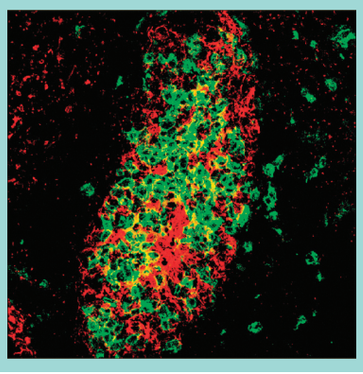
European Journal of Immunology

In this issue

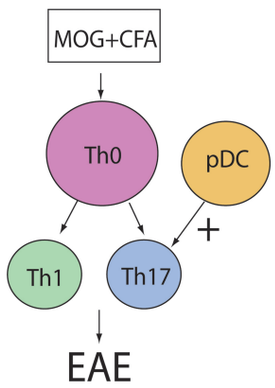


Cover image

The cover image is a colour inverted figure taken from *Role of DOCK2 and DOCK180 in fetal thymus colonization* by Lei *et al.* (*pp*. 2695–2702). By co-staining sections of frozen embryos for CD45 and keratin, the authors elegantly show that a combination of DOCK2 and DOCK180, two closely related CDM family molecules, plays a significant role in prevascular fetal thymus colonization.

(*pp 2925–2935*)

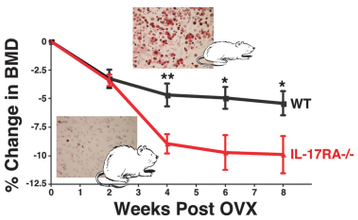
Plasmacytoid DC promote priming of Th17 and EAE



Plasmacytoid DC (pDC) produce large amounts of type I IFN upon activation and are implicated in the pathogenesis of systemic autoimmune diseases. In this issue, Isaksson *et al*. show that pDC are important for the initiation of the organ-specific autoimmune disease EAE. The presence of pDC during initiation of EAE promotes clinical signs of the disease, inflammation and demyelination of the CNS. Type I IFN mediate this effect to some extent, but the interaction between pDC and Th17 cells appears to be central. The numbers of autoimmune Th17 cells, but not Th1 cells, are much higher in the presence of pDC during priming. In contrast, pDC deficiency later in the disease process leads to exacerbated clinical signs of EAE. These observations are relevant not only for EAE and MS, but also for other autoimmune diseases involving pDC.

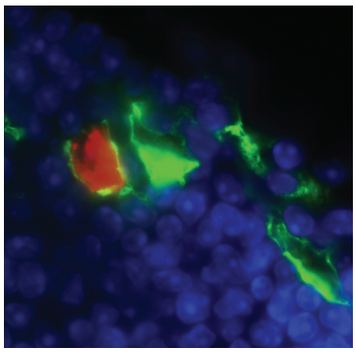
IL-17, bone, and fat: A surprising relationship

(*pp 2831–2839*)



Osteoporosis affects millions of women worldwide. The pathogenesis of osteoporosis is linked to inflammatory cytokines including TNF-α, IL-1 and IL-6. Mice deficient in these cytokines are protected from bone loss following ovariectomy (OVX), the standard model of post-menopausal osteoporosis. IL-17, the hallmark cytokine of Th17 cells, cooperates closely with TNF-α, IL-6 and IL-1 to drive inflammation. IL-17 is also directly bone-destructive in the context of rheumatoid arthritis. Accordingly, one would expect IL-17 to play a similar pro-inflammatory, bone-destructive role in osteoporosis. In this issue, Goswami *et al.* demonstrate that IL-17 receptor-deficient mice (IL-17RA$^{-/-}$) unexpectedly exhibited accelerated bone loss following OVX, and also became overweight. Leptin, a cytokine associated with fat metabolism and satiety, was also increased in IL-17RA$^{-/-}$ mice. *In vitro*, IL-17 suppressed the adipogenesis and leptin production of 3T3-L1 cells. Combined with recent reports showing that IL-17 promotes osteoblastogenesis, these findings suggest that IL-17 protects bone during estrogen deficiency, probably by favoring osteoblastogenesis over adipogenesis.

(pp 2809–2821)

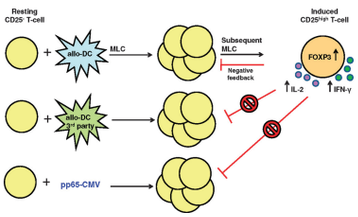


Dengue and the macrophage paradox

Dengue virus is transmitted by mosquitoes and causes a systemic inflammation with high fever that can progress into dengue hemorrhagic fever or dengue shock syndrome. In patients and in mouse models, the virus is most easily detected in macrophages, which are believed to play a key role in establishing and spreading dengue infection in the body. In this issue, Fink *et al.* show, contrary to expectations, depleting macrophages in a mouse model of infection leads to an increase in systemic infection. This, together with the observation that macrophages infiltrate infected lymphoid organs in large numbers, suggests that macrophages play a dual role in dengue infection – while macrophages are important for establishing infection, macrophages are also critical for virus control.

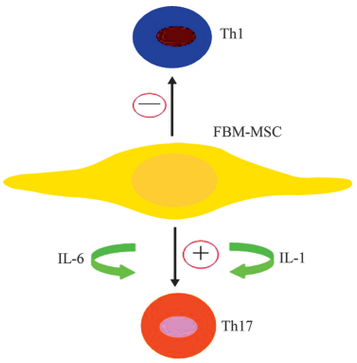
Induced Treg: Just what we need in BMT?

(pp 2703–2715)



Induced human $CD4^+CD25^+$ T cells have been shown to express FOXP3, similar to the naturally occurring regulatory T cells (nTreg). The inhibitory capacity of these induced cells is, however, under debate. In this issue, Stroopinsy *et al.* investigate functional characteristics of $CD4^+CD25^{high}$ $FOXP3^+$ cells derived from $CD25^-$ precursors following allo-stimulation. Intriguingly, the resultant $CD4^+CD25^{high}$ population concurrently exhibited the regulatory markers FOXP3, CTLA-4, GITR and the inflammatory cytokines IL-2 and IFN-γ. Similarly to nTreg, induced $FOXP3^+IFN\text{-}\gamma^+$ cells were shown, for the first time, to markedly inhibit alloreactive T-cell expansion. In contrast to nTreg, the induced cells did not suppress proliferation against a third party stimulator or cytomegalovirus, suggesting specific suppressive capacity, targeted against the original stimulus only. While selective suppressive capacity of induced $FOXP3^+IFN\text{-}\gamma^+$ cells would allow prevention of graft-*versus*-host disease, their prominent inflammatory cytokine expression would preserve graft-*versus*-infection and -tumor responses. Such unique duality makes these cells ideal for use as post-transplant graft-*versus*-host disease prophylaxis.

(pp 2840–2849)



Mesenchymal stem cells: Immunosuppressant or immunostimulant?

Mesenchymal stem cell (MSC) treatment is considered an attractive therapeutic option to dampen inflammation. Th17 cells are a new effector $CD4^+$ T-cell lineage with distinct cytokines profiles and are thought to be involved in inflammatory and autoimmune diseases. Given the suppressive effects of MSC on T cells, it is possible that MSC may also have the same effect on Th17 cells. On the contrary, in this issue, Guo *et al.* demonstrate that fetal bone marrow-derived MSC (FBM-MSC) promote the expansion of Th17 cells *in vitro*, with IL-6 and IL-1 being two soluble mediators involved in this process. FBM-MSC also decreases the percentage of Th1 cells. This study therefore demonstrates an unanticipated immuno-enhancing function of FBM-MSC on Th17 cells.

