# Keynote Lecture V
# The Role of Innate Immunity in Autoimmune Diseases

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After graduating in Chemistry at Monash University, Melbourne, Liew took a PhD in Immunology at the John Curtin School of Medical Research, Australian National University. He joined the Wellcome Research Laboratories, Beckenham, Kent, UK in 1977 and moved to the Gardiner Chair and Head of the Department of Immunology, Glasgow University in 1991. He has also been Director of the Glasgow Biomedical Research Centre since 2002.

His main research contributions have been in the understanding of the role of CD4+ T cell subsets in infection and inflammation. His group was the first to show the heterogeneity of CD4+ T cells and their functional role in Leishmania infection. He also showed that nitric oxide plays a central role in the destruction of intracellular pathogens and in mediating inflammatory pathology. More recently, his group demonstrated that Interleukin (IL)-15 plays an important role in rheumatoid arthritis and anti-IL-15 antibody is at advanced stage of clinical trial for treating arthritis.

He was elected Fellow of the Royal Society of Edinburgh in 1995, Fellow of the Academy of Medical Science in 1999, and was awarded the Sheikh Hamdan Prize in 2002. He was elected President of the European Federation of Immunological Societies (EFIS) 2003-2006.

Toll is the founder of a group of pattern recognition receptors, which play a critical role in the innate immunity in *Drosophila*. At least 13 distinct Toll-like receptors (TLRs), recognizing pathogen-associated molecular pattern (PAMPs), have now been identified in humans. Most investigations on TLRs have focused on cells of the innate system. We have investigated the expression and role of TLRs on T cells. We have found that naïve human T cells expressed high levels of cell surface TLR2 after activation by anti-T cell-receptor (TCR) antibody and Interferon-α. Activated cells produced elevated levels of cytokines in response to the TLR2 ligand, bacterial lipopeptide (BLP). Furthermore, $CD4^+CD45RO^+$ memory T cells from peripheral blood constitutively expressed TLR2 and produced IFNγ in response to BLP. BLP also markedly enhanced the proliferation and IFNγ production by $CD45RO^+$ T cells in the presence of IL-2 or IL-15. Thus, TLR2 serves as a co-stimulatory receptor for antigen-specific T cell development and participates in the maintenance of T cell memory. This suggests that pathogens, via their PAMPs, may contribute directly to the perpetuation and activation of long term T cell memory in both antigen dependent and independent manner.

Since BLP (and indeed other PAMPs) are highly conserved in bacteria, this finding would predict that control mechanisms must exit to limit the continuous activation of the immune system to avoid autoimmunity. We have now found a potential key regulatory mechanism involving other members of the Toll-IL-1R family to limit the excessive activation of TLR2 signaling.

The Toll-IL-1 receptor (TIR) superfamily, defined by the presence of an intracellular TIR domain, initiates innate immunity via NF-κB activation, leading to production of pro-inflammatory cytokines. ST2 is a member of the TIR family that does not activate NF-κB and has been suggested as an important effector molecule of type 2 T helper cell responses. We have demonstrated that the membrane bound form of ST2 (ST2L) negatively