Acquired immunodeficiency syndrome

Laying the groundwork for neutralizing AIDS-linked virus

from Jerome E. Groopman

WITH what success does the human immune system produce antibodies that neutralize the human T-lymphotropic virus type III (HTLV-III) — the virus that is aetiologically linked to the acquired immunodeficiency syndrome (AIDS)? And can the neutralizing antibodies be exploited for prophylaxis or therapy of AIDS? Two papers elsewhere in this issue[1,2] report that such antibodies are present in some sera both from AIDS patients and from people who have been exposed to the virus but are asymptomatic. The relatively low titres of neutralizing antibodies in HTLV-III-infected persons should not dissuade investigators from pursuing their clinical relevance; the feline leukaemia virus often elicits low titres of neutralizing antibodies *in vivo*,[3]. yet vaccines of some effectiveness, which exploit at least in part this antibody response, have recently been developed.

Several studies that would help to define the significance of HTLV-III neutralizing antibodies *in vivo* immediately suggest themselves. Comparison of the titres and types of these antibodies in asymptomatic and AIDS patients can readily be accomplished. Particularly interesting would be longitudinal studies to examine whether the neutralizing antibodies persist in the sera of those who remain relatively healthy despite exposure to the virus but diminish in those to progress to AIDS. Of course, the clinical situation may not be so simple. Like visna virus, to which it bears some similarity, HTLV-III may alter its surface antigenic determinants over time and 'escape' from the protective effects of neutralizing antibodies[4,5]. Serial culture of HTLV-III with testing of neutralizing antibodies on the host's own isolates is one approach to determine if *in vivo* there are selection pressures that favour the emergence of antigenically altered virus. Initial reports of apparently healthy adults in Central Africa who are both antibody positive and virus positive for HTLV-III should make this population particularly valuable in addressing the clinical role of neutralizing antibody[6]. Because antigenic determinants on the gp120 envelope protein of the gp41 transmembrane protein of the virus[7-9] are likely to be the primary sites of interaction with the putative cellular receptor for HTLV-III[10,11], it is to be predicted that neutralizing antibodies are directed against gp120 and/or gp41 determinants. The wide antigenic variability in envelope-related antigens from different HTLV-III isolates[12] makes testing the ability of geographically-distant sera to neutralize geographically-distant isolates a valuable means of identifying conserved epitopes for neutralizing antibodies.

Recently, a retrovirus that cross reacts in serological tests with HTLV-III has been isolated from African Green monkeys[13]. Studies on the neutralization of HTLV-III by sera from these monkeys and of the ability of human HTLV-III neutralizing antibodies to recognize the surface determinants of the monkey virus may also help to localize highly conserved epitopes that would interact with cell-surface receptors for the viruses.

HTLV-III, LAV and ARV — all clearly variants of one type of human retrovirus — have been cloned and sequenced, thereby providing ready access to recombinant (made by recombinant DNA technology) viral peptides[14-17]. Peptides of the envelope protein can be used *in vitro* to absorb out the neutralizing activity and localize the epitopes that elicit antibodies. It is of interest to determine whether some neutralizing antibodies might react with the putative gene products (termed sor, P′, Q and 3′ORF, E′, F) that may have functional roles, particularly in the activiation of cellular genes (transactivation). The availability of these products will allow the reverse test: do polyclonal or monoclonal antibodies raised in animals against any of these gene products have *in vitro* neutralizing capacity? To obtain the equivalent human antibodies, it may be possible to use B-cells from people with neutralizing antibodies.

Ultimately, *in vitro* studies will be needed to determine the clinical significance of neutralizing antibodies for either prophylaxis or therapy of HTLV-III infection. Initial tests of prophylaxis with hyperimmune globulin and of therapy with pools of high-titre neutralizing antibodies can be undertaken in primates which are susceptible to infection with HTLV-III. Simple vaccination with native or recombinant peptides that elicit neutralizing antibodies may not be sufficient to protect primates against challenge with HTLV-III, but such an approach can readily be examined. The role of the cellular immune response (in addition to the antibody response) in preventing or suppressing human retroviral infection is still unaddressed. Innoculation of primates with forms of HTLV-III that are defective in functional genes but still display structural antigens, or with recombinant constructions of HTLV-III with other viruses, such as vaccinia, should permit the study of both cellular immune and antibody responses.

The HTLV-III research community will now coordinate its clinical and scientific forces to build on the new observation of neutralizing antibodies in the hope of constructing strategies to outwit this threatening human retrovirus. □

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Lasers

Dynamic holograms from crystals

from Malcolm Gower

WHEN certain crystals are exposed to spatially non-uniform light fields, light-induced refractive index changes occur, caused by the migration and retrapping of charges. Known as the photorefractive effect, the phenomenon was first reported nearly twenty years ago as the mechanism responsible for the self-focussing of laser light in crystals of $LiNbO_3$ and $LiTaO_3$, and has since been observed for many more crystals, including CdS, InP and GaAs. It was soon recognized that photorefractive crystals used as three dimensional media for holographic recording (volume holograms) could contain extremely high densities of information, up to 10^{12} bits per cm^3, yet retain exposure sensitivities comparable to those of the best photographic emulsions (at least 100 μJ per cm^2). But, unlike conventional media, photorefractive crystals can be used for dynamic or 'real-time' holography in which the writing and reading processes occur virtually continuously and simultaneously. Recently there have been some remarkable discoveries in the field that may lead to a host of applications in real-time optical data processing — from optical image amplifiers, enhancers and pattern recognizers to optical switches and memories[1].

Unlike the relatively slow serial proces-