Program

Theme: Chronic Inflammation (innate immunity)

Time: Thursday the 12th of May 2016
University of Copenhagen, Denmark

Place: Auditorium 29.01.32, The Panum Institute, University of Copenhagen, Nørre Allé 20, 2200 Copenhagen N

Organizers: Graduate School of Immunology and Infectious Diseases and Danish Society of Immunology

13.15	Welcome
13.20	Catherine D Andersen, Fairfield University, Connecticut, USA: Impact of obesity and dyslipidemias on immunity
14.00	Eitan Okun, Bar Ilan University, Israel: DAMPs as mediators of sterile inflammation in aging-related pathologies
14.40	David Magne, University of Lyon, France: Inflammation: a culprit for vascular calcification in atherosclerosis and diabetes.
15.20	Coffee Break
15.40	Gunnar Houen, Statens Serum Institute, Copenhagen: Innate immune system in chronic inflammation.
16.20	Stephen Moss, University College London Institute of Ophthalmology, London: Chronic inflammation and age-related macular degeneration
17.00	Closing remarks

Abstracts, May 12th, 2016

The Immune System in Health and Disease

Theme: Chronic Inflammation (innate immunity)

Impact of obesity and dyslipidemias on immunity

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Obesity is associated with metabolic disturbances that cause tissue stress and dysfunction. Clinical presentation of metabolic dysfunction includes dyslipidemias, insulin resistance, and systemic markers of chronic inflammation, which correspond to the increased risk of chronic disease observed on obesity. It has been well established that innate and adaptive immune cells play important roles in the pathogenesis of obesity-related chronic diseases, as evidenced by leukocyte activation and dysfunction in metabolic tissues such as adipose tissue, liver, pancreas, and the vasculature. However, recent findings highlight the substantial impact that obesity has on immunity and pathogen defense, including the disruption of lymphoid tissue integrity, alterations in leukocyte development, phenotypes, and activity, and the coordination of innate and adaptive immune responses. Further, dyslipidemias and impaired lipoprotein metabolism appear to directly influence immune cell activity and profiles. Together, the pathophysiology of obesity and dyslipidemias may have important clinical implications for immunity.

DAMPs as mediators of sterile inflammation in aging-related CNS pathologies

Ravit Madar1, 2, 3 and Eitan Okun1, 2, 3
1 The Mina and Everard Goodman faculty of Life sciences
2 The Leslie and Susan Gonda Multidisciplinary Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel
3 The Paul Feder Laboratory on Alzheimer's disease research

Accumulating evidence indicates that aging is associated with a chronic low-level inflammation, termed sterile-inflammation. Sterile-inflammation is a form of pathogen-free inflammation caused by mechanical trauma, ischemia, stress or environmental conditions such as ultra-violet radiation. These damage-related stimuli induce the secretion of molecular agents collectively termed danger-associated molecular patterns (DAMPs). DAMPs are recognized by virtue of specialized innate immune receptors, such as toll-like receptors (TLRs) and NOD-like receptor family, pyrin domain

containing 3 (NLRP3). We hypothesize that TLRs activated by DAMPs mediate sterile-inflammation, affecting aging and age-related CNS pathologies.

Inflammation: a culprit for vascular calcification in atherosclerosis?

David Magne
Institute of Molecular and Supramolecular Chemistry and Biochemistry, University of Lyon, France

Plaque calcification is a hallmark of atherosclerosis and the calcium score as emerged as a strong independent predictor of acute cardiovascular events. A large number of evidences indicate that inflammatory cytokines likely play a role in calcification and that crystals, in turn, may exert pro-inflammatory effects. However, recent data suggest that this presumed exclusively negative impact of calcification on atherosclerosis plaques may be too simplistic. Indeed, if the first microcalcifications seems to be pro-inflammatory and harmful, the bone metaplasia that eventually forms in advanced plaques likely stabilizes the plaques. In this contradictory context, we will discuss some recent important studies on the relationship between inflammation, calcification and plaque stability. In addition, we will consider recent data suggesting that tissue nonspecific alkaline phosphatase (TNAP) likely participates to plaque calcification and inflammation, and represent a promising target to determine the effects of calcification on plaque progression and stability.

Innate immune system (deficiencies) in chronic inflammation

Gunnar Houen
Statens Serum Institut, Copenhagen, Denmark

The innate immune system has a vital role for initial control of infections and for activation of the adaptive immune system. Consequently, deficiencies of innate immunity predispose to infections and to inflammatory and autoimmune syndromes associated with chronic infection. This will be illustrated for selected human herpes-viruses and for the systemic autoimmune disease lupus erythematosus.

Chronic inflammation and age-related macular degeneration

Stephen Moss, Jennifer Williams, Camilla Pilotti and John Greenwood
UCL Institute of Ophthalmology, 11-43 Bath Street, London EC1V9EL, UK

Age-related macular degeneration (AMD) is the most common blinding eye disease in western societies, affecting around 1:10 individuals by the age of 60, rising to 1:4 by age 75. With life expectancy increasing, AMD presents a major health care challenge with important consequences for quality of life and independence. Although the genetics of AMD is complex, more than 50% of all cases are linked to specific high-risk polymorphisms in genes associated with the alternative

pathway of complement activation, most notably *Cfh*. Despite this clear association, the underlying biology and cellular pathophysiology of AMD remains poorly understood. Our approach has been to use mouse models deficient in certain complement genes, but these have major limitations. More recently we have therefore switched to conditional gene knock-outs and these have provided new insight into the regulation of complement homeostasis in the retina that I will discuss in my presentation.