Program
Theme: Autoimmunity/Tolerance

Time: Thursday the 26th May 2016
University of Copenhagen

Place: Room 22.1.29, The Panum Institute, University of Copenhagen, Nørre Allé 20, 2200 Copenhagen N

Organizers: Graduate School of Immunology and Infectious Diseases, Danish Immunological Society and Copenhagen Cluster of Immunology

13.15	Welcome
13.20	Finn Sellebjerg, Rigshospitalet, University of Copenhagen, Copenhagen (finn.t.sellebjerg@rh.regionh.dk): Treatment of multiple sclerosis
14.05	Koen Venken, Ghent University Hospital (Koen.Venken@ugent.be): Immune regulation in the gut: disurbances in Spondyloarthritis?
14.50	Gregory F. Sonnenberg, Cornell University, New York (gfsonnenberg@med.cornell.edu): Immune regulation of intestinal health and disease
15.35	Coffee Break
15.55	Bonnie Dittel, BloodCenter of Wisconsin, Wilwaukee (bonnie.dittel@bcw.edu): Suppression of autoimmunity by regulatory B cells
16.40	Lars Iversen, Aarhus University Hospital, Aarhus (Lars.Iversen@clin.au.dk): The pathogenesis of psoriasis
17.25	Closing remark

Abstracts, May 26th, 2016

The immune System in Health and Disease

Theme: Autoimmunity/Tolerance

Treatment of Multiple Sclerosis

Finn Sellebjerg, Danish Multiple Sclerosis Center, Rigshospitalet, University of Copenhagen

Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system. In the majority of cases, the disease has a relapsing-remitting disease course with recurrent relapses. Relapses are initiated by systemic immune cells. Activated T cells, B cells and monocytes migrate into the brain or spinal cord, where they initiate focal lesions with demyelination and axonal damage. This results in disruption of inter-neuronal signaling and ensuing neurological symptoms.

Treatment of MS is mainly based on the prevention of pathogenic immune activation or interference with leukocyte migration. Since the 1990'ies treatment with recombinant interferon-beta has been in general use. The interferons have a multitude of effects, but their main effects are thought to relate to inhibition of leukocyte migration and induction of regulatory cells. Glatiramer acetate, a mixture of synthetic polypeptides also has a broad range of immunoregulatory effects. Fingolimod interferes with lymphocyte egress from lymph nodes by blocking sphingosine-1-phosphate signaling, and the monoclonal antibody natalizumab interferes directly with leukocyte migration into the CNS by blocking alfa-4-integrins. The monoclonal antibody alemtuzumab depletes lymphocytes by binding the CD52 molecule. This is highly efficacious in relapsing-remitting MS, but selective B cell depletion also has surprisingly high efficacy. Finally, interference with interleukin-2 (IL)-2 signaling by treatment with the IL-2-receptor alfa chain antibody daclizumab has shown efficacy, presumably by a combination of interference with innate lymphoid cell differentiation and inhibition of T cell activation.

In summary, a wide variety of therapeutic strategies have shown efficacy in relapsing-remitting MS. The remarkable efficacy of B cell depleting antibodies is driving research into new aspects of MS immunopathogenesis. Unfortunately treatment of the later, progressive stages of MS is still not successful.

Immune regulation in the gut: disturbances in Spondyloarthritis?

Koen Venken
Laboratory for molecular Immunology and inflammation, Department of Rheumatology, VIB Inflammation Research Center, Ghent University, Ghent University Hospital, Belgium

