

DATE:
Tuesday,
29 April 2008

VENUE:
Centre for Life Sciences
Auditorium, Level 1

TIME:
4.00 - 5.00 pm



Immune Recognition and the Atkins Diet

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Abstract

$\alpha\beta$ T cell receptors interact with peptide and lipid-laden MHC and CD1 molecules respectively. The MHC is highly polymorphic engendering the ability to bind a wide array of peptides, whilst the CD1 family are monomorphic members binding distinct lipids. Structural studies on TCR-pMHC complexes have revealed markedly different docking strategies utilised by the TCR in recognising peptides of canonical and non-canonical length. Recently, we have also determined how a TCR can recognise a glycolipid presented by CD1d. This latter interaction, which has been probed via extensive mutational analyses, is more typical of innate pattern receptor recognition events. These variations on a theme are discussed in the context of peptide and lipid-mediated recognition by a TCR.

Biography

Prof. Rossjohn's principal contribution to biomedical health lies in providing an understanding of processes central to infection and immunity. Moreover, alongside collaborators from Adelaide, his interest in bacterial toxins included the characterization of a novel toxin from pathogenic *E. coli* that is the causative agent for outbreaks of haemolytic uraemic syndrome in Australia, and overseas.

The flip-side to infection, immunity, represents the 2nd main arm of his research program. In collaboration with colleagues from Melbourne and Queensland, his research is aimed at understanding the structural basis of adaptive and innate immunity, which includes peptide and lipid presentation, T-cell mediated graft rejection and T-cell mediated autoimmune disorders. His research on T-cell repertoire selection provided a basis for understanding biased TcR gene usage in Epstein-Barr Virus and Influenza infection, ubiquitous human pathogens. Subsequently he demonstrated that super-bulged MHC-I restricted epitopes could also generate an anti-viral T-cell response, which provided insight into the minimal requirements of MHC restriction, the process of positive selection, as well as having important implications for epitopes used in peptide-based vaccine design. The team also demonstrated the structural basis for MHC Class 1b-mediated responses in adaptive immunity, which is important in *Cytomegalovirus* and *M. tuberculosis* infection. In transplantation, T cells recognise the foreign MHC complexes on the graft and initiate an alloreactive response that ultimately leads to allograft rejection. The findings on alloreactivity, provided a basis why certain MHC alleles represent a significant alloreactive barrier to clinical transplantation, and also provided insight into the mode of action of the therapeutic antibody, OKT3, an immunosuppressant used to prevent transplant rejection. Furthermore, his team has made contributions to autoimmunity, having determined the structure of a key autoantigen in multiple sclerosis and a key antigen protecting the fetus from the maternal immune system. Recent research in Celiac disease has important implications for how the disease is diagnosed and treated in certain human populations with a genetic background that predisposes them to this disease. The team's recent findings provided important insights into how microbial lipids are recognised by NKT cells and have important implications for glycolipid-based vaccine development.

Prof. Rossjohn, alongside his colleagues, has published more than 115 papers, including articles in *Nature*, *Cell*, *Science*, *Nature Immunol.*, *Immunity*, *J. Exp. Med.*, *Nature Structural Biology*, *EMBO J.*, *PNAS*, *Nature Reviews Immunology* and *Nature Reviews Drug Discovery*.

ALL ARE WELCOME

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