



# NSI Meeting Announcement

Date: Thursday, March 22<sup>nd</sup>, 15:00 – 15:45

Venue: Auditorium 2 (red), Rikshospitalet

## Guest lecture

by

## Professor Marco Colonna

Washington University School of Medicine, Department of Pathology  
and Immunology, St. Louis, Missouri, USA

### ***“Plasmacytoid dendritic cells in anti-viral immune responses”***

One critical question about the generation of host anti-viral responses is how plasmacytoid dendritic cells (PDC) and dendritic cells (DC) sense viruses. PDCs recognize RNA and DNA viruses through Toll-like receptor (TLR)7 and TLR9. Detection occurs in early endosomes, does not require active viral replication and leads to the prompt release of high amounts of type I interferons (IFNs), which act on surrounding cells inducing bystander activation. TLR7/9 signaling in pDCs is inhibited by DAP12-dependent cell surface receptors.

DCs have evolved additional strategies based on the ability to recognize dsRNA intermediates, which are generated during replication of RNA viruses and some DNA viruses. TLR3 detects dsRNA in endosomes; this pathway allows recognition of dsRNA associated with dying cells that enter the endosomal route. TLR3 also allows recognition of viruses that use receptor-mediated endocytosis to gain entry into the cell.

However, viruses that directly access the cytoplasm may evade TLR3 detection. Thus, DCs are equipped with cytosolic sensors of dsRNA. Recent studies demonstrate that the RNA helicase encoded by the melanoma differentiation gene 5 (MDA-5) is a critical component of cytosolic recognition of dsRNA. MDA-5-deficient DCs are incapable of producing type I IFNs in response to the synthetic analog of viral dsRNA, poly(I:C), and do not respond to picornaviruses *in vitro*, such as the encephalomyocarditis virus (EMCV). Moreover, MDA-5-deficient mice succumb earlier to lethal doses of EMCV *in vivo*. Collectively, these studies demonstrate that pDCs and DCs detect viruses through multiple sensors that trigger type I IFN responses through distinct pathways.

**Refreshments will be served from 14:45**

**Welcome all!**



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