

Viral cancers

AIDS virus at the centre*Los Trois Ilets, Martinique*

"RESEARCH in viral-associated cancers has come of age", said Peter Fischinger, deputy director of the National Cancer Institute (NCI) at a three-day conference here co-sponsored by the National Institutes of Health (NIH) and the Association pour la Recherche sur le Cancer (ARC).

Initial enthusiasm for the possible role of viruses in cancer accompanied the discovery in the 1960s that Epstein-Barr virus is associated with Burkitt's lymphoma. But that enthusiasm abated when little evidence was found to implicate other viruses with human cancers.

Today, the enthusiasm has returned. Nasopharyngeal cancer, a much more significant worldwide health problem than Burkitt's lymphoma, has also been linked to Epstein-Barr virus. Hepatitis-B virus DNA has been found in hepatocellular carcinomas. Different variations of human papilloma virus have been identified in 80 per cent of human papillomas, and, according to Harald zur Hausen of the Deutsches Krebsforschungszentrum at Heidelberg, it is likely that some form of human papilloma virus will be found in all forms of human cervical cancer.

Probably the most significant reinforcement of interest in cancers associated with virus comes from the discovery that a

Infection mechanism?

NCI's Robert Gallo now believes that transmission of HTLV-III/LAV infection is through cells, not virus particles. His scenario for spread of infection suggests that when a donor cell is recognized by a recipient cell, there is a mixed lymphocyte reaction. This in turn releases lymphokines which activate the initiating sequences of the viral genes, including the transactivating transcription gene (*tat*), which in turn causes viral expression in the newly infected host. This mechanism would explain why HTLV-III/LAV is not highly contagious, requiring some transmission of body fluid containing lymphocytes.

Gallo also reported five new cases of HTLV-II infection, and suggested there is some evidence that this virus is also spreading.

Although evidence for brain infection by HTLV-III/LAV is now undisputed, the exact target for infection is still in doubt. Luc Montagnier of the Pasteur Institute believes glial cells are infected directly, and has *in vitro* evidence to support this. Gallo, however, believes that brain involvement comes from monocyte macrophages migrating to the brain, possibly turning into microglial cells.

Joseph Palca

human retrovirus, HTLV-I, causes adult T-cell leukaemia, and that another human retrovirus, HTLV-III/LAV, causes acquired immune deficiency syndrome (AIDS).

In 1985, NCI spent \$135 million on viral cancer research, approximately 12 per cent of its budget. Whether that level of support will continue is unknown. Both NCI director Vincent DeVita and NIH director James Wyngaarden were forced to bow out of this conference at the last minute to devise a new budget for NIH under the guidelines set forth in the recently passed Gramm-Rudman legislation (see *Nature*, **318**, 495; 1985).

Although HTLV-III/LAV has not been directly associated with cancer, the explanation may be that patients are killed by opportunistic infections seen in AIDS before cancers can develop. According to Max Essex of the Harvard School of Public Health, many more cats die from opportunistic infection associated with feline leukaemia virus than die from leukaemia.

A possible human parallel is seen in Japan; Isao Miyoshi of the Kochi Medical School reports seeing infections similar to those seen in AIDS patients in individuals infected with HTLV-I. There may be more of these patients, but so far no one has thought to look for them. Ironically, it may yet turn out that HTLV-III/LAV will cause cancer if AIDS patients can be kept alive long enough to exhibit it.

The explosion in AIDS research has produced several interesting and potentially important discoveries. Evidence for heterosexual transmission of HTLV-III/LAV continues to grow. In 1979, 12 per cent of AIDS patients in Haiti were female; now, the number has grown to 30 per cent, and is expected to grow to 40 per cent in the next two years.

Conflict continues about what constitutes an effective therapy for AIDS. Research at the Pasteur Institute in Paris has focused on HPA-23, a compound that can block HTLV-III/LAV production *in vitro* and apparently *in vivo*. Sam Brower of NCI believes that a therapy that blocks viral replication is insufficient, and that the need is for an agent that will restore the helper/inducer T cells destroyed by HTLV-III/LAV infection. One such compound appears to be 3' azido-3'-deoxythymidine (AZT), now in clinical trials at NIH. A major advantage of AZT is it can be taken orally, an important consideration as it will have to be taken for life.

There are also indications that a new generation of assays for HTLV-III/LAV is not too far off. An important first step achieved in a preliminary form by Biotech Research Laboratories in Rockville,

Maryland, is the purification of viral coat proteins, which may also play an important role in vaccine development.

There was some tension at the meeting between NCI and Pasteur Institute researchers over the recent lawsuit by the French over the granting of a patent for an HTLV-III/LAV antibody test (see *Nature* **318**, 595; 1985). Both Luc Montagnier, the Pasteur researcher who first reported the association of a retrovirus with AIDS, and Robert Gallo, the NCI researcher whose work led to the US patent, attended the meeting. Nomenclature became somewhat confusing as the virus was alternately referred to as "HTLV-III/LAV", "LAV/HTLV-III", "LAV" or "HTLV-III" depending on the nationality and affiliation of the speaker. Future collaborations are not likely to suffer because of the current contretemps.

But Gallo complains of one unpleasant side effect of the lawsuit; he has been ordered to make photocopies of all notes and data relating to his work by US government lawyers acting in the lawsuit; this, Gallo maintains, will set back his research schedule.

ARC, the French co-sponsors of the meeting, have taken an active interest in viral associated cancers, especially in their relevance to health issues in underdeveloped countries. They also pride themselves on bringing together researchers around the world to tackle problems of mutual interest. In March 1984, a conference in Marseilles on cancers of the Mediterranean included Arab and Israeli researchers.

Says Gerard Milhaud, a member of ARC's scientific advisory board, "We got the Israelis and the Arabs together for a meeting. Bringing Montagnier and Gallo together was easy." **Joseph Palca**

Polish astronomers

THREE Polish astronomers from the Copernicus Astronomical Centre in Torun are expected to go on trial this week for possession of an illegal radio transmitter. Drs Jan Hanasz, Zygmunt Turlo and Leszek Zaleski, all members of the Polish Astronomical Society, were arrested on 26 September, together with Mr Piotr Lukaszewski, a technician from a local factory, charged with an offence against public order and possessing the transmitter.

They had used it to put out a television broadcast calling for a boycott of the forthcoming general elections, which they categorized as "undemocratic".

The astronomers last weekend called on Western colleagues to take note of their case, urging that, under prevailing conditions in Poland, the normal methods of making one's viewpoint felt were not available.

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