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 the latest member of the IL-1 family. It is the ligand of ST2, which is expressed mainly on activated 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 alternatively activated macrophages (M2). IL-33 signals via MyD88, the canonical pathway shared by all members of the IL-1 family. Additionally, IL-33 activates type II cytokines via mTOR (mammalian target of rapamycin). IL-33 mRNA is expressed early during infection of the intestinal-dwelling nematode Trichuris muris in mice and IL-33 treatment enhances resistance to Trichuris infection by inducing Th2. Furthermore, IL-33 reduces the pathology and mortality of experimental cerebral Malaria infection in mice by activating M2. Importantly, IL-33 also effectively attenuates sepsis by mobilising the innate cells neutrophils, to the site of infection and helps to clear the pathogens. Thus IL-33 is evolutionally preserved for the host defence against infections. However, IL-33 can also induce Type 2 innate lymphoid cells (ILC2), which mediate airway inflammation. Furthermore, IL-33 contributes to the severity of mucocytis accompanying chemotherapy (Irinatecan). Blocking IL-33 prolongs the treatment and effectiveness of chemotherapy in colorectal cancer. In contrast, IL-33 appears to restore the long-term potentiation in a murine model of Alzheimer’s disease. Therefore, IL-33 is a double-edged sword and targeting IL-33 should be approached with caution.

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 (2008-2012). 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.