GENETIC ASPECTS OF EBV-ASSOCIATED MALIGNANCIES

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EBV is strongly associated with two malignancies, Nasopharyngeal carcinoma (NPC) and Burkitt's lymphoma (BL). Of the two main aspects of genetic consideration, more information is emerging concerning genetic mechanisms of carcinogenesis in BL. Genetic factors responsible for excess cancer occurrence are better understood in NPC than in any other common human cancer.

The two malignancies in which there is strong suspicion of EBV involvement are Nasopharyngeal carcinoma (NPC) and Burkitt's lymphoma (BL). EBV is also associated with a variety of lymphoproliferative diseases including malignant lymphoma but apparently not including Hodgkin's disease (Purtilo, 1983). The program for this symposium indicates that mechanisms and models of BL aetiology are to receive close attention, as will recent developments in oncogene molecular biology. These presentations can be expected to deal with one of the two main aspects of genetic consideration, namely that of genetic mechanisms of background incidence cancer development. Since my overview is the only one scheduled to address NPC, I will focus on the second main aspect of genetic factors responsible for excess NPC occurrence in high risk groups.

Chromosomal aberrations are thought to play a central role in neoplasia, allowing the generalisation that all cancer is in one sense a genetic disease. For many cancers there are no distinguishing cytogenetic features detectable.
at the microscopic level. In BL there are exciting developments at the chromosomal and DNA molecular levels using cytogenetic banding and oncogene probe technologies. The emerging molecular description of genetic phenomena involving oncogene activation epitomises the former aspect of genetic consideration concerning genetic processes underlying background cancer occurrence (Klein, 1981, 1983). To date, there is no information in NPC similar to the chromosomal rearrangements identified in BL. There is a pressing requirement to apply cytogenetic and molecular biological techniques to assess whether there are chromosomal alterations accompanying NPC and, if so, whether they occur in either background or in excess incidence patient populations, or both.

The epidemiological data does not suggest a major role for genetic elements in the excess risk for BL. Rather it seems that the excess incidence reflects interactive environmental exposure events. In complete contrast, the maintenance of high NPC incidence among Chinese is perhaps the best example of an epidemiological pattern suggesting an important genetic component (Simons and Shanmugaratnam, 1982). Furthermore, NPC stands alone as the only common human malignancy in which the strong genetic effect suspected of underlying excess incidence has been assigned to a polymorphic gene system for which the chromosomal localization is known.

Some introductory comments about genetics and neoplasia may be useful in order to better comprehend concepts of genetic-environment interaction, so that the evidence for genetic effects in NPC can be better appreciated. Comments which suggest some confusion in conceptual comprehension of the role of genetic and environmental factors in cancer causation include the following:

(i) the HLA gene complex comprises only a minute fraction of the human genome so HLA genes can not be that important;

(ii) the HLA BW46 gene is only present in Chinese, so the genetic findings are not relevant to NPC patients of other ethnic groups;

(iii) incidence estimates among Hawaiian and mainland USA Chinese patients indicate a decline in US-born Chinese NPC incidence, so environmental effects are predominant, although genetic factors cannot be excluded;

(iv) the high NPC incidence maintained among overseas