Spondyloarthritis (SpA) refers to a cluster of rheumatic diseases showing common clinical, genetic and pathophysiological characteristics, affecting nearly 1-2% of the Western population. Typical disease manifestations consist of sacroiliitis and spinal inflammation next to peripheral arthritis. Intriguingly, there seems to be a close relationship between intestinal and joint inflammation as

more than 50% of SpA patients display microscopic signs of gut inflammation of which 5-10% develops Crohn's disease. Conversely, up to 30% of patients with inflammatory bowel disease develop a SpA-like articular disease. The gut immune system harbors a number of highly specialized T cells with potent immune modulatory properties. Innate-like T cells, such as invariant natural killer T (iNKT) cells, Mucosal associated invariant T (MAIT) cells and γδ-T Cells, are present in circulation but are predominantly found at mucosal and epithelial barrier sites where they serve an essential role in modulating host-microbial interplay. These cells can release a broad spectrum of cytokines upon T cell receptor (TCR) activation but also after TCR-independent stimulation, acting as a 'bridge' between innate and adaptive immune responses. Interest in how potential disturbances in these immune regulatory mechanisms may influence diseases like SpA, linking gut and joint inflammation, is a topical issue.

Immune regulation of intestinal health and disease

Gregory F. Sonnenberg
Department of Medicine, Gastroenterology Division, Department of Microbiology & Immunology, and the Jill Robert's Institute for Research in Inflammatory Bowel Disease, Weill Cornell Medical College, Cornell University, New York, NY, USA

The human immune system is critical to protect against infection with pathogenic microorganisms. However, inappropriate immune responses against our own tissues or non-harmful environmental triggers such as beneficial commensal bacteria that normally colonize the body's barrier surfaces can promote autoimmune or chronic inflammatory diseases. Indeed, emerging studies in patient populations indicate that abnormal host immune responses to commensal bacteria are causally-linked to the pathogenesis and progression of numerous chronic infectious, inflammatory and metabolic diseases, such as HIV, inflammatory bowel disease (IBD) and cancer. The focus and long-term research goals of the Sonnenberg Laboratory are to interrogate functional interactions between the mammalian immune system and intestinal commensal bacteria in the context of health and disease. The laboratory employs cutting-edge immunologic and microbiologic approaches to interrogate these interactions in both basic mouse models and translational patient-based studies. Recent studies in the laboratory have identified a critical role for innate lymphoid cells in orchestrating host relationships to defined subsets of commensal bacteria. Delineating these complex interactions will lead to a better understanding of the pathogenesis of multiple chronic inflammatory diseases, and direct the future development of novel therapeutic strategies targeting commensal bacteria-dependent chronic inflammation.

Suppression of Autoimmunity by Regulatory B Cells

Bonnie N. Dittel and Avijit Ray
BloodCenter of Wisconsin, Blood Research Institute, Milwaukee, WI, USA

Autoimmunity occurs when the immune system inappropriately attacks self-tissues resulting in inflammation that can lead to extensive tissue damage and even death. While treatment options for many autoimmune diseases are limited they are largely treated with disease-modifying therapeutics that slow but do not stop the progression of disease. Thus new cellular targets that can be harnessed

to attenuate autoimmune responses need to be identified. To that end, B cells with regulatory activity (Breg) have emerged as a potential cellular target. B cells have been shown to attenuate the severity of autoimmune disorders by a variety of mechanisms including production of IL-10, IL-35 or TGF-beta or by expression of FasL. In our studies, we have shown that Breg suppress autoimmunity by the maintenance of $CD4^{+}Foxp3^{+}$ Treg homeostasis by inducing their proliferation in a GITRL-dependent manner. These cumulative studies indicate that Breg could be a viable target for the treatment of autoimmunity.

The Pathogenesis of Psoriasis

Lars Iversen

Department of Dermatology, Aarhus University Hospital, P. P. Orumsgade 11, 8000 Aarhus C, Denmark

Psoriasis is a common, chronic inflammatory skin disease most often appearing in the form of well-demarcated, scaly plaques. Its pathogenesis is still not fully understood; however, infiltrating subsets of T cells, including Th1, Th17, and γδ T cells are known to play an important role. These T cells secrete an array of specific cytokines, including TNFα, IFNγ, IL-17A, IL-17F, and IL-22. Especially TNFα and IL-17A play a key role in disease pathogenesis and antibodies targeting these specific cytokines are now used in the treatment of psoriasis. In recent years also specific intracellular signalling pathways that are important in the disease pathogenesis have been identified and most recently IκBζ was demonstrated as a key protein for the IL-17A–driven effects in psoriasis.