TUMOUR VIRUSES

Pulling Together

from a Correspondent

To mark the sixty-fifth birthday and retirement of their director, Professor O. Mühlbock, the Netherlands Cancer Institute organized in Amsterdam last week (May 12–15) a verbal *Festschrift*—a conference on RNA tumour viruses and oncogenesis with particular emphasis on the role of the host genome in the response of an animal to tumour viruses. And for once the murine mammary tumour viruses were as fully discussed as the avian and murine sarcoma leukaemia virus complexes; there are, of course, more virologists—most of them Mühlbock's pupils—studying mouse mammary tumour viruses in Holland than in any other country with the possible exception of the United States.

Once the stage had been set by a series of speakers who surveyed the history of the subject, the conference got down to first discussing the genetic factors influencing oncogenesis by avian viruses. Svoboda (Czechoslovakia) summarized a series of experiments showing that Rous sarcoma virus (RSV) can be rescued from transformed mammalian cells by fusion with chick fibroblasts if the transformed cells carry the group specific antigens of the avian tumour viruses. By contrast, if the transformed mammalian cells lack the group specific antigens, RSV cannot be rescued by fusion with chick fibroblasts.

Payne (UK) then reviewed the elegant genetic analysis of the control of susceptibility of chicks to avian sarcoma and leukaemia viruses which have won him and his colleagues renown. Susceptibility to viruses of subgroups A, B, and C is controlled by three corresponding loci, the allele for susceptibility being dominant to that for resistance. Susceptibility to viruses of subgroup E—the new designation of the Bryan high titre sarcoma virus genome and RAV.60—is, however, more complex; in addition to a locus with dominant susceptibility and recessive resistance alleles there is a second epistatic inhibitor locus. The dominant and widespread allele of this inhibitor locus (I^0) renders cells resistant to E subgroup viruses even when the cell is homozygous for the susceptibility allele.

Weiss (UK) then reported fascinating experiments which show that all chick cells carrying the group specific antigens of the avian viruses can provide a helper function for RSV.E, and chick factor, otherwise called RAV.0 or RAV.60, can be obtained from these cells. Chemical carcinogens and ultraviolet and X-irradiation all promote this activation and release of the resident RAV.60 or RAV.0 leukosis virus.

Furthermore, even cells which lack detectable group specific antigens may act as helper for RSV.E and occasionally leukosis virus seems to be rescuable from these cells. Hanafusa (USA) reported essentially similar results and conclusions as Weiss. It is beginning to look as if all chick cells, even those of wild Malaysian jungle fowl, carry the leukosis virus RAV.60 (or RAV.0).

The Dutch school of murine mammary tumour virologists have come to much the same conclusion about their system. Hageman and Bentvelzen (Holland) suggest that no strain of mice is free of mouse mammary tumour virus (MMTV), and Bentvelzen's impressive experiments clearly indicate that several strains of MMTV are transmitted vertically by egg and sperm rather than in milk. He believes that every mouse carries the genes to specify an MMTV, and that the development of mammary carcinoma depends on the "derepression" of these genes and their replication as a virus.

Whether mammary carcinoma develops depends on hormonal factors (Boot, Holland) and on the host's genotype. Dux and Mühlbock (Holland) reported that alleles of the H2 histocompatibility locus play an important part in regulating the response of an animal to strains of MMTV; the H2b allele, for example, inhibits oncogenesis by C3H-MTV (Bittner agent).

Boyse (USA) and Lilly (USA) described the striking parallels between the influence of histocompatibility antigens on the response to MMTV and murine leukaemia viruses. As Boyse so

eloquently explained, the H2 locus, the TLA locus and the G9 locus, all part of the murine linkage group IX, are implicated in murine leukaemogenesis. Leukaemic cells of strains of animals which are, when healthy, TLA⁻ and G9⁻ carry at least two TL antigens and the G9 antigen. These loci seem to be switched on by leukaemogenesis, and although not committing himself Boyse raised the possibility that the G9 locus might be part of a murine leukaemia virus genome present in all mice. Murine leukaemogenesis might well boil down to the activation of a latent murine leukaemia virus genome transmitted vertically in mice which in the environment of the thymus might transform target lymphoid cells.

On the final morning Spiegelman (USA) reviewed the state of play with reverse transcriptase, noted in passing that visna and slow pneumonia viruses have now been shown to transform cells *in vitro*, reported that the B-type particles (or are they C-type?) in human milk contain reverse transcriptase, and left the stage for Temin (USA) to expound his provirus theory. Temin argued that gene amplification may be important in normal differentiation and may be mediated by messenger RNA and reverse transcriptase. Cell transformation might result from the amplification of transforming genes either introduced by a transforming virus or resident but not normally expressed in a differentiated cell but induced to amplify by the virus. His was a thought provoking climax to a noteworthy conference.

New Soft X-Ray Source Discovered

As well as the exciting developments from the experiments on board the Uhuru X-ray satellite, the by now conventional sounding rocket techniques continue to add to the list of known X-ray sources. Below 2 keV, the lower limit of the sensitivity of Uhuru's detectors, sounding rockets remain the prime source of experimental data. The latest development in this field is the discovery of a soft X-ray source in the Aries-Taurus region. This discovery was made by the large team of high energy astronomers working at Nagoya University; their full report of the discovery will be published next week in *Nature Physical Science*.

At 0.2–0.5 keV, the source is brighter than NGC 1275, the Seyfert galaxy recently found to be an X-ray source, which appears in the same part of the sky. But at higher energies the relative brightness of the new source decreases until it can no longer be detected above 1 keV. NGC 1275 is still detectable at the higher energy range, and this points, not unexpectedly,

to a different mechanism operating in the new source. The statistics available so far do not really allow any definite estimate of the source's spectral characteristics, but it is a very soft source, and the spectrum is at least not inconsistent with the familiar exponential form with kT between 0.3 and 0.5 keV. A lower limit on the total energy flux from the source in the observed range is roughly 2×10^{-9} erg cm⁻² s⁻¹.

Comparison with Sco X-1, the brightest known X-ray source within our galaxy, shows just how wide the classification "X-ray source" is—Sco X-1 has a very hard X-ray tail to its spectrum (above 40 keV), as well as a softer, varying component at 1–10 keV, and if the energy mechanism is thermal the effective temperature in the source is roughly 50 million K. Indeed, it is now little more help to say that an object is an X-ray source than to say that it is a star. With the further development of high energy astronomy, more specific classifications will undoubtedly become clear.