Mini symposium at the Institute of Molecular Medicine, SDU, J.B. Winsløws Vej 25, auditorium Odense

Friday January 29, 2016 (10:30 – 12:00)

- all are welcome

10:30
Complement Regulation - Lessons Learned from Patients
Professor Peter F. Zipfel
Department of Infection Biology, Hans Knöll Institute, Jena, Germany

11:15
Structural studies of complement proteases and their complexes
Professor Gregers Rom Andersen
Department of Molecular Biology and Genetics, Aarhus University, Denmark

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Professor Peter F. Zipfel
Complement Regulation - Lessons Learned from Patients
The human organism is constantly exposed to microbes and infectious agents and consequently has developed a complex and highly efficient immune defense which is aimed to recognize and eliminate such infectious agents. The response of the human host to infectious agents forms a double edged sword of immunity. The immune system has to keep a tight balance between attack on foreign surfaces and protection of host surfaces. In its proper function the immune response is aimed to recognize, attack and eliminate invading infectious agents and this response is beneficial for the host. However when the activated immune response like the complement system is not properly controlled and deregulated, effector compounds can attack and damage self-surfaces and this results in disease. In addition pathogens which cause infections and disease protect themselves from the damaging and harmful host immune weapon and use specific immune escape strategies. The complement system forms the first defense line of innate immunity and aids in the elimination of microbes and modified self-cells. Defective regulation of this cascade type system results in infections and in pathology. This can result in

diseases, like severe renal diseases hemolytic uremic syndrome (HUS) and dense deposit disease (DDD), in age related macular degeneration a common form of blindness and also in other forms of autoimmune diseases.

Professor Gregers Rom Andersen

Structural studies of complement proteases and their complexes

The proteolytic cascade of the complement system is initiated when pattern-recognition molecules (PRMs) bind to ligands, resulting in the activation of associated proteases. In the lectin pathway of complement, the complex of mannan-binding lectin (MBL) and MBL-associated serine protease-1 (MASP-1) initiates the pathway by activating a second protease, MASP-2. Here we present a structural study of a PRM/MASP complex and derive the overall architecture of the 450 kDa MBL/MASP-1 complex using small-angle X-ray scattering and electron microscopy. The serine protease (SP) domains from the zymogen MASP-1 dimer protrude from the cone-like MBL tetramer and are separated by at least 20 nm. This suggests that intracomplex activation within a single MASP-1 dimer is unlikely and instead supports intercomplex activation, whereby the MASP SP domains are accessible to nearby PRM-bound MASPs. This activation mechanism differs fundamentally from the intracomplex initiation models previously proposed for both the lectin and the classical pathway.