SIgN

SIgN Immunology Seminar

Dr Francesca Fallarino

Department of Experimental Medicine and Biochemical Sciences
University of Perugia, Italy

Indoleamine 2,3-dioxygenase: as an inducer and amplifier of regulatory T cell functions

Host
Prof Paola Castagnoli
Singapore Immunology Network, A*Star

Date
Tuesday, 6 November 2012

Time
11am – 12pm

Venue
SIgN Seminar Room,
Immunos Building
Level 4
Biopolis

Regulation of tryptophan metabolism by indoleamine 2,3-dioxygenase (IDO) in dendritic cells (DCs) is a highly versatile modulator of immunity. In inflammation, interferon γ (IFN-γ) is the primary IDO inducer to prevent hyperinflammatory responses, but the enzyme is also responsible for longer-term, self-tolerance effects. Treatment of mouse plasmacytoid DCs (pDCs) with transforming growth factor β (TGF-β) confers regulatory effects on IDO that are mechanistically separable from its enzymic activity. In particular, IDO appears to be involved in intracellular signaling events responsible for self-amplification and maintenance of a stably regulatory phenotype in pDCs. Thus IDO has a dual immunoregulatory function driven by distinct cytokines. The IFN-γ–IDO axis is pivotal in generating and sustaining the function of T_{reg} cells through the combined effects of tryptophan starvation and kynurenines acting via the aryl hydrocarbon receptor of T cells. A second tonic, non-enzymic function of IDO contributes to TGF-β–driven tolerance in non-inflammatory contexts, including fetomaternal tolerance and tolerance to self. The latter function is part of a regulatory circuitry in pDCs whereby—in response to TGF-β—the kinase Fyn mediates tyrosine phosphorylation of IDO-associated immunoreceptor tyrosine-based inhibitory (ITIM) motifs, resulting in downstream effects that regulate gene expression and preside over proper, local homeostatic balance between immunity and tolerance.