In the news

T-CELL VACCINE FOR MS

Following the promising results of a multiple sclerosis vaccine trial in a small group of patients, a large-scale trial has been initiated to test the efficacy of a personalized T-cell vaccine in patients with multiple sclerosis.

The vaccine, known as Tovaxin by its developers, the Texas-based company PharmaFrontiers, is now to be tested in 100 patients with multiple sclerosis. David McWilliams, of PharmaFrontiers, told *BBC News* that "if earlier results were replicated in this study, it might be possible to slow or even halt the progress of the condition." (8 March 2006).

The vaccine is made from the patients' own T cells, which are cultured in the laboratory in the presence of myelin antigens that are targeted by T cells in the disease and irradiated before being returned to the patient. The hope is that an immune response is triggered against the injected myelin-reactive T cells, thereby priming the patient's immune system for elimination of the disease-causing cells. "If that's the case, the earlier we can [vaccinate] after diagnosis the better", McWilliams told *New Scientist* (9 March 2006).

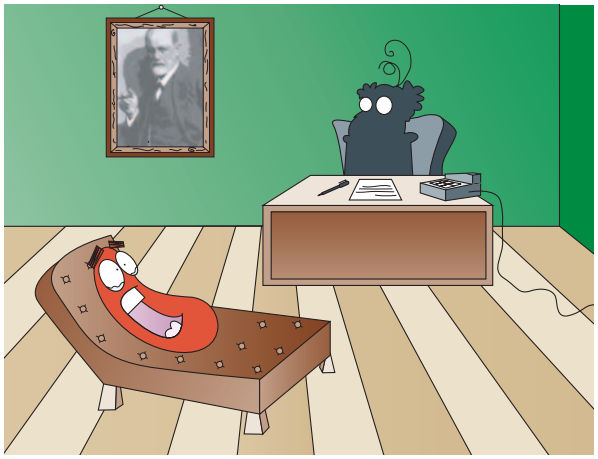
However, Richard Rudick of the Mellen Center for Multiple Sclerosis Treatment and Research in Cleveland, Ohio, is cautioning against over-enthusiasm for the new vaccine as "None have worked so far. This one may, but we don't know yet." (*Guardian*, 9 March 2006). In addition, there is no guarantee that normal T cells will not also be eliminated following vaccination.

Nevertheless, good news might await multiple sclerosis sufferers as the US Food and Drug Administration is expected to lift its ban on prescribing natalizumab (Tysabri; Biogen Idec/Elan). Natalizumab works by blocking the migration of myelin-reactive cells to the brain, and it has been recently reported to be better than existing interferon-β treatments (*The New England Journal of Medicine*, 2 March 2006).

Lucy Bird

REGULATORY T CELLS

Getting down to the specifics



It is now becoming clear that naturally occurring $CD4^+CD25^+$ regulatory T (T_{Reg}) cells not only keep self-reactive T cells in check but also hamper efficient control of microbial infection. However, whether the role of T_{Reg} cells in infection results from specific recognition of foreign antigen or from bystander activation through self-antigen remains a matter of debate. Now, Yasmine Belkaid and colleagues show for the first time that T_{Reg} cells can respond specifically to microbial antigens.

In earlier work, this group showed that, after infection of mice with the parasite *Leishmania major*, T_{Reg} cells accumulate in the skin and draining lymph nodes, where they impede effector-T-cell-mediated clearance of the pathogen. To assess the specificity of these T_{Reg} cells, the authors tested the ability of the cells to proliferate *in vitro* in response to *L. major*-infected bone-marrow-derived dendritic cells (BMDCs). Surprisingly, most of the $CD4^+CD25^{hi}$ T cells isolated from the skin-draining lymph nodes of chronically infected mice proliferated under these conditions. These $CD4^+CD25^{hi}$ T cells were indeed T_{Reg} cells (and not activated $CD4^+$ effector T cells, which also express CD25) because they were shown to express the T_{Reg}-cell-specific marker

T-CELL MEMORY

Less is more

Protective immunity to pathogens requires memory T cells that survive for many years after initial exposure to the infectious agent. The identity of the factors that influence the maintenance of naive and memory T cells *in vivo* remains highly sought after and is the subject of a recent study by Marc Jenkins and colleagues published in *Science*. They show that clone size markedly influences the survival of naive T cells and their memory-cell progeny.

To study *in vivo* T-cell survival, the authors first tracked polyclonal naive $CD4^+$ T cells after adoptive transfer to congenic recipients. Although most of the two million transferred cells died within the first 2 months, with an estimated half-life of 50 days, 10% of the cells were still detectable a year after transfer. However, when one million monoclonal naive $CD4^+$ T cells from T-cell receptor (TCR)-transgenic (DO11.10) mice were transferred to histocompatible mice, the half-life of these cells was only 12 days.

The authors proposed that the poor survival rates of monoclonal- compared with polyclonal-cell populations might be related to clone size. To enable the