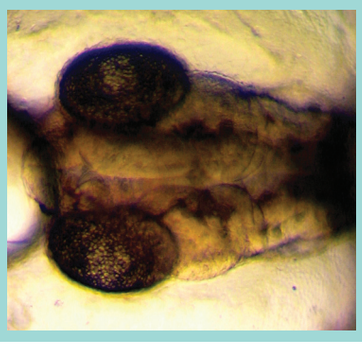
European Journal of Immunology

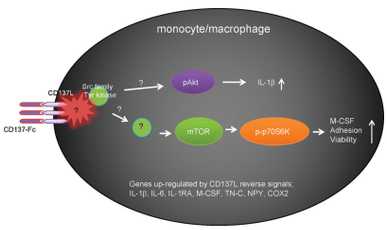
In this issue



Cover image

This cover is specifically designed to celebrate the 2nd European Congress of Immunology (www.eci-berlin2009.com), to be held September 13–16, 2009 in Berlin. The cover consists of a collage of images from Iwanami *et al.* (*pp* 2606–2616) with Berlin's historic Bradenburg Gate, *Brandenburger Tor*, in the forefront (image of the Brandenburg Gate © ImageState). Iwanami *et al.'s* elegant study shows that, in addition, to defective thymus development, teleosts with mutations in *KIAA1440*, TRRAP, and *SKIV2L2* also exhibit defective development of multiple organs, thus identifying previously unknown roles of these genes in organ development.

(pp 2617–2628)

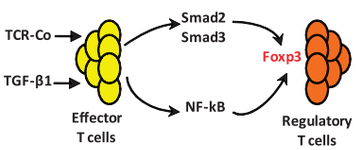


Modulating innate immunity *via* CD137 ligand

Reverse signaling through CD137L, a member of the TNF family, has been shown to modulate cellular immune responses. The molecular mechanisms underlying these effects, however, remain elusive. In this issue, Kim *et al.* demonstrate that in mouse myeloid cells, cross-linking of CD137L with rCD137-Fc protein phosphorylates Src family tyrosine kinase(s). It activates both Akt and mTOR/p70S6 kinase in parallel *via* unidentified pathways. CD137L reverse signal-mediated mTOR/p70S6 kinase pathway enhances cell viability, adhesion and M-CSF expression. The Akt pathway, on the other hand, is responsible for induction of IL-1β. While TLR signals are responsible for initial activation of innate immune cells, reverse signaling through CD137L may serve as a fine-tuning device when innate immune cells make physical contact with T cells.

Molecular mechanisms for Treg induction

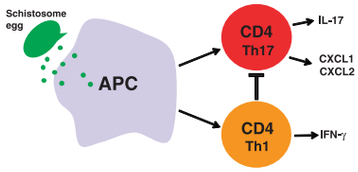
(pp 2571–2583)



Cellular therapy using Treg is an appealing option for the prevention of autoimmune diseases. One method of inducing Treg from effector T cells is through T-cell stimulation in the presence of exogenous TGF-β1. Given that the extent of Foxp3 expression in Treg correlates with their regulatory function, increasing Foxp3 levels remains a key goal to enhance efficacy of cellular therapy in clinical trials. In this issue, Jana *et al.* show that both Smad3 and Smad2 are required for TGF-β1-induced Foxp3 expression. In contrast, T-cell stimulation *via* the NF-kB pathway is more complex with evidence for both a positive effect on Foxp3 expression *via* IL-2 production, and a repressive effect through the activation of p50, one of the main NF-kB subunits. Understanding the differential effects of these pathways may facilitate the optimization of Treg-generation for the prevention and treatment of autoimmune diseases in the future.

(pp 2470–2481)

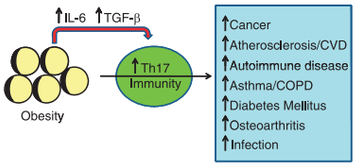
Th1 cells regulate a Th17-mediated severe form of murine schistosomiasis



The role of Th1 *vs*. Th17 cells in inflammatory diseases remains a controversial issue. In murine schistosomiasis, both Th1 and Th17 cells are induced in its severe form: the hepatic egg-induced granulomatous inflammation. In this issue, Rutitzky *et al.* use the T-bet-deficient mice, which have impaired Th1 immunity, to study the relative importance of the Th1 and Th17 subsets in murine schitosomiasis. T-bet-deficient mice have exacerbated immunopathology with increased neutrophil-infiltration and hyperactive DC/CD4$^+$ T cells in the lesions. In the infected T-bet$^{-/-}$ mice, the absence of IFN-γ correlates with an increase in IL-23p19, IL-17, IL-22 and TNF-α, and with a decrease in IL-4, IL-5 and IL-10. The study also shows a decrease in markers for alternatively activated macrophages and Treg. Overall, the findings demonstrate that Th1 cells regulate Th17 cell-mediated immunopathology; however, they do not exclude a pathogenic role of the Th1 subset in the absence of Th17 cells.

Th17 biased immunity: The link between obesity and inflammatory disease?

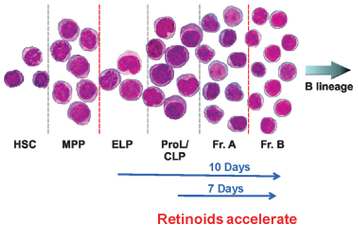
(pp 2629–2635)



The incidence of obesity is increasing worldwide and is becoming a major global cause of morbidity and mortality. Obesity has been epidemiologically linked to numerous inflammatory conditions including atherosclerosis, autoimmune disease, asthma, diabetes mellitus, and cancer. The cause of this association is unclear. In this issue, Winer *et al*. show that obesity favours a pro-inflammatory Th17-biased immune response, providing one plausible mechanism to explain the relationship between obesity and inflammatory disease. T cells from obese, but not lean, mice immunized with the CNS protein myelin oligodendrocyte glycoprotein (MOG) show enhanced IL-17 secretion resulting in the development of severe, early onset, autoimmune demyelination. Obese mice were also more prone to developing Th17-mediated colitis. These results highlight the importance of obesity's impact on the immune system and on the development of chronic inflammatory disease.

(pp 2515–2524)

Retinoids set the pace



Retinoids appear to control some rate-limiting events during B-cell development. Progression of the B-cell lineage is remarkably accelerated when retinoids are added to adult lymphoid progenitor cultures. In this issue, Chen *et al.* demonstrate that there is more complexity to the system. In contrast to retinoids' effect on adult lymphoid progenitor cultures, retinoids inhibit B lymphopoiesis in fetal progenitor cultures. Interestingly, the authors also show that retinoids have an inhibitory effect on adult progenitors when cells are exposed at high doses or for prolonged periods. Taken together, the data suggest that fetal lymphoid progenitors may be exposed to retinoids in the fetal environment and hence the unexpected response to retinoids observed in culture. More importantly, the results suggest that endogenous retinoids may regulate B lymphopoiesis.

