

observed much less variance in concentration even with a greater sampling frequency and could not detect any deviation during the period of the Maunder minimum or any of the spikes which Zeller attributes to solar flare or supernovae events. Moreover, he detected a seasonal variation with summer maxima in parallel with variations in sulphate. Delmas also found that nitrate concentrations in the

Dome C core have been relatively constant over the last 30,000 years. To complicate the picture even further, in a detailed profile at James Ross Island he found virtually no seasonal variability. In view of the potentially great value in using nitrate to trace past solar fluctuations the conference agreed that high priority should be given to resolving these seemingly incompatible data series. □

## A virus associated with human adult T-cell leukaemia

from Robin Weiss

RECENT virological, serological and epidemiological evidence strongly indicates that a newly discovered retrovirus is the aetiological agent of certain types of adult T-cell lymphoma/leukaemia. The virological evidence first came from R.C. Gallo's laboratory at the US National Cancer Institute<sup>1</sup> where the retrovirus was isolated from a T-lymphoma cell line established in culture from a patient with mycosis fungoides. In this issue of *Nature* Poiesz *et al.* (see p.268) report the isolation of a similar virus from a patient with Sézary syndrome, while Kalyanaraman *et al.* (see p.271) show that the two patients' sera (and that of a patient's spouse) contain antibodies which specifically react with the major core protein of the virus.

Mycosis fungoides and Sézary syndrome are clinical variants of cutaneous T-cell lymphoma and leukaemia, respectively, that occur as rare diseases in adults<sup>2</sup>. The retrovirus particles produced by these tumours are not evident until the tumour cells are grown in culture, although a second biopsy from the first patient released virus within 24 h of its being placed in culture. Until 5 years ago it was very difficult to maintain normal or malignant T cells in culture; however, a specific T-cell growth factor (TCGF) discovered in Gallo's laboratory<sup>3</sup> enables T cells to proliferate *in vitro* for long periods, and this aided the detection of the virus.

### Properties of HTLV

The virus, called HTLV (for human T-lymphoma virus), seems to be quite distinct from the numerous types of animal retroviruses previously described. By its morphology and the molecular weight of virion proteins, HTLV most closely resembles bovine leukosis virus, which causes lymphoma in cattle. However, the human and bovine viruses seem unrelated antigenically or by nucleic acid homology.

Following Gallo's report of virus production from T-lymphoma cultures, an

independent virus isolate has been made in Japan<sup>4</sup> from a previously established malignant T-cell line<sup>5</sup>. Now Miyoshi and his colleagues, in a paper shortly to be published in *Nature*, claim that co-cultivation of the T-leukaemia cells with umbilical cord leukocytes leads to the transformation of the cord leukocytes into a TCGF-independent cell line producing retrovirus particles. This is the first experimental evidence for infectious transmission and cell transformation with HTLV.

### Origin of HTLV

Gallo's laboratory has not succeeded in transforming animal or human cell lines with HTLV, but they have not tested cord lymphocytes nor used co-cultivation. They think that T lymphocytes from some relatives of patients may support the replication of HTLV. At a recent meeting of the Leukaemia Research Fund in England, Gallo reported individual isolates of HTLV from four cutaneous T-lymphoma patients. From one patient an Epstein-Barr virus-positive B-lymphoblast line was also developed: this line was negative for HTLV, suggesting that HTLV is specifically associated with the tumour cells. Serological tests on some hundreds of American normal individuals or patients with diseases other than T-cell malignancies have been negative for antibodies reacting with the HTLV p24 core protein. By no means all T-cell leukaemia patients are positive either; the virus appears to be associated with a particularly malignant, fast growing form of tumour. Gallo thinks that all four patients (three black and one white) from whom HTLV has been isolated have Caribbean connections and that the virus may be more commonly found there.

The most striking epidemiological studies, however, come from Japan. There is a relatively high incidence of patients in major Japanese cities presenting an aggressive form of adult T-cell leukaemia. Uchiyama *et al.*<sup>6</sup> noted that 13 out of 16 patients with this form of disease were born and grew up on the west coast of Kyushu,

Japan's extreme south-west island. A more recent study<sup>7</sup> of 272 T-cell leukaemia cases shows a remarkable clustering of places of birth, in the Kagoshima and Nagasaki prefectures of Kyushu. Sera from all the leukaemia patients tested and from 25% of healthy adults sampled react positively with Miyoshi's virus isolate<sup>4</sup>. Through Yohei Ito, Gallo has found that Japanese sera also recognize his viral p24 antigen.

Several viruses are implicated as aetiological factors in human malignancies; Epstein-Barr virus in Burkitt's lymphoma and nasopharyngeal carcinoma are the classic examples. The association of hepatitis B virus infection with liver cancer has become apparent although it is curious that this virus does not even merit passing mention in two major compendia on tumour viruses published as recently as 1980<sup>8,9</sup>. Cancer of the uterine cervix may well have an infectious agent as an aetiological factor, for which herpes simplex and papilloma viruses are under suspicion. During the 1970s claims for isolating human retroviruses have perhaps been made too frequently and prematurely. While some proved to be animal viruses acquired during laboratory procedures, others remain enigmatic, such as the virus-like particles seen in full-term placentae<sup>10</sup>. Four laboratories — Bentvelzen's in Holland, Gallo's at the National Institutes of Health, Kaplan's at Stanford and Kirsten's in Chicago — have independently isolated from human tissues retroviruses related to those of gibbons and baboons. These isolates are generally dismissed as laboratory contaminations. I am reluctant to disclaim their human provenance so lightly, although admittedly human antibodies which were thought to bind to these viruses specifically now appear to recognize heterophile carbohydrate groups present on the viral glycoproteins<sup>11,12</sup>.

### Role in malignancy

The striking features of the T-cell leukaemia virus are its unique biochemical properties, its association with a particular subset of T-cell lymphoma/leukaemias and the geographical clustering of that disease in Japan. The discovery of this new virus followed the successful development of culture methods for T cells. The epidemiological findings would not have been possible without careful classification of leukaemias into B- and T-cell classes and further subclasses. A fascinating and important story is unfolding on the viral aetiology of a human malignancy. □

Robin Weiss is at the Institute of Cancer Research, London.

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