treatment. The state of the remaining genome has not yet been investigated.

While no restriction studies have been made on EBV as yet, Sugden (Karolinska Institute) reported the first EBV-transcription studies. He found a more extensive transcription of the viral genome (up to 30–50%) in the producer P3HR-1 line than in the non-producer Raji line, as expected. The viral RNA sequences detected in Raji cells were a subset of those found in P3RH-1 cells; they were sufficient to code for approximately 10 proteins. EBNA is the only known viral function in transformed non-producer lines.

Immunological factors

Henle stressed the curious differences in antibody patterns between different EBV-associated diseases. Burkitt lymphoma patients with ongoing disease tend to form antibodies against one particular subcomponent of the early antigen complex (R). Mononucleosis and nasopharyngeal carcinoma patients preferentially make antibodies to another component (D). Since all known strains of EBV induce both antigens approximately simultaneously, during their cycle, these differences in the host response probably reflect the way in which the various antigens becomes available to the immune system. Considerable discussion followed the report of Henle that anti-EBNA antibodies appear very late, several months after the onset of infectious mononucleosis and are frequently low or absent in Hodgkin's disease (HD). Henle attributed this to the intranuclear nature of the antigen and postulated that considerable time is required before enough EBNA positive cells have been destroyed by the immune response. In HD the response would be often deficient.

The question why lymphoma, HD and other patients with EBV-genome negative tumours sometimes develop elevated EBV-antibody titres, was approached by P. H. Levine and colleagues (National Institutes of Health), and by Johansson and colleagues (Karolinska Institute), respectively. Both dealt with the possibility that tumour-induced immunosuppression may be responsible, but in different ways. Levine found no evidence for any relationship between the lymphocytotoxicity reaction of Herberman against established lymphoma lines, and EBV titres. This reaction is mediated by non-T lymphocytes, however. Johansson found a correlation between T-cell depression, as judged by PHA, Con A, and PPD lymphocyte stimulation or skin tests, and increased anti-EBV (VCA) titres. No such correlation was found with reactivity to a B cell mitogen (PWM). The notion that T-cell suppression may be crucial receives support also from the demonstration by Aiuti that two congenitally T-cell deficient children had significantly elevated anti-EBV (VCA and EA) titres that fell to normal after thymus grafting and appearance of T cells in the circulation. It is likely that T cells play some regulatory part in maintaining the anti-EBV titre at a relatively low level from year to year in normal individuals. Depending on one's viewpoint, this could be attributed to T-cell mediated surveillance against dormant, potentially neoplastic cells, or to some T-cell dependent antibody, acting either against dormant cells or against the spreading of periodically reactivated virus.

Sabin withdraws claim

THE persistent irreproducibility and frustration to which Zur Hausen has alluded (see Klein on this page) is not confined to attempts to demonstrate herpesvirus DNA or antigens in cervical carcinomas. Albert Sabin has been obliged to withdraw his claim made early last year that a nonvirion antigen of HSV is associated with a large number of human cancers and can be found early in infection of guinea-pig cells *in vitro* (see *Nature*, **247**, 334; 1974).

The history of frustration has extended over a period of five months during which Sabin has been trying to trace the reasons for his failure to reproduce the results he and Tarro reported last year (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 1032–1036 and 3225–3239; 1937). The irreproducibility of the results remains unexplained and Sabin's most recent paper (*Proc. natn. Acad. Sci. U.S.A.*, **71**, 3248–3252, 1974) contains a detailed admission of defeat.

The difficulty in which Sabin now finds himself weakens the case for HSV as the aetiological agent of certain cancers; hopes of shedding light on oncogenesis through a study of the function of early HSV proteins are correspondingly dimmed.

Marek's disease and herpes simplex

An important development in the field of Marek's disease is the establishment by Kato of three permanent lines which Nazerian has shown carry 70-80 genomes per cell. IUDR can activate antigen production in a small proportion of the cells. The lines had T-lymphocyte characteristics, confirming the suspicion that the disease is due to malignant T-cell proliferation. P. M. Biggs (Houghton Poultry Research Station) showed that bursectomy did not increase the incidence of the malignant lesion. Powell found that the established lines can serve as targets for *in vitro* lymphocytotoxicity tests. Preliminary evidence suggests that MDV-induced tumour cells may have a distinctive membrane antigen: clearly better antigen definition and immunological characterisation are urgently needed in the MD system. The disease seems to be uniquely suitable for studies on immune surveillance against tumours induced by a naturally occuring virus, with genetic differences in susceptibility and a corresponding contrast between self-limiting and malignant lesions. Biggs summarised the remarkable success story of vaccination against the malignant form, first with attenuated MDV, and later with a partially crossreactive but non-pathogenic turkey herpesvirus (HTV). It is interesting that without protecting birds from infection or reducing virus shedding the vaccine was nevertheless capable of preventing the development of malignant disease. It is probable, although unproven, that this is due to immunisation against tumour-associated antigens. The situation may be analogous to the successful protection of hamsters inoculated with polyoma or SV40 virus when newborn, by a second virus dose.

There is now increasing evidence that the HSV-transformed lines carry viral genomes. Frankel pointed out that viral RNA is often more easily detectable than viral DNA. Summers reported the detection of viral DNA using restriction fragments as the hybridisation probe.

Though laboratory models of HSV transformation have achieved a status of increased reproducibility, this cannot be said about the attempts to demonstrate herpesviral genomes or their antigenic footsteps in human cervical carcinomas. Zur Hausen said that this search has resulted in "persistent irreproducibility and persistent frustration, rather than persistent infection". This was countered by the argument that fractional genomes may be very difficult to demonstrate, as also evident from the *in vitro* transformed cell studies. The epidemiological evidence that links HSV type 2 infections to cervical carcinoma is circumstantial at best. While some careful studies suggest a relationship, at least in certain geographical areas and certain socio-economic groups, the suspicion still prevails that the venereally transmitted type 2 infection may be another covariable of promiscuity, particularly the early onset of sexual life and multiple partners, factors that are known to have a role in the genesis of cervical carcinoma, rather than being an aetiological factor in itself. But recent epidemiological studies of the Melnick group where controls and cancer patients have been matched with regard to sexual history speak against this.