



The Norwegian Society for Immunology hereby announces the June 2011 Guest Lecture:

Effects of Polymorphic Killer Cell Immunoglobulin-like Receptors on Resolution of Hepatitis C Virus

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Date: Tuesday, 21st of June 2011
Venue: Seminar room A3.3067, Rikshospitalet
(one floor up from IMMI)
Time: 14.00-15.00

Program

14.00-14.15: Refreshments
14.15-14.00: Guest Lecture and discussion

Resolution of hepatitis C virus (HCV) infection is influenced by host polymorphisms of killer cell immunoglobulin-like receptors (KIR) and their human leukocyte antigen (HLA) class I ligands. Previously reported genomic analyses suggest that weak inhibitory combinations of KIR and HLA (and hence stronger immunity) are associated with modestly increased rates of spontaneous HCV resolution. Genomic typing alone, however, fails to examine critically important features of KIR biology, including polymorphisms that affect receptor density, frequency, and function. We used flow cytometry and genomic analyses to examine the combined effects of KIR expression and of compound KIR and HLA types on HCV resolution. Our results indicate that HCV persistence is associated with NK cell expression of strong inhibitory KIR in the context of their HLA ligands. Patients with the weakest inhibitory KIR2DL and HLA-C pairs, in the absence of confounding inhibitory KIR3DL1 and HLA-A or -B pairs, resolved HCV at rates approaching 50%, as compared with a cohort specific rate of 23%. Among patients with strong inhibitory KIR and HLA interactions, HCV resolution is associated with increasing numbers of putatively licensed NK cells. These results indicate that KIR and HLA interactions on NK cells may have profound, rather than modest, influences on HCV immunity, and that HCV persistence stems in part from inadequate NK cell activation.

Results from a preliminary clinical study of innate immune polymorphisms and treatment related outcomes among 492 patients with chronic HCV will also be presented. This study was performed in patients that underwent liver biopsy during consideration for interferon- α based treatment between 1992 and 2010. The study suggests that hepatic inflammation and fibrosis may be accelerated by current therapies in patients who fail to clear the virus. Patients who cleared the virus were protected from cirrhosis after stratification by baseline liver fibrosis stage and adjustment for clinical and behavioral risk factors. Unexpectedly, treatment failures had a markedly increased hazard of developing cirrhosis (HR = 3.73, CI 1.12-12.40) compared to never treated patients. As treatment induced viral clearance is achieved in only a subgroup of patients, previously approved treatment regimens for HCV may cause more cirrhosis than they prevent.