NSI Symposium

It's all about specificity: Immunological specificity in adaptive immunity, cancer, and autoimmunity

Tuesday, June 4th, Auditorium Grønt, Rikshospitalet, Oslo

16:15 **Andreas Plückthun**, Laboratory for Protein Engineering, Department of Biochemistry, University of Zürich, Switzerland
Protein Engineering in the developments of new therapeutics

17:00 **Johanna Olweus**, Laboratory for Experimental Immunotherapy, Department of Cancer Research, University of Oslo, Oslo University Hospital, Oslo
T-cell receptors from healthy donors to target cancer

17:45 **Donna Farber**, Columbia Center for Translational Immunology, Columbia University, USA
Human immunity in space and time

BBQ free of charge with open bar (from 19:00)
Venue: Lawn outside Café Eric, Domus Medica (new building)

Please sign up by May 31: https://nettskjema.uio.no/a/118166

We are looking forward to your attendance!

The Norwegian Society for Immunology

Andreas Plückthun
University of Zürich
Department of Biochemistry
Switzerland

Title: Protein Engineering in the developments of new therapeutics

Over the last decades, both the generation of therapeutic antibodies from synthetic antibody libraries and therapeutic proteins those of new non-antibody scaffolds, e.g. the DARPins, have progressed from the academic research lab to late stage clinical trials or even the market (e.g., www.morphosys.com, www.molecularpartners.com). Nonetheless, modern protein engineering can do much more. This presentation will show how the engineering of stealth adenovirus, not carrying any viral genes, can be made to infect arbitrary cells in vivo based on their surface markers, and thereby to produce a cocktail of therapeutics in situ. These exciting new opportunities, in conjunction with new analytical tools also developed from advanced protein engineering, may extend the possibilities beyond what is possible with classical antibody technology today.

Biography

Andreas Plückthun, Ph.D., is a Professor of Biochemistry of the Department of Biochemistry at the University of Zurich, Switzerland. His research is centered on protein engineering. His contributions have included many aspects of antibody engineering, expression technology, design of synthetic antibody libraries, the development of ribosome display, development of new scaffolds (the DARPin technology), and the directed evolution of G-protein coupled receptors towards high stability, which has allowed determination of several crystal and NMR structures of GPCRs.

In 2003 he was elected as member of the German Academy of Science (Leopoldina). His work has been published in over 430 papers, which have been cited over 42,000 times (h-index 114). He is an inventor on more than 20 patent families.
He is the winner of the 2016 Christian Anfinsen Award of the Protein Society for “pioneering contributions to protein engineering”. In 2005 he received, together with a team from Molecular Partners, the deVigier Award and the Swiss Technology Award. In 2002 he received the J. P. Morgan Chase Award of The Tech Museum of Innovation (San Jose, USA), the Wilhelm-Exner-Medal (Vienna, Austria) and The Jury’s Grand Prix of the European Grand Prix for Innovation Awards (Monaco). In 2000, he received the Karl-Heinz-Beckurts Award (Germany) and in 2001 he became a finalist in the World Technology Awards in the Biotechnology category. Before that, he received the Young Investigator's Award of the German Industry Fund and was elected member of EMBO.

He has founded 3 companies: in 1992, he co-founded the Munich biotech company MorphoSys AG (TecDAX: MOR). In 2004 he co-founded the biotech company Molecular Partners AG in Zurich (SIX: MOLN). In 2014, he cofounded G7 Therapeutics, now divested to Heptares/Sosei.

He studied chemistry at the University of Heidelberg (Germany) and received his graduate education at the University of California at San Diego, where he obtained a Ph.D. in 1982 with Prof. Edward Dennis. He was a postdoctoral fellow at the Chemistry Department of Harvard University (1982-85) where he worked with Prof. Jeremy Knowles. From 1985 until 1993, he was group leader at the Genzentrum and Max-Planck-Institut für Biochemie in Martinsried (Germany). He was appointed to the faculty of the University of Zürich (Switzerland) as a Full Professor of Biochemistry in 1993.

Johanna Olweus
University of Oslo
Oslo University Hospital
Laboratory for Experimental Immunotherapy

