maintained in adults compared to children. The mechanism explaining this phenomenon is not clear, although it might result from the limited capacity of children to produce antibodies to non-protein antigens, such as GPI. Furthermore, these findings suggest that anti-GPI immunity is probably not responsible for the incredibly high fever thresholds that are often observed in parasitemic children [3].

Therefore, although laboratory studies provide tantalizing evidence of a role for anti-GPI antibodies in protection against severe malaria, clearly, more detailed studies are required to determine if similar mechanisms operate during human *P. falciparum* infection. In the face of ongoing anti-malarial drug resistance and continued problems with insecticide use, this possibility will no doubt receive further attention as the desperate search for a malaria vaccine continues.

1 Schofield, L. *et al.* (2002) Synthetic GPI as a candidate anti-toxic vaccine in a model of malaria. *Nature* 418, 785–789

2 De Souza, J. *et al.* (2002) Prevalence and boosting of antibodies to *Plasmodium falciparum* glycosylphosphatidylinositols and evaluation of their association with protection from mild and severe clinical malaria. *Infect. Immun.* 70, 5045–5051

3 Boutlis, C. *et al.* (2002) Antibodies to *Plasmodium falciparum* glycosylphosphatidylinositols: inverse association with tolerance of parasitemia in Papua New Guinean children and adults. *Infect. Immun.* 70, 5052–5057

Sarah Hudson Keenihan
keenihan@namru2.med.navy.mil

Where do memory T cells come from?

Immunological memory provides cellular recall for the rapid and efficient mobilization of immune forces against pathogens previously encountered. During a primary immune response to new pathogens or antigens, naïve T cells become activated, undergo proliferative expansion and differentiate into effector cells. Although most activated or effector cells die after antigen is cleared, a proportion of these primed cells persist as memory T cells. The identity and functional properties of the effector cells that perish versus those that survive as memory T cells are not known. Moreover, it is not known whether the two types of effector CD4 T cells, interferon (IFN)-γ-producing Th1 cells and interleukin (IL)-4 producing Th2 cells, have similar capacities for memory generation.

Wu *et al.* [1] have begun to address these questions in a recent intriguing study. Using a combination of cytokine capture techniques and *in vivo* adoptive transfers, they demonstrated that the persisting memory T-cell population derives from activated cells that are not producing IFN-γ. Antigen-specific Th1 effector cells were generated *in vitro* or *in vivo* from DO11.10 mice expressing a transgenic T-cell receptor specific for ovalbumin and MHC class II. The resultant Th1 population was sorted into IFN-γ^+ and IFN-γ^- cells and transferred *in vivo* to unmanipulated, syngeneic murine hosts. Several days post-transfer, they detected the persistence of both IFNγ^+ and IFN-γ^- transferred cells; however, after one week *in vivo*, the IFN-γ^+ cells literally disappeared from lymphoid and lung tissue, whereas IFN-γ^- cells persisted. Although Wu *et al.* did not examine other tissues that might serve as reservoirs for activated T cells, such as the lamina propria of the gut, these results strongly suggest that the precursors to long lived memory T cells reside in the IFN-γ^- fraction of activated cells. Once cells have differentiated fully to produce IFN-γ, they cannot convert to long lived memory T cells.

Interestingly, this survival dichotomy between cytokine producers and non-producers does not seem to occur with Th2 cells, where IL-4^+ and IL-4^- fractions have similar survival potentials *in vivo*. Thus, development of memory depends crucially on the type of response, the cytokines produced and the differentiation state of activated cells. These findings have profound implications for vaccine design because it might be advantageous to establish conditions that do not promote full differentiation to Th1 effector cells, to optimally promote a long lived memory response.

1 Wu, C-Y. *et al.* (2002) Distinct lineages of Th1 cells have differential capacities for memory-cell generation *in vivo*. *Nat. Immunol.* 3, 852–858

Donna L. Farber
dfarber@smail.umaryland.edu

DC–tumour fusions: every which way but allo[2]

The resurgence of interest in cancer immunotherapy is primarily the result of a shift in focus, from the use of monoclonal antibodies to target tumours (magic bullets), to the use of antigen-presenting cells (APCs) to elicit anti-tumour cytotoxic T-lymphocyte (CTL) responses. The relative success of this approach is, with hindsight, scientifically obvious when one considers that it is CTLs, rather than antibodies, that clear tumours. Thus, the central question for cancer immunotherapy is, how does one elicit an effective anti-tumour CTL response? The surprisingly universal answer that is emerging is that this requires the stimulation of T cells by a specific APC, the dendritic cell (DC). These studies show that the key element of triggering an effective anti-tumour immune response is getting tumour antigens into DCs, which can then deliver both the antigen-specific and costimulatory signals required for the induction of CTLs from naïve T cells.

'the key element of triggering an effective anti-tumour immune response is getting tumour antigens into DCs'

Although there are several methods for loading DCs with tumour antigens, the paucity of defined tumour-specific antigens, together with the emerging evidence for the individuality of patient tumours, means that the most promising approaches to DC-based cancer immunotherapy are those using whole tumour-cell lysates or fusion hybrids to load DCs with tumour antigens. The fusion hybrids are particularly interesting because they would enable the

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