



NSI and CIR
Meeting Announcement
Date: Tuesday, Sept 9th, 15:00 – 15:45
Venue: Seminar room A3.3067, RH



Guest lecture

Professor Sally Ward

Department of Immunology, UT Southwestern Medical Center, Dallas

“The role of FcRn in IgG homeostasis: from protein engineering to imaging single molecules in 3D”

Antibodies represent a rapidly expanding class of therapeutics and diagnostics. The MHC Class I-related receptor, FcRn, plays a pivotal role in regulating the transport and distribution of immunoglobulinG (IgG) in vivo. The binding site for FcRn on IgG has been mapped and involves several well conserved residues at the CH2-CH3 domain interface of the Fc region. FcRn-IgG interactions are characterized by marked pH dependence, with relatively tight binding at pH 6.0 that becomes progressively weaker as near neutral pH is approached. This pH dependence allows IgG molecules to interact with FcRn in acidic early endosomes following uptake into cells, followed by recycling/transcytosis and exocytic release at the cell surface.

The engineering of IgGs with higher affinity for FcRn is of considerable interest since it can be used to produce antibodies with longer in vivo half lives, but only if the pH dependence of the interaction is retained. Conversely, engineered IgGs with increased affinity for FcRn at both acidic and near neutral pH can act as potent inhibitors of FcRn. Such engineered antibodies (‘Abdegs’, for antibodies that enhance IgG degradation) can lower the levels of endogenous IgG and therefore have potential uses as therapeutics.

From the point of view of using antibodies as therapeutic agents and from a cell biological perspective, it is important to understand how FcRn performs its function as a salvage receptor in cells. We are using a combination of fluorescence imaging approaches, including single molecule and multifocal plane microscopy, to analyze how FcRn and its IgG cargo traffick within live endothelial cells. These studies are giving a dynamic, high resolution view in three dimensions as to how IgG salvage and recycling occurs.

Refreshments will be served from 14:45

Welcome all!



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www.norwegianimmunology.org

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