**The role of cytokine in infection and inflammation**

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**ABSTRACT**

Cytokines are hormones of the immune system. Cytokine-targeting represents a major triumph in immunology scientifically, clinically and commercially. There is therefore considerable interest in discovering novel cytokines. I will illustrate the pleiotropic role of some of the novel cytokines by focusing on interleukin (IL)-33. IL-33 is a member of the IL-1 family. It is the ligand of ST2, which is expressed mainly on Th2 cells, epithelial cells, neuronal cells and mast cells. IL-33 can skew a predominantly Th1 cell population to Th2 cells phenotype in vivo. Furthermore IL-33 potently induces Type 2 innate lymphocyte (ILC2) and alternatively activated macrophages (M2), leading to the differentiation of regulatory T cells (Tregs).

I will present some recent finding on the role of IL-33 in cerebral malaria and Alzheimer’s disease. IL-33 reduces the pathology and mortality of experimental cerebral Malaria in mice by activating ILC2, which induces M2 that enhance the differentiation of a subset of Tregs, which suppress the inflammatory response. A combination treatment of IL-33 with artesunate and chloroquine is a promising new approach for treatment of cerebral malaria, a devastating condition with unmet clinical need. Alzheimer’s disease is characterized by an accumulation of β-amyloid in the brain that triggers chronic neuroinflammation and leads to microglia activation, and synaptic and neuronal dysfunction. Systemic injection of IL-33 reversed synaptic plasticity impairment and cognitive deficits in APP/PS1 mice (a model of Alzheimer’s disease) and reduced soluble β-amyloid levels and amyloid plaque deposition by promoting the recruitment and uptake of β-amyloid by microglia. In addition, intraperitoneal injection of IL-33 modulates the innate immune response by polarizing microglia towards an anti-inflammatory phenotype and reducing the expression of pro-inflammatory genes, such as Nlrp3, IL-1β and IL-6 in the cortices of APP/PS1 mice. In humans, IL-33 expression was decreased in the brain of patients with Alzheimer’s disease, and levels of serum sST2 are elevated in patients with mild cognitive impairment. Furthermore, genetic studies have linked IL33 and ST2 single nucleotide polymorphism to Alzheimer’s disease. Therefore, mobilization of innate immunity by IL-33 to prevent and clear established β-amyloid accumulation represents a new treatment paradigm for Alzheimer’s disease.

**ABOUT THE SPEAKER**

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 was the founding Director of the Glasgow Biomedical Research Centre.

Liew’s main research interest has been the role of CD4+ T cell subsets, nitric oxide and cytokines in infection and inflammation. He demonstrated the key role of interleukin (IL)-15 and IL-18 in rheumatoid arthritis. More recently, he is investigating the biology of IL-33, a new member of the IL-1 family.

Liew was elected Fellow of the Royal Society of Edinburgh in 1995, Fellow of the Academy of Medical Science in 1999, and Fellow of the Royal Society in 2012. He was awarded the Sheikh Hamdan Prize for Medical Research Excellence in 2002 and was President of the European Federation of Immunological Societies (EFIS, 2003-2006). He was Editor-in-Chief of the European Journal of Immunology (2006-2011). He chairs the Biomedicine Research Panel, Hong Kong, and was a member of the UK MRC Infection and Immunity Board, and President of the European Congress of Immunology 2012.