Preface

O.

Ohio

Hino

Tokyo, Japan

Guest Editor

Cancer is a heritable disorder of somatic cells. Environment and heredity both operate in the origin of human cancer. These environmental and genetic determinants of cancer can be classified into four groups designated 'on-codemes' by Knudson in 1985. Oncodeme 1 is the irreducible 'background' level of cancer due to spontaneous mutagenesis. Oncodeme 2 is 'environmentally induced' cancer, whose causative agents are chemical carcinogens, radiation, or viruses. Oncodeme 3 is basically 'environmentally induced' cancer, but there are genetically determined differences among persons, e.g. the activation or inactivation of carcinogens. Oncodeme 4 is 'hereditary' cancer. Only a small proportion of cancers belong to this group, although recently several predisposing 'cancer' genes have been discovered and there is a social impact. However, most human cancers are believed to belong to oncodemes 2 and/or 3 (about 80%), for which the probability of the occurrence of carcinogenic steps is increased, although the number of steps is not decreased. Oncodeme 1 would contain the 20% that would remain if 'environmentally induced' cancers (oncodemes 2 and/or 3) were prevented.

Human viral carcinogenesis belongs to oncodemes 2 and/or 3 and greatly influences the incidence of somatic genetic events in virus-infected organs or tissues, by increasing the number of target cells, or the proliferation of once-hit stem cells, eventually leading to cancers. These conditions may be designated the 'hypercarcinogenic state'. Our goal is to lead the 'hypercarcinogenic' to the 'normo- or hypocarcinogenic' state and to prevent cancer development.

This special issue describes the latest achievements in the study of five types of human viral (HBV, HCV, HPV, EBV and HTLV-I) carcinogenesis.

Velhagen et al. studied the function of an antisense promoter within the HBV X gene. They show that the product of an ORF under the promoter transactivated c-myc, and discuss its possible role in HBV-associated hepatocarcinogenesis. Koike summarizes the findings obtained in the HBV X transgenic mouse developing hepa-tocellular carcinoma. Schaerer and Gerilch provide a broad review of the transforming activity of HBV DNA in vitro and point out that it and the transactivating activity of HBV X might be independent of each other. London and colleagues studied the epidemiology of HBV-associated hepatocellular carcinoma in China and propose GSTM1 (the μ form of glutathione-S-transferases) and EPHX (microsomal epoxide hydrolase) to be the candidate genetic factors which determine the susceptibility to HBV-associated cancer. Shimotohno introduces recent findings on the virological analysis of HCV, and speculates that the critical events for cancer development may occur in the early stage of HCV infection. Kajino and co-workers discuss viral hepatocarcinogenesis with respect to 'genomic instability'.

Beyer-Finkler et al. provide evidence for the multiclonal development of HPV-associated cancer. Kondoh et al. report that the activation of c-myc/SLF is required for the development of testicular tumor in their HPV 16 E6E7 transgenic mice, and that the amplification of E6E7 expression is required for the progression of the tumor. Both Kanda and Katase and their co-workers present data revealing the association of HPV 16 infection and the development of cervical carcinoma. The former group shows that antibody against the HPV 16 virion protein L2 is more frequently detected in the sera of cervical cancer/ dysplasia patients than in the healthy female. In their prospective study, Katase's group shows that HPV16, 33 and

© 1995 S. Karger AG, Basel

52 are associated with the progression of cervical intraepithelial neoplasia.

Homer et al. propose a hypothesis that BHFR1, the EBV homologue to bcl-2, protects cells against apoptotic death and contributes to cancer development. Kawanishi observes that nitric oxide suppresses the replication of EBV, and speculates that the effect may be mediated by the inhibition of ribonucleotide reductase. Takada and colleagues compare the phenotype of EBV-positive and EBV-negative cell clones with the same origin, and show that the malignant phenotype is more evident in an EBV-positive clone.

Fujii's group reports that even in the absence of Tax, cellular AP-1 activates the transcription of HTLV-I mRNAs from the LTR. Yoshiki establishes the rat model of HTLV-I infection, and describes the characteristics of the model animal. Tajima and Cartier summarize the epidemiological data of HTLV-I infection in Japan. They suggest that the development of symptomatic ATL may be related to the nutritional condition in childhood, and to the HLA haplotype of the infected patients.

We hope that this special issue will be helpful in the understanding of human viral carcinogenesis and in orienting future work with the aim of reaching a 'normo-or hypocarcinogenic state' from 'hypercarcinogenic states' and thus preventing human cancers.

126

Hino

Preface