sponse to particular infectious agents determine the protective value of the immune response, IL-2$^-$ mice would be expected to show striking susceptibility to certain types of infectious agents.

Schimpl also reported that the relatively subtle abnormalities of young IL-2$^-$ mice give way to a striking lymphadenopathy and splenomegaly in older mice, associated with an increase in immature B lymphocytes and granulocytes in the spleen. This is followed by an almost total loss of B220$^+$ cells, first from the bone marrow and later from the spleen. Most animals die within 2 to 6 months of age. Detailed study of these mice, now in progress, should yield illuminating information about the normal physiological functions of IL-2 and the consequences of an unbalanced cytokine network.

W. Müller (Univ. of Cologne) described experiments on mice in which the IL-4 and IL-10 genes had been inactivated by gene targeting; these mice are referred to as IL-4T (for targeted) and IL-10T, respectively. The IL-4T mice had already been described[5], but this was the first report of the phenotype of the IL-10T animals.

The IL-4T mice have an abnormality that is essentially predictable from studies *in vitro* (showing that IL-4 regulates IgG1 and IgE production by controlling immunoglobulin class switching to these isotypes[6,7]) and from experiments *in vivo* (showing that antibodies to either IL-4 or its receptor completely prevent increases in serum IgE to helminthic infection or to polyclonal B cell activation, stimulants that often increase serum IgE levels 100-fold or more[8]). Not surprisingly, then, the IL-4T mice had no detectable serum IgE and markedly diminished IgG1. They failed to produce IgE in response to nematode infection and showed a strikingly diminished production of IgG1, but not of other IgG isotypes, in response to conventional thymus-dependent immunization.

These results have several implications. First, it is now abundantly clear that IL-4 is absolutely essential for production of IgE. Second, IL-4 is a physiological switch factor for IgG1, which had been in doubt, although it cannot be the only one because some IgG1 is made by the IL-4T mice. Finally, the reciprocal phenotypes of the IL-4T and the IL-2$^-$ mice, in terms of the dominant types of serum immunoglobulin, emphasize the different regulatory properties of the two lymphokines, and of the T cells that produce them. They lead to the prediction that IL-4T mice will show diminished production of other Th-2 products and that they will overproduce IFN-γ.

Interleukin-10 is a more recent entrant on the cytokine scene but the range of its activities is impressive and growing, typical of this class of molecules for which the description "pleiotropic and redundant" has been popular. A particularly provocative observation (M. Howard, DNAX, and ref.9) is that treatment of normal mice with monoclonal anti-IL-10 antibody from birth causes a striking reduction of serum IgM concentrations and the elimination of CD5$^+$ B cells, which had been postulated to be the principal source of serum IgM[10]. These effects seem to result from the action of IL-10 as a "cytokine synthesis inhibitory factor" (the activity under which it was initially described)[3]. Indeed, anti-IL-10 treatment causes the overproduction of IFN-γ and anti-IFN-γ reverses the effects of anti-IL-10. Somewhat disappointingly, the IL-10T mice had normal serum IgM levels and showed no evidence of the overproduction of IFN-γ. These observations imply that the effects obtained by *in vivo* neutralization of IL-10 with antibody may have a more complex explanation, or that IL-10T mice may have activated mechanisms to correct the abnormalities that would normally result from the absence of the cytokine.

The IL-10T mice tended to be smaller than their IL-10 'sufficient' littermates, and some of them died early in life. Although the reasons are not yet known, detailed study of these valuable animals will offer much information regarding the contribution of IL-10 to the cytokine network.

Studies of the consequences of deleting key players in the regulation of the immune system provide a striking glimpse of how the immune system controls itself in the course of immune responses. Further analyses of the resistance of these mice to various infections will provide much insight into the contribution of different cytokines to protective responses and into the complex interplay between these potent molecules. □

William E. Paul is in the Laboratory of Immunology, NIH National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892, USA.

1. Schorle, H., Holtschke, T., Hünig, T., Schimpl, A. & Horak, I. *Nature* **352**, 621–624 (1991).
2. Paul, W. E. *Cell* **57**, 521–524 (1989).
3. Mosmann, T. R. & Moore, K. W. *Immun. Today* **12**, A49–A53 (1991).
4. Mosmann, T. R. & Coffman, R. L. *A. Rev. Immun.* **7**, 145–173 (1989).
5. Kühn, R., Rajewsky, K. & Müller, W. *Science* **254**, 707–710 (1991).
6. Vitetta, E. S. *et al. J. exp. Med.* **162**, 1726–1731 (1985).
7. Coffman, R. L. *et al. J. Immun.* **136**, 4538–4541 (1986).
8. Finkelman, F. D. *et al. Proc. natn. Acad. Sci. U.S.A.* **83**, 9675–9678 (1986).
9. Ishida, H., Hastings, R., Kearney, J. & Howard, M. *J. exp. Med.* (in the press).
10. Hayakawa, K., Hardy, R. R., Parks, D. R. & Herzenberg, L. A. *J. exp. Med.* **57**, 202–218 (1983).

RÉSUMÉ

Defence costs

A fresh twist in the evolutionary struggle between brood parasites and their hosts is described in a study of the yellow-browed leaf warbler, a presumed former host of cuckoos. Sharp-eyed leaf-warbler females strongly discriminate against eggs of other species, turfing them out of the nest. But K. Marchetti (*Proc. R. Soc.* B**248**, 41–45; 1992) has found that the birds are sometimes too picky for their own good and reject their own eggs. This cost of egg discrimination could lead to the selective loss of host defences, which in turn would make the leaf-warbler population vulnerable to re-exploitation by cuckoos. That, says Marchetti, might explain the survival of brood parasitism despite its burden on the host species.

Tickled by light

FISH without contractile pupils adjust to light and dark by changing the lengths of their visual receptors. The rods, which sense dim light, shorten on dark adaptation and the cones lengthen. This allows weak incident light to get at the rod outer segments first, whereas in bright light they are shielded by the retinal pigment layer. Now K. Pagh-Roehl *et al.* (*Cell Motil. Cytoskel.* **21**, 235–251; 1992) have found that elongation of the rods can be reproduced in a dark-adapted preparation *in vitro*. The contractile element of the rod inner segment contains actin filaments, which push outwards by elongating at their slow-growing ('pointed' ends), while depolymerizing at the barbed ends. How they are induced to do this is not clear.

Superfluid solution

THE next assault on the solar-neutrino problem may use a new kind of neutrino detector devised and tested by S. R. Bandler *et al.* (*Phys. Rev. Lett.* **68**, 2429–2432; 1992). The snag has been that most detectors are sensitive only to high-energy neutrinos, so neglecting the contribution from hydrogen-burning nuclear reactions in the Sun's core. Gallium detectors go but part way to resolving the difficulty. Bandler *et al.* note that a neutrino passing through superfluid helium can create one of the exotic menagerie of collective quantum excitations, such as rotons, possible in this material, which persist until they reach the superfluid's surface. Here they dissipate their energy by evaporating a few atoms which can condense on a nearby ultracold wafer. The resulting thermal pulse of the wafer signals the neutrino's arrival. The detector's main advantage, besides the low threshold energy, is that the superfluid bath can be made as large as necessary to maximize the number of scattering events without compromising sensitivity, which depends on the wafer's mass.