millimetre wavelengths, the 3.8-metre United Kingdon Infrared Telescope (UKIRT) atop Mauna Kea, at submillimetre wavelengths, and NASA's Kuiper Airborne Observatory, at far-IR wavelengths.

The resultant radio to optical spectrum (see the figure) shows that the quasar has a flat radio spectrum and becomes transparent at millimetre and shorter wavelengths. It therefore appears that at millimetre and submillimetre wavelengths we are observing the core of the radio emission. This observation makes it all the more worthwhile to develop millimetre-wavelength very-long-baseline interferometry (VLBI), which will allow the angular structure of the core to be determined.

Studies of the variability of quasars at millimetre wavelengths have been rather few until recently. Now, two groups, E. Epstein *et al.* (*Astr. J.* **87**, 499; 1982) and Ennis, Neugebauer and Werner (*Astrophys. J.* **262**, 451; 1982), have published monitoring projects at 3.3 and 1 mm respectively. Unfortunately, new observations only serve further to subvert straightforward interpretation of the observed brightness changes. Sometimes the millimetre variations are correlated with those seen at longer wavelengths, and sometimes they are not. Even when they are connected, the simple models found in the literature do not seem to explain the details of the observations. Moreover, the connection with optical brightness changes is far from clear. Clearly, further observational and theoretical advances are necessary.

Neugebauer and Werner (*Astrophys. J.* **262**, 460; 1982) bears on the radio-quiet QSO problem. They detected no radio-quiet QSOs at 1 mm, so clearly the optical–IR spectrum must cut off at wavelengths substantially shorter than this.

A further curious result is the failure to detect QSOs that have been observed to be weak radio sources, implying that the radio spectrum does not rise steeply from long to short wavelengths as would be the case for a self-absorption cutoff. This behaviour is consistent with Scheuer and Readhead's (*Nature* **277**, 182; 1979) relativistic beaming model, but other observations seem to indicate that this is not the entire explanation.

Fortunately, we can expect further development of millimetre and submillimetre astronomy in the near future. Resurfacing and expansion of the NRAO 36-foot dish (now called the '12-metre' telescope) and the introduction of new millimetre-wave dishes (for example, the upcoming British 15-m dish atop Mauna Kea) should at least partially compensate for the demise of the proposed US 25-m project. Continued advances in submillimetre detectors and the deployment of IR satellites will further assure a place for millimetre and submillimetre astronomy at the forefront of quasar research. □

Vaccine development

Hybrid vaccinia virus for mass hepatitis immunization?

from A.J. Beale

IN this issue of *Nature* (p.490), Smith, Mackett and Moss from the National Institutes of Allergy and Infectious Diseases in Bethesda, Maryland, describe the successful selection of vaccinia virus into which the gene for hepatitis B virus surface antigen has been inserted. The modified virus grows well in cell culture and hepatitis B virus agglutinin (HBsAg) is released into the culture fluid in a form indistinguishable from the native antigen present in the serum of carrier individuals. Even more exciting is their observation that rabbits infected with the hybrid vaccinia virus produce high titres of antibody to the HBsAg, more than those required to provide protection in man. The authors suggest that this type of hybrid vaccinia virus might be ideally suited to mass immunization campaigns in areas of the world where control measures are urgently needed but existing vaccines are too expensive to make or administer. The success of the WHO campaign for the global eradication of smallpox gives added force and credibility to that point of view.

Moss and his colleagues devised a means of introducing foreign DNA into vaccinia virus so that the polypeptide encoded by the new DNA is produced during the growth cycle of the virus. A chimaeric gene consisting of vaccinia virus promoter sequences fused to the coding sequence for the desired foreign protein was flanked by vaccinia virus DNA in a plasmid vector. One such foreign protein used in early experiments was herpes virus thymidine kinase. In order to make vaccinia useful as a general expression vector, plasmids with restriction enzyme sites next to the vaccinia thymidine kinase promoter or another vaccinia promoter engineered in the thymidine kinase gene were constructed. Transfection of vaccinia virus-infected cells with the plasmid allowed recombination to take place. The recombinants containing the foreign protein-coding sequences could be selected by looking for thymidine kinase vaccinia plaques or the presence of herpes virus thymidine kinase.

The recloned vaccinia containing the HBsAg-coding sequences were used to vaccinate two rabbits; typical vaccinia lesions were produced and, in addition, high titres of antibodies were seen to last for at least 31 days. These preliminary results hold promise that many other antigens may be expressed in the same way and used as vaccines, either as a means of producing antigens in culture or, more imaginatively, to use them as combination vaccines. Several problems in developing vaccines by new technology may thus be solved. Although rDNA techniques should enable protective antigens to be produced in large quantities, some antigens are poorly expressed or poorly immunogenic when produced in *Escherichia coli*, as is the case with foot-and-mouth disease virus VP1 or HBsAg. Again, the presentation of the immunogen to the host may be below the optimum, and it is commonly thought that a new generation of adjuvants or a deeper understanding of the nature of immunogenicity will be required before it will be easy to elicit the range of immune responses necessary for clinical immunity.

The cost of vaccines, and particularly of their administration, are vital factors in determining the success of an immuniza-

Oncogenic Intelligence

Oncogene, not polymorphism

from Peter Newmark

THE 15 April issue of *Science* contains a retraction of a paper published there two months ago and the subject of this column in *Nature* **301**, 654 (1983). In their paper (*Science* **219**, 853; 1983) R.J. Muschel, G. Khoury, P. Lebowitz, R. Koller and R. Dhar claimed that polymorphism rather than somatic mutation accounted for the single base change that distinguishes the c-*ras*^{H} oncogene of T24 bladder carcinoma cells from that in normal tissue gene banks and accounts for the ability of the former to transform NIH 3T3 cells.

At best their evidence — for the same base change in the c-*ras*^{H} gene of both normal and tumour tissues of an individual with bladder cancer as in T24 cells — was decidedly preliminary. At worst, as they have since discovered, it was all accounted for by contamination. Further tests have convinced them that neither normal nor tumour tissue of their patient had the mutation that characterizes the c-*ras*^{H} oncogene of T24 cells.

Polymorphism remains a possible explanation of the T24 mutation but the attempt by Muschel *et al.* to make that explanation stick should now be counted as a casualty of the fierce competition that abounds between oncogene laboratories. □

Peter Newmark is Deputy Editor of Nature.

0028-0836/83/140476-02$01.00