertoire (as well as the BCR and TCR repertoires) in human health and disease and on the discovery and preclinical development of enzyme and antibody therapeutics for cancer and for inborn errors of metabolism.

Professor Georgiou was elected to the National Academy of Engineering (2005), National Academy of Medicine (2011) and the American Academy of Arts and Sciences (2016). He is also a Fellow of the American Institute for Biological and Medical Engineers (AIMBE), the American Academy of Microbiology and the American Association for the Advancement of Science (AAAS). He is the author of >260 research publications and co-inventor of 87 issued or pending US patents, more than 65% of which (comprising 24 distinct technology suites) have been licensed to 27 pharma & biotech companies. He founded GGMJD (1999; acquired by Maxygen in 2000), Aeglea Biotherapeutics (2013-Present; NASDAQ: AGLE) and Kyn Therapeutics Inc. (2015-Present) and currently serves as a Director and Chairman of the SAB for both companies. In 2013, Georgiou was selected as one of the top 20 Translational Researchers by Nature Biotechnology

Victor Greiff

Department of Immunology
University of Oslo



Deciphering the complexity of B-and T-cell repertoires

The adaptive immune system recognizes antigens via an immense array of antigen-binding antibodies and T-cells. The interrogation of antibody and T-cell receptor repertoires (also called immune repertoires) is of high relevance for understanding the adaptive immune response in (autoimmune) disease and infection. We and others have recently shown that immune repertoires are much more predictable than previously thought, which is of incredible importance for the precise manipulation and prediction of adaptive immunity. However, as of yet, we lack the computational methods that enable us to understand the construction rules according to which immune repertoires are assembled. Specifically, (i) on the repertoire-level, we lack mathematical methods to measure repertoire similarity across individuals. We will show preliminary results of a network approach that allows quantifying immune repertoire similarity based on the multidimensional combination of immunological features. (ii) On the sequence level, we lack detailed understanding of antibody-antigen binding. Therefore, we mined antibody-antigen crystal structures in order to understand the sequence structure of the antibody sequence motifs (binding rules) that mediate antigen binding. (iii) Finally, there exists currently no comprehensive machine learning framework for immune receptor analysis. We will show a draft of a general software architecture for an open source platform that enables large-scale machine learning analysis on immune receptor data. Taken together, we have developed computational tools that pave the way towards understanding the molecular construction rules of adaptive immunity on the repertoire and single sequence level.

Ida Lindeman

Department of Immunology
University of Oslo



Simultaneous transcriptional characterisation and clonal inference of autoreactive plasma cells in coeliac disease

Objectives: Plasma cells (PCs) are terminally differentiated lymphocytes of the B-cell lineage secreting large amounts of antibodies. PCs are especially abundant in the lamina propria of the small intestine. Coeliac disease (CD) can be characterised by plasmacytosis in the lamina propria and the presence of high numbers of disease-specific PCs, of which most target the autoantigen transglutaminase 2 (TG2) and a smaller fraction target gluten peptides. The contribution of PCs toward the pathogenesis of CD has yet to be resolved.

Methods: We sorted single CD38⁺ TG2-specific, gliadin-specific or non-TG2/gliadin-specific PCs from untreated CD patients, CD patients on a gluten-free diet and non-CD controls. We performed single-cell RNA-sequencing of the sorted cells and reconstructed their B-cell receptors and identified clonally related cells with the computational tool BraCeR.

Results: A significantly higher fraction of the disease-specific compared to non-disease-specific intestinal PCs in untreated CD patients (n=10) were CD19⁺CD45⁺, a compartment of PCs that has previously been shown to be short-lived. Furthermore, we found that intestinal PCs express mRNA for molecules associated with antigen presentation and cross-talk with T cells, such as HLA class II, cytokines and cytokine receptors. Lastly, we investigated clone-specific transcriptional signatures among the disease-specific PCs.

Conclusion: Our findings support previous reports showing that PCs may have functions in addition to antibody secretion. These results suggest that PCs may have a more active role in immunological diseases than previously thought, through cross-talk with helper T cells. We anticipate that our findings could provide a basis for studies involving targeted therapy against PCs in CD and potentially also in other autoimmune diseases.