IMMUNOLOGY

The worm and the virus

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INTEREST in the possible interactions between parasites and AIDS, particularly in Africa, has taken a new turn with a report in the latest issue of *Journal of Experimental Medicine*[1]. In it, Jamal Khalife and colleagues describe the unexpected discovery that one of the surface antigens of the helminth worm *Schistosoma mansoni* contains an epitope that is identical to one of the regulatory proteins of the human immunodeficiency virus HIV-1. The finding bears on the controversy as to whether there is a causal relationship between the occurrence of schistosomiasis and AIDS, and also opens up a number of possibilities concerning the interactions between these pathogens.

Schistosomes evade the immune response by coating themselves with host molecules within a few days of penetrating the skin. Each adult worm carries a forest of acquired substances — including various blood groups, major-histocompatibility-complex molecules, immunoglobulins and albumin — which mask the worm antigens that might act as targets for immune attack[2]. It is therefore difficult to determine exactly which antigens are specific to the parasite and which have been acquired from the host. The schistosome antigen described by Khalife *et al.*[1] is apparently worm-derived, and is a glycoprotein of relative molecular mass 170,000 (M_r, 170K) which appears on the surface of the invading larval schistosome after about three days, while it is still in the skin, and persists into the adult stage. It is of interest not only because it shares an epitope with one of the HIV-1 regulatory proteins, but because it also induces protection against challenge with *S. mansoni* in rats and induces a specific antibody response in humans.

The antigens of HIV-1 are coded for by nine genes, the best known being *gag* and *env*, which code for the structural elements (the core and envelope proteins), and *pol* which codes for enzymes. But there are also six regulatory genes, among them *vif* which codes for the virion infectivity factor, Vif, concerned with entry of free virus into the host cell[3]. Vif is a small protein which occurs on free virus particles, in the cytoplasm of infected cells and in the fluid surrounding them. But only a proportion of individuals infected by HIV-1 develop antibodies to Vif and its importance in AIDS is not clear[4].

Khalife *et al.* have identified a 14-amino-acid epitope common to the HIV-1 Vif antigen and to the 170K antigen of *S. mansoni*. This peptide induces monoclonal antibodies that recognize both HIV-1 and the surface of *S. mansoni*, and it is also recognized by some, but not all, individuals infected with either HIV-1 or *S. mansoni*. In rats, passive administration of the monoclonal antibody reduced the parasite load by 34–49 per cent, which is comparable with the best results obtained using antibodies against more conventional antigens[5].

The immediate significance of this finding is not clear but its implications are wide ranging. *Schistosoma mansoni* and HIV-1 frequently occur together in Africa and there is some seroepidemiological evidence that there is a positive correlation between the two infections[6]. This has been disputed[7], but the lack of correlation relates to the better known *S. mansoni* antigens and the structural antigens of the virus, and both viewpoints will have to be revised in the light of these new discoveries. Practical consequences include the possibilities that *S. mansoni* infections might actually inhibit the invasion of cells by HIV-1, or that HIV-1 infections might contribute to immune responses against *S. mansoni*. In this context, concepts of a cocktail vaccine against *S. mansoni* might have to be revised if it is found that one of the components actually interferes with HIV-1 — even though this might appear at first glance to be beneficial — because the balance between protection and pathology in schistosomiasis is so delicate.

The actual interactions between HIV-1 and *S. mansoni* are likely to be much more complex than they would first appear. *Schistosoma mansoni* infections induce the production of a number of cytokines including interleukin-1, interferon-γ and tumour necrosis factor, but interleukin-1 and tumour necrosis factor stimulate HIV-1 enhancers and thus act as cofactors in AIDS[8]. Similarly, cells infected with HIV-1 produce cytokines that are capable of modifying immune responses[9], and there is every reason to suspect that the cytokines would affect *S. mansoni*. The existence of a common epitope also leaves open the possibility that the virus shares antigens with other parasites, such as the malaria organism, with which it appears to have a seroepidemiological association[10].

The biological function and possible origins of the common Vif–170K antigen are also of interest. There are many similarities between HIV-1 and the simian immunodeficiency virus, including the presence in each of a Vif molecule[11]. It would be very interesting to know more about a molecule that was common to the two organisms that are now pathogens before humans came on the evolutionary scene. Is it a schistosome structural or functional antigen, or was it acquired from its simian host? If so, could it possibly have come from a virus with which the host had come to terms? □

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Schistosoma mansoni, one of three species of fluke which cause schistosomiasis.

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