Title: T-cell receptors from healthy donors to target cancer

Recent advances in cancer immunotherapy have greatly improved life expectancy for patients with widespread (metastatic) cancer. Two of the most successful strategies are inhibition of negative immune regulation by checkpoint inhibition, and transfer of T cells gene-modified to express artificial immune receptors called chimeric antigen receptors (CARs). Allison and Honjo were awarded the Nobel Prize in physiology or medicine in 2018 for the therapeutic concept of checkpoint inhibition, and Adoptive Cell Therapy was named Clinical Cancer Advance of 2018 by the American Society of Clinical Oncology due to the impressive effectiveness of CAR19 T cell therapy in the treatment of B-cell malignancies. In checkpoint inhibition, the effector mechanism is the endogenous T-cell receptor (TCR) repertoire of the patient, recognizing peptides encoded by mutations (neoantigens) presented on major histocompatibility complex (MHC) molecules on the surface of tumor cells. However, the TCR repertoire of the patient is in most cases insufficient at mediating cures. CAR19 T cells, on the other hand, recognize tissue-specific self-antigens on the target cell surface, such as CD19, specific for B cells. It has, however, proven difficult to identify tissue-specific cell surface antigens that can be safely targeted in other cancers. As a consequence, existing immunotherapies rarely cure metastatic cancer and are available only for subgroups of patients, calling for alternative options. In my talk, I will discuss the possibility that TCRs identified from healthy donors can be used for genetic modification of T cells in adoptive cell therapy to target a wide range of cancers. We have demonstrated that healthy donor T cells provide a rich source of TCRs reactive to neoantigens, responding to five-fold more mutations than the patient's own tumor-infiltrating T cells. Moreover, we have demonstrated that healthy donor T cells can recognize a wide range of peptides derived from normally expressed tissue-restricted self-antigens when presented on mismatched HLA. Recognition of such self-peptides in complex with foreign HLA is the basis for graft rejection, and we hypothesize that this immune response can be used to "reject" cancer. As TCRs can recognize peptides independently of cellular localization, the number of potential self-antigens that can be targeted by TCRs is vastly increased relative to CARs.

Biography

Johanna Olweus is a physician-scientist with a Ph.D. in hematopoietic stem cell biology and over 10 years of experience in cell-based cancer immunotherapy. During her Ph.D. studies (University of Bergen, Norway), she deciphered the earliest stages of lineage commitment from human hematopoietic stem cells by ultrasensitive multiparameter measurements of cytokine receptors using flow cytometry. During these studies and postdoctoral work at Becton Dickinson Immunocytometry Systems in San José, USA, she discovered together with Fridtjof Lund-Johansen a new lineage of dendritic cells defined by high expression of CD123 (IL-3Ralpha), now known as plasmacytoid dendritic cells. Following clinical training to specialize in Immunology and Transfusion Medicine in Oslo, Norway, she built up a research group focused on studies of T cell-based cancer immunotherapy. Her training in transplantation immunology inspired her to work towards the following goal: to utilize the powerful immune responses of graft-versus-tumor-reactivity and graft rejection to reject cancer cells in a specific and controlled manner. Since 2008 she holds the position as Head of the Dept of Cancer Immunology at the Institute for Cancer Research at Oslo University Hospital and Professor at the University of Oslo. She is also the Director of K.G. Jebsen Center for Cancer Immunotherapy, which started in 2013 and is now in its second term.

Donna Farber
Columbia Center for Translational Immunology
Columbia University, New York, USA

Title: Human immunity in space and time

Research in our laboratory is focused on immunological memory and specifically on memory T cells as essential mediators of protective immunity. While it was previously thought that memory T cells mediate their protective responses through rapid migration and surveillance through tissues, it is now become clear that localization and establishment of non-circulating memory T cells resident in tissue sites is integral to immune protection. We are incorporating fundamental studies on mouse models with novel translational approaches on human samples to investigate tissue immune responses. We have identified a new subset of non-circulating tissue-resident memory T cells (TRM) in the lung that mediate optimal protective immunity in a mouse model of influenza infection. Current studies into mechanisms for how memory T cells become targeted to and maintained in the lung use total transcriptome profiling and bioinformatics approaches. We have identified novel roles for specific integrins and inflammatory mediators in this process, and are studying the signaling pathways involved in resident memory T cell generation and functional recall. For our translational studies, we have established a unique collaboration and research protocol with the organ procurement organization for the New York Metropolitan area (LiveOnNY ; http://www.donatelifeny.org/) and transplant surgeons at New York Presbyterian (NYP) where we obtain multiple lymphoid and mucosal tissues from research-consented human organ donors. These studies are part of an NIH-funded Program on “Tissue compartmentalization of human lymphocytes”, involving immunologists, molecular biologists and computational biologists in five institutions to study human adaptive and innate lymphocyte compartmentalization and maintenance in human tissues throughout the human lifespan. Additionally, because memory T cells are critically important to generate in vaccines, we have ongoing studies on infant immunity, to investigate how protective responses can be established in babies who are most susceptible to infection and immune pathologies. These infant studies involve both mouse models and also sampling of site-specific responses in human infants intubated due to virus infection in collaboration with clinicians in the Pediatric Critical care Division at Morgan Stanley/NYP.

Biography

Dr. Farber received her undergraduate degree in Microbiology from the University of Michigan, her Ph.D. in Biochemistry and Molecular Biology at the University of California, Santa Barbara and did postdoctoral training in the Section of Immunobiology at Yale University and at the Pasteur Institute in Paris, France. She started her laboratory at the University of Maryland and moved to Columbia University in 2010 where she is currently the George H. Humphreys, II Professor of Surgical Sciences and Professor of Microbiology and Immunology, and recently became Chief of the Division of Surgical Sciences. Dr. Farber’s research for the past 22 years is focused on immunological memory, and recently, on how the immune response is compartmentalized in tissue sites in mouse infection models and in humans. For human studies, Dr. Farber set up a unique resource to obtain multiple tissues from organ donors, enabling novel investigation of human immunity throughout the body over age and genetic diversity.