INFECTIOUS DISEASE

A new tool for testing malaria vaccines

Vaccines directed against circumsporozoite (CS) proteins of *Plasmodium falciparum* (a causative agent of malaria) are undergoing Phase I human trials at present. One of the goals of these vaccines is to generate neutralizing antibodies specific for sporozoites (the pre-erythrocytic, blood-stage form of the parasite). But, *P. falciparum* does not infect rodents, and it is not possible to assess the efficacy of vaccine-induced neutralizing antibody responses in the lab. Now, researchers at New York University have developed an animal model for testing vaccine-induced antibody responses by modifying a rodent species of malaria.

Hybrid parasites were generated by targeting a CS-deficient form of the rodent malaria parasite *Plasmodium berghei* with a plasmid encoding *P. falciparum* CS repeat regions (CS(Pf)). To assess whether the modified rodent parasites would be useful for measuring protective antibody responses, mice were immunized with a vaccine containing *P. falciparum* CS repeats and then exposed to mosquitoes infected with the CS(Pf)-modified parasite . The vaccine generated sterile immunity in the immunized mice, and protection was specific for *P. falciparum* CS repeats. Sera from immunized mice protected naive recipients from infection when challenged with mosquitoes infected with CS(Pf)-modified parasites. Depletion of $CD4^+$ T cells did not affect the level of protection of immunized mice, which indicates that protection was mediated predominantly by antibodies.

These CS(Pf)-modified rodent parasites are a powerful and safe new tool for the analysis of vaccine-induced antibody responses. By expressing T-cell epitopes from the *P. falciparum* CS protein, it should be possible to develop hybrid parasites for the analysis of T-cell responses.

Elaine Bell

References and links

ORIGINAL RESEARCH PAPER Persson, C. *et al.* Cutting edge: a new tool to evaluate human pre-erythrocytic malaria vaccines: rodent parasites bearing a hybrid *Plasmodium falciparum* circumsporozoite protein. *J. Immunol.* **169**, 6681–6685 (2002)

FURTHER READING Richie, T. L. & Saul, A. Progress and challenges for malaria vaccines. *Nature* **415**, 694–701 (2002)

IN BRIEF

LYMPHOID ORGANOGENESIS

Different cytokines induce surface lymphotoxin-αβ on IL-7 receptor-α cells that differentially engender lymph nodes and Peyer's patches.

Yoshida, H. *et al. Immunity* **17**, 823–833 (2002)

The interleukin-7 receptor-α (IL-7Rα)$^+$ 'inducer' cells for Peyer's patch (PP) and lymph node (LN) development are phenotypically similar, and both must be triggered to express lymphotoxin-αβ (LTαβ) for their function. But, there are differences in the molecular requirements for PP and LN development. The development of PPs, but not LNs, requires IL-7, whereas LN development requires signals through RANK ligand (RANKL). This study shows that in *Traf6*$^{-/-}$ mice, in which RANKL signalling and LN development is blocked, IL-7 can stimulate the expression of LTαβ on LN inducer cells and treatment with soluble IL-7 restores LN formation. This indicates that the inducer cells for LNs and PPs are functionally similar also.

TRANSPLANTATION

$CD4^+CD25^+$ alloantigen-specific immunoregulatory cells that can prevent $CD8^+$ T-cell-mediated graft rejection: implications for anti-CD154 immunotherapy.

van Maurik, A. *et al. J. Immunol.* **169**, 5401–5404 (2002)

Blockade of the CD40–CD154 co-stimulatory pathway using CD154-specific antibodies can promote the long-term survival of allografts in animal models, and there is some evidence that this is mediated, in part, by $CD4^+$ regulatory T cells. But, in some situations, anti-CD154 therapy fails owing to the initiation of graft rejection by CD154-independent $CD8^+$ T cells. This study shows that anti-CD154 treatment at the time of transplantation allows the development of $CD4^+CD25^+$ regulatory T cells, which, if present in sufficient numbers, can suppress rejection mediated not only by $CD4^+$ T cells, but also by $CD8^+$ T cells. This phenomenon, known as linked unresponsiveness, is an important clinical goal.

ANTIBODY RESPONSES

A critical role for IL-21 in regulating immunoglobulin production.

Ozaki, K. *et al. Science* **298**, 1630–1633 (2002)

The authors generated IL-21 receptor (IL-21R)-deficient mice and found that although T-cell function was normal in these animals, the levels of IgG1 and IgG2b were reduced and the level of IgE was increased. However, this B-cell-intrinsic defect is less severe than that seen in mice and humans that are deficient for the cytokine-receptor common γ-chain (which is shared by IL-21R), indicating that normal B-cell responses must involve an additional cytokine(s). Mice that were deficient for both IL-21R and IL-4 had markedly impaired production of all antibody isotypes. So, this study shows that co-operation between IL-4 and IL-21 is essential for antibody responses.