

Systems Immunology Seminar

Friday, August 24, Auditorium 1 (Grønt), Rikshospitalet

Session 1.

Chair: Victor Greiff

13:00 Sai Reddy, Department of Biosystems Science and Engineering, ETH Zürich, Switzerland
Molecular decryption of antibody responses

13:50 Fridtjof Lund-Johansen, Department of Immunology, Oslo University Hospital
Antibody-based proteomics

14:15 Eivind Heggernes Ask, Department of Cancer Immunology, Oslo University Hospital
Immune repertoire dynamics during chemo-immunotherapy of diffuse large B-cell lymphoma

14:40 Coffee break

Session 2.

Chair: Shuo-Wang Qiao

15:00 Aimee S. Payne, Department of Dermatology, University of Pennsylvania, USA
Targeting autoimmunity with CAAR T cells

15:50 Asbjørn Christophersen, Department of Immunology, University of Oslo
Gluten-specific CD4+ T cells have a narrow phenotype

BBQ with open bar (from 16:30)

Venue: Lawn outside Café Eric, Domus Medica (new building)

Free of charge. Please sign up at <http://norwegianimmunology.org/meetings/events/> before August 10

Welcome!

The Norwegian Society for Immunology
UiO FOCIS Centre of Excellence



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Molecular decryption of antibody responses

The ability to predict and correspondingly manipulate antibody responses is highly valuable for biotechnology and medicine. To achieve this requires a greater molecular understanding of antigen selection and specificity in antibody repertoires. In this presentation I will describe how we are decrypting antibody repertoires by identifying antigen-associated molecular patterns. Detection of these patterns is based on the principle of convergent selection: different individuals exposed to the same antigen respond with antibodies that converge to similar sequence space. Molecular convergence is specifically identified by bioinformatic recoding of high-throughput sequencing data of antibody repertoires into constituent biochemical sequence space. By combining this approach with a statistical learning framework we are able to accurately predict antigen exposure and potential antigen specificity based on antibody sequences alone.

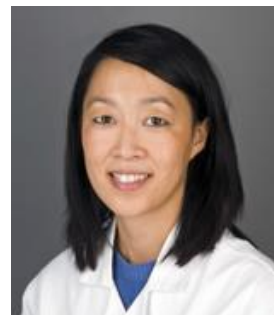
I will also highlight recent work in our group aimed towards engineering antibodies at high-throughput in mammalian cells through genome editing. We have recently established a technique known as homology-directed mutagenesis (HDM), which is able to generate mutagenesis libraries directly in mammalian cells using CRISPR-Cas9. HDM enables several of the most essential methods of antibody engineering, which are usually only possible in microbial or in vitro systems (e.g., phage, yeast), to be performed directly in mammalian cells. This includes generation and screening of synthetic libraries for antibody discovery and affinity maturation. Finally, by combining HDM with high-throughput sequencing, we are able to perform deep mutational scanning on antibodies in order to decrypt their antigen-recognition sequence landscape.

Brief Biography

Sai Reddy is faculty in the Department of Biosystems Science & Engineering, ETH Zurich, Switzerland. His research group uses methods in systems and synthetic biology to study and manipulate immune responses for applications in biotechnology, vaccination, and immunotherapy. Sai Reddy holds B.S. (2003) and M.S. (2004) in Biomedical Engineering from Northwestern University (Evanston, IL, USA). He completed his Ph.D. thesis at Ecolé Polytechnique Fédérale de Lausanne (EPFL, Switzerland) in Bioengineering and Biotechnology (2008). Sai Reddy did post-doctoral research at the University of Texas, Austin (2008-2011).

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Targeting autoimmunity with CAAR T cells

Pemphigus vulgaris is a paradigm for autoantibody-mediated disease in humans. As with most autoantibody-mediated diseases, current therapy for pemphigus aims to suppress antibody production, with consequent risks of morbidity or mortality from infection. We recently described a novel gene-engineered cellular immunotherapy that uses the autoantigen targeted in pemphigus, desmoglein 3, to direct T cell cytotoxicity against anti-desmoglein 3 B cells. These "chimeric autoantibody receptor" (CAAR) T cells demonstrated efficacy in an experimental pemphigus vulgaris model without detectable off-target effects. We will discuss challenges and opportunities in translating these novel immunotherapies to first-in-human clinical trials.

Brief Biography

Aimee S. Payne is an Associate Professor of Dermatology at the University of Pennsylvania. Her career interest has been in pemphigus: diagnosing and treating patients with this potentially fatal autoimmune disease, and performing research to better understand disease, with the goal of improving therapy. Dr. Payne received her BS in Biology from Stanford University and her MD/PhD from Washington University School of Medicine, followed by residency and postdoctoral fellowship training in Dermatology at the University of Pennsylvania. Her research has focused on three major areas of investigation: 1) cloning and characterization of B cell repertoires to understand how autoimmunity occurs in pemphigus, which has discovered common features of the B cell response among patients; 2) cell biologic studies to identify mechanisms for loss of cell adhesion, which has identified the p38/MK2 axis as a key regulator of desmosome adhesion in keratinocytes; and 3) patient-oriented research to improve pemphigus therapy, which has led to a better understanding of B cell depletion strategies in pemphigus as well as novel strategies for targeted therapy of disease.