MACQUARIE University
SYDNEY·AUSTRALIA

Biomolecular Frontiers Research Centre (BMFRC)

Special Seminar

Monday 14th March, 12-1pm

F7B322

Hosted by the Biomolecular Frontiers Research Centre

Prof Leonard C Harrison

Title: CD52 glycan mediates immune suppression by binding sialic acid binding Ig-like lectin (Siglec) receptors

Abstract:
Immune cells use a range of mechanisms to regulate each other and maintain homeostasis. In testing the hypothesis that paracrine mechanisms limit T-cell proliferation, we discovered that antigen-activated T cells with high expression of the GPI-anchored glycoprotein CD52 suppress other T cells. We showed that suppression is due to phospholipase C-mediated release of soluble CD52, which binds to the sialic acid binding Ig-like lectin (Siglec)-10 receptor on human T cells; this leads to decreased phosphorylation of T-cell receptor-associated tyrosine kinases Lck and ZAP-70, and impaired T-cell activation (1). The significance of CD52 in vivo is reflected by the acceleration of diabetes onset in the non-obese diabetic mouse, a model of autoimmune (type 1) diabetes, after depleting high CD52-expressing T cells.

Mature CD52 is a small peptide (12 aa) with at least one O-glycan and a single N-linked glycan. Nanomolar concentrations of recombinant CD52-Fc suppress not only T cells but also innate immune cells (monocytes, dendritic cells) by inhibiting the NFkB pathway, and at higher concentrations induce apoptotic cell death. Direct studies with recombinant proteins show that immune suppression by CD52 requires that it first capture the danger-associated molecular pattern protein, HMGB1. CD52-HMGB1-Siglec interactions depend on the CD52 N-glycan, the detailed structure of which will elucidate the biological functions of CD52.

(1) Bandala-Sanchez et al. Nature Immunol 14:741-748, 2013.

Brief Bio: Leonard C Harrison
Len Harrison is a Senior Principal Research Fellow of the NHMRC, and Professor in the Population Health and Immunity Division at the Walter and Eliza Hall Institute of Medical Research. At the Royal Melbourne Hospital, he was Director of Diabetes and Endocrinology 1981-87 and Director of Immunology and Allergy 1987-2010. His early research was on the structure-function of the insulin receptor, leading to a C.J. Martin Fellowship at the National Institutes of Health, USA. Subsequently, in Melbourne, he pioneered pre-clinical diagnosis and prediction of type 1 diabetes, identified proinsulin as a key autoantigen in type 1 diabetes and initiated trials of a nasal insulin vaccine for type 1 diabetes prevention. His research is now focused on epigenetic mechanisms of immune regulation in early life. He has authored over 550 scientific papers and is the recipient of various awards including the Wellcome (Glaxo) Australia Medal, Susman Research Prize (Royal Australasian College of Physicians),

Kellion Medal (Australian Diabetes Society) and Rumbough Award for Scientific Excellence and Lifetime Achievement Award (Juvenile Diabetes Research Foundation).