IN BRIEF

T CELL RESPONSES

Autocrine transforming growth factor-β1 promotes in vivo Th17 cell differentiation

Gutcher, I. *et al. Immunity* **34**, 396–408 (2011)

Foxp3$^+$ regulatory T cells promote T helper 17 cell development in vivo through regulation of interleukin-2

Chen, Y. *et al. Immunity* **34**, 409–421 (2011)

CD4$^+$CD25$^+$Foxp3$^+$ regulatory T cells promote Th17 cells in vitro and enhance host resistance in mouse *Candida albicans* Th17 cell infection model

Pandiyan, P. *et al. Immunity* **34**, 422–434 (2011)

Transforming growth factor-β (TGFβ) is secreted by regulatory T (T_{Reg}) cells and is thought to be important for promoting both the development and the anti-inflammatory functions of these cells. More recently, TFGβ was shown to be involved in the differentiation of pro-inflammatory T helper 17 (T_H17) cells; this was somewhat counter-intuitive, as T_{Reg} cells can inhibit pro-inflammatory T_H17 cell responses in mouse models of disease (such as experimental autoimmune encephalomyelitis (EAE)). Three studies in *Immunity* now add an additional layer of complexity to the story. By conditionally depleting TGFβ expression in T_{Reg} cells or in both T_{Reg} cells and effector T cells, Gutcher *et al.* showed that autocrine production of TGFβ by T_H17 cells, rather than paracrine responsiveness to T_{Reg} cell-derived TGFβ, is required for T_H17 cell differentiation and the development of EAE. Chen *et al.* came to a similar conclusion, showing that T_H17 cells still develop normally when T_{Reg} cells are unable to express TGFβ. However, these authors found that conditional depletion of T_{Reg} cells did, in fact, inhibit T_H17 cell development *in vivo*. This effect was shown to result from the loss of T_{Reg} cell-mediated consumption of interleukin-2 (IL-2), which inhibits T_H17 cells. Pandiyan *et al.* echoed the findings of both studies, showing that IL-2 consumption by T_{Reg} cells, and not their ability to secrete TGFβ, allows this subset to promote T_H17 cell development. Furthermore, they found that in mice infected with *Candida albicans*, T_{Reg} cell-mediated support of T_H17 cell differentiation enhanced fungal clearance and recovery from infection. Pandiyan *et al.* suggest that T_{Reg} cells are not just important for suppressing immune responses — they can also contribute to protective immunity by supporting inflammatory T_H17 cell responses during infection.

VACCINES

An inactivated cell-culture vaccine against yellow fever

Monath, T. P. *et al. N. Engl. J. Med.* **364**, 1326–1333 (2011)

Although there is a highly effective vaccine for yellow fever (a lethal viral disease spread by mosquitoes in the tropics), this live attenuated vaccine can have serious side effects. Thus, there is a need for a safer, non-replicating vaccine, particularly for immunocompromised individuals. The first Phase I study of such a vaccine in healthy humans has shown promising results. A single injection of a high dose of XRX-001 (which comprises whole inactivated virus adsorbed to aluminium hydroxide) induced the development of virus-specific neutralizing antibodies in 46% of the study group. Furthermore, following a booster injection of XRX-001, 100% of the subjects developed neutralizing antibodies. The next important issue to address is whether XRX-001 can induce long-lasting protective immunity against yellow fever, in a similar manner to the live attenuated vaccine.