IMMUNE REGULATION

‘Eggstra’ clues to helminth infections

Schistosomes — the parasitic worms that are the causative agent of schistosomiasis — chronically infect ~200 million individuals in 76 countries, mainly in tropical and sub-tropical areas. When adult *Schistosoma mansoni* begin to produce eggs, the host immune response is biased towards a T helper 2 (T_H2)-cell response, with the key cytokine driving this polarization being interleukin-4 (IL-4). Recent research has greatly increased our understanding of how microbial components can drive the development of T_H1 responses — but so far, we have had little understanding of the microbial components that drive T_H2 responses. Now, Gabriele Schramm *et al.*, reporting in the *Journal of Biological Chemistry*, have characterized a factor in *S. mansoni* eggs that could be responsible for the switch to a T_H2 response.

Previously, work in the same laboratory established that the IL-4-inducing factor in *S. mansoni* eggs was a secreted glycoprotein. In the current study, a protein, which the authors named IPSE (IL-4-inducing principle from *S. mansoni* eggs), was isolated and characterized. Size determination gave a molecular weight of 40 kDa; this decreased to ~20 kDa under reducing conditions, so the authors suggest that IPSE is a homodimer. Analysis indicated that IPSE is identical to antigen α_1, a factor that was identified previously in *S. mansoni* eggs but has not been fully characterized.

In response to exposure to *S. mansoni* egg antigen extract (SmEA), basophils degranulate rapidly and release IL-4 and other inflammatory mediators. Is IPSE alone responsible for these effects? The results of functional *in vitro* assays in which human basophils were incubated with whole SmEA, SmEA fractions and recombinant IPSE, and the fact that antibodies raised against recombinant IPSE inhibited the activation of basophils by SmEA, indicated that IPSE is the sole factor responsible for the basophil-activating effects of SmEA. In addition, it was already known that the presence of IgE is required for SmEA to have an effect on basophils. Further analysis confirmed that IPSE can bind IgE, indicating that it is the crosslinking of receptor-bound IgE that accounts for IPSE-mediated basophil activation.

The characterization of IPSE could prove to be an important step forward in our understanding of the ways in which microbial products can polarize the T-cell response to T_H2 cells. Research to characterize the nature of the interaction between IPSE and IgE is now underway.

Sheilagh Clarkson, Associate Editor,
Nature Reviews Microbiology

References and links

ORIGINAL RESEARCH PAPER Schramm, G. *et al*. Molecular characterization of an interleukin-4-inducing factor from *Schistosoma mansoni* eggs. *J. Biol. Chem*. 6 March 2003 (DOI:10.1074/jbc.M300497200)

FURTHER READING Pearce, E. J. & MacDonald, A. S. The immunobiology of schistosomiasis. *Nature Rev. Immunol*. **2**, 499–511 (2003)

IN BRIEF

T-CELL MEMORY

CD4⁺ T cells are required for secondary expansion and memory in CD8⁺ T lymphocytes.

Janssen, E. M. *et al. Nature* **421**, 852–856 (2003)

Requirement for CD4⁺ T-cell help in generating functional CD8⁺ T-cell memory.

Shedlock, D. J. & Shen, H. *Science* **300**, 337–339 (2003)

Defective CD8⁺ T-cell memory following acute infection without CD4⁺ T-cell help.

Sun, J. C. & Bevan, M. J. *Science* **300**, 339–342 (2003)

Understanding how memory responses are generated is crucial if we are to develop improved vaccine strategies. Three recent papers have addressed the issue of whether T-cell help is required for the generation of functional CD8⁺ memory T cells. For primary CD8⁺ T-cell responses to certain antigens, CD4⁺ T cells are required to ‘license’ antigen-presenting cells (APCs) — thought to be mediated by CD40 signalling — to generate a response. But primary CD8⁺ T-cell responses to infectious agents do not often require T-cell help, because microbial products provide their own immunostimulatory signals for the direct activation of APCs. These studies now show that CD4⁺ T-cell help is necessary during the priming phase, but not during the recall response itself, to generate an effective CD8⁺ memory T-cell response.

CELL DEATH AND IMMUNITY

Essential role for caspase 8 in T-cell mediated homeostasis and T-cell mediated immunity.

Salmena, L. *et al. Genes Dev.* **17**, 883–895 (2003)

The role of caspase-8 in immunity is uncertain as disruption of the gene is lethal during embryogenesis. In this new study, mice with a T-cell-specific caspase deficiency were shown to have normal thymic output of T cells but decreased numbers of peripheral T cells. T-cell clonal expansion was also impaired — apparently owing to reduced survival rather than a defect in T-cell activation — and the mice were unable to mount effective anti-viral responses.

T-CELL ACTIVATION

ISKAP-55 regulates integrin adhesion and formation of T cell–APC conjugates.

Wang, H. *et al*. *Nature Immunol.* **4**, 366–374 (2003)

A function for the T-cell adaptor protein SKAP55 has long been sought. An initial clue to its role came from previous observations that SKAP55 binds to another T-cell adaptor, ADAP, a regulator of integrin clustering. This study shows that similar to APAP, increased expression of SKAP55 in cell lines or primary mouse T cells potently upregulates the formation of T-cell-APC (antigen-presenting cell) conjugates *in vitro*. It seems that SKAP55 mediates this effect by upregulating integrin clustering and adhesion. So, SKAP55 joins ADAP as a crucial component of the still poorly understood ‘inside out’ signalling pathway that regulates conjugate formation.