SAIDS SYMPOSIUM

SIMIAN AIDS PROVIDES A USEFUL MODEL

DAVIS, Calif.—The chimpanzee is still the only non-human species known to be susceptible to infection with the human immunodeficiency virus (HIV). However, at least two separate subfamilies of retroviruses (SRV and SIV) are capable of causing immunosuppression in macaques. Studies of AIDS pathogenesis, treatment, and immunoprotection can use each of these animal models. This was clear from the presentations of scientists from the seven United States Primate Centers and other institutions in the U.S.A. and abroad who met here late in September to discuss simian AIDS (SAIDS).

Investigators from the Southwest Foundation (Texas), Yerkes (with the Centers for Disease Control, Georgia), and the Frederick Cancer Research Center at the National Institutes of Health (Maryland) reported results on HIV infection or immunization of chimpanzees. Although almost all HIV-inoculated chimps are persistently infected and mount an immune response similar to that of humans, no AIDS-like disease has developed as of two years after infection. While scientists can recover the virus from peripheral blood lymphocytes and bone marrow, they have been unable to isolate it from plasma, saliva, or cerebral spinal fluid. And none of the chimps has yet developed signs of central nervous system infection.

Experiments to investigate transmission routes show that oral exposure to cell-free HIV does not cause infection of chimps, whereas vaginal exposure succeeds in establishing infection. The virus is not spread by simple cage contact, but animals infected with one strain of HIV can be superinfected with a different strain of the virus. This supports the idea that when a human vaccine is developed, it will need to be multivalent.

A number of groups have used HIV envelope proteins to induce a vigorous humoral or cellular antibody response (including neutralizing antibodies) in chimps and macaques. These envelope antigens are derived from genetically engineered gp120, synthetic peptides from gp41 and gp120, recombinant vaccinia virus expressing gp41 and gp120, and native gp120 obtained from HIV particles. Whether any of the preparations will afford protection from HIV challenge remains to be determined.

Investigators at five primate centers (California, Oregon, Washington, Wisconsin, and New England)

Genetic organization of several retroviruses. Open reading frames corresponding to viral genes are labeled for SRV-1 (SAIDS type D retrovirus-serotype 1), human T-cell lymphotropic virus Type II (HTLV-II), and the human immunodeficiency virus (HIV). See text for a description of how simian retroviruses are being studied as models for human AIDS.

and the National Institutes of Health reported their experience with SAIDS type D retrovirus (SRV) in several species of macaques. SRV is closely related to the prototype type D retrovirus—the Mason-Pfizer monkey virus. Although immunologically unrelated to HIV, SRV provides an excellent model for studying the mechanisms of retroviral-induced immunosuppression.

At the three West Coast centers, SRV and its associated diseases are highly prevalent and account for a significant mortality in the macaque colonies. At the Wisconsin and New England centers, the virus represents a less acute problem, and it appears to be absent from the Delta (Louisiana) and Yerkes (Georgia) centers. Different manifestations of SAIDS are associated with two distinct serotypes, SRV-1 and SRV-2. Each has been molecularly cloned and sequenced, and the cloned California type D isolate (SRV-1) has been used to induce SAIDS. Resistance to infection with this virus is correlated with the presence of neutralizing antibodies, and an inactivated whole virus vaccine is effective in preventing experimentally induced disease.

Researchers at the New England, Delta, Yerkes, California, and Washington centers are studying another simian virus that is more closely related to HIV. SIV (STLV-III), a lentivirus, is highly prevalent in healthy HIV-seropositive sooty mangabeys in primate centers and zoos. It is found less frequently in healthy African green monkeys (from Africa, not the Caribbean) and, in low prevalence, in immunosuppressed macaques.

Like its human counterpart, SIV replication is largely restricted to T4 lymphocytes, but it does not appear as genetically diverse. Isolates from the various centers are quite similar by criteria such as restriction mapping, peptide mapping, and amino acid sequencing. Cloned SIV shows varying degrees of nucleotide homology with HIV. The most, about 50 percent, is found in the *gag* and *pol* genes. Of particular interest are HIV isolates called HTLV-IV, which were obtained from healthy West African prostitutes, and appear very similar to SIV by restriction enzyme analysis and immunological cross-reactivity. SIV can be experimentally transmitted in macaques and induces a persistent infection characterized by a humoral antibody response and mild immunosuppression. Although passage of SIV in human T cells appears to rapidly attenuate its virulence, initial attempts to immunize against experimental infection using an inactivated virus vaccine have been unsuccessful. Nevertheless, infection of macaques with SIV promises to be another useful model for pathogenesis, treatment, and prevention of a retroviral-induced, AIDS-like disease.

In order to make the most of the opportunities afforded by these animal models, cooperation and sharing of reagents and other resources among the different primate centers is of the utmost urgency. In this vein, the California center has established a reference unit to help monitor the seroepidemiology of SAIDS and its associated retroviruses.

—Murray Gardner