about 20 per cent of the mass of each head. This result confirms almost all previous studies on the shape of myosin heads; no well-substantiated gross difference in head shape has ever been observed in any two different biochemical states of the head, such as in the presence and absence of ATP[10], the molecule which is hydrolysed by myosin to produce force. Perhaps all these data are trying to tell us something that many have been reluctant to accept.

To put these conclusions into perspective, the figure illustrates some of the changes in head configuration on actin that would produce an axial displacement of the 'neck' end of the head of between 4 and 10 nm, as required from studies of muscle mechanics[11], and it indicates how some of these (*d* and *f*) can probably be excluded by the neutron-scattering data. Other evidence is now accumulating[12] that the initial and final stages of the attachment phase of myosin heads in the contractile cycle do represent two distinct attitudes of myosin heads on actin. With the new neutron-scattering data, this result imposes severe constraints on the structural events that might be involved in the contractile cycle. For example, models *c*, *d* and *f* in the figure would all be excluded. □

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AIDS

Novel HIV systems

Robin A. Weiss

IN VIVO models are much needed for AIDS research to test potential antiviral drugs and vaccines. Besides man, only chimpanzees and gibbons have been found to be susceptible to infection with human immunodeficiency virus type 1 (HIV-1). These apes are in extremely short supply in captivity, and are rightly classified as protected or endangered in the wild. The second AIDS virus, HIV-2, has been reported to infect macaques such as the rhesus monkey. It is not yet clear whether any of these non-human primate species, or any other animals, are susceptible to HIV-induced AIDS. The paper by G. Jay and colleagues on page 606 of this issue[1] is the latest of several new reports which use various animal models of the disease.

The HIV-related simian immunodeficiency viruses (SIV) have been isolated from Old World monkeys such as macaque, sooty mangabey, African green monkey and mandrill[2]. Serological evidence indicates that SIV naturally infects African green monkeys, whereas it has not been found in wild-caught macaques in Asia and appears to be restricted to captive primate colonies. SIV infection of African green monkeys and mangabeys is apparently asymptomatic, but macaques develop AIDS, as indeed they do after inoculation with the mangabey virus (SIV_{SMM}). The infection and disease caused by SIV in macaques promises to be of great importance for understanding pathogenesis and for the development of therapeutic agents and vaccines that may be applicable to human AIDS. Nonetheless, animal models of HIV infection itself would benefit the fight against AIDS.

Several promising leads have recently been published to indicate that research on HIV might usefully be conducted with lagomorphs and rodents. T. J. Kindt's group recently reported[3] that two T-cell lines and one macrophage line of rabbit cells transformed by oncogenic viruses can be infected *in vitro* with HIV-1. O.E. Varnier's group[4] has now shown that rabbits inoculated with HIV-1 or virus-producing cells develop persistent infections. This results in seroconversion and the ability to rescue virus from rabbit leukocyte cultures up to 7 months after HIV-1 inoculation. Rabbits were first used for human retrovirus research by I.Miyoshi's group[5], which showed that human T-cell lymphotrophic virus (HTLV-1) infection readily occurs and is transmitted from dam to offspring via the milk. There is no evidence that rabbits succumb to HTLV or HIV disease. The rabbit/HTLV-1 system, however, has been successfully used for testing vaccinia-based HTLV-1 recombinant envelope vaccines[6], and similar usage now appears possible for HIV.

Another approach to devising animal systems is to manipulate mice to become susceptible to HIV infection. The generation of transgenic mice carrying the human CD4 receptor gene has been much discussed, but currently seems unpromising as murine cells expressing human CD4 in culture are refractory to HIV infection and replication[7]. Two groups now show that mice with severe combined immune deficiency (SCID, an inherited immunodeficiency syndrome) can be engrafted with human haematopoietic cells to reconstitute human T- and B-lymphocytes. Because SCID mice are immunodeficient, they accept the human cells as a xenograft.

D. E. Mosier *et al.*[8] inoculated human peripheral blood leukocytes into SCID mice and obtained mice that give a specific human immunoglobulin response to challenge with tetanus toxoid, an antigen to which the human donors had been previously immunized. Interestingly, human cell lymphomas also appear in the engrafted SCID mice and these are positive for Epstein–Barr virus.

I. L. Weissman's group[9] inoculated SCID mice with human fetal liver cell suspensions containing haematopoietic stem cells. These cells, and cells from human fetal thymus and lymph node, provide mature T cells and B cells of human origin in the peripheral blood of the mice. The experiments on the reconstitution of SCID mice by human cells open a new horizon for studying *in vivo* haematopoietic cell differentiation and leukaemia. Each animal, however, has to be individually reconstituted. It remains to be seen whether these mice can be infected with HIV, can make human cell immune responses to the virus, or reacquire immunodeficiency.

Recently, two groups at NIH have made transgenic mice carrying all or part of the HIV-1 genome. It has been reported at conferences that M. Martin's group has inserted a full-length, recombinant HIV provirus into mice which were, of course, kept in strict containment facilities. In the paper in this issue[1], Jay's group reports that lesions resembling Kaposi's sarcoma appear in the skins of transgenic mice expressing the *tat* gene of HIV-1. If, indeed, these are endothelial cell lesions that mimic human Kaposi's sarcoma, the result implies that a single viral gene exerts a proliferative effect independent of viral replication and the induction of immunodeficiency.

These findings pose as many questions as explanations. For instance, as HIV genomes are not generally present in human Kaposi's sarcoma cells, does the *tat* protein act to stimulate a paracrine growth factor? And if Kaposi's sarcoma is directly linked to HIV infection, why is this tumour virtually unknown in haemophiliacs with AIDS? Together with the late G. Khoury, Jay had previously reported[10] that mice transgenic with the *tat* gene of HTLV-1 develop peripheral nerve lesions resembling von Recklinghausen's neurofibromatosis. Clearly, there is much to be learned from the action of single viral genes expressed in transgenic animals. □

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