SIgN Immunology Seminar



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The role of cytokine in infection and inflammation

Date
Friday
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Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Host
Prof Ren Ee Chee
Singapore Immunology Network

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, intra-peritoneal 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.