Mechanisms of DNA Tumor Virus Transformation
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Mechanisms of DNA Tumor Virus Transformation

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Leonard J. Rosenthal  Washington, D.C.

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Leonard J. Rosenthal, PhD
Department of Microbiology & Immunology,
Georgetown University Medical Center,
Washington, D.C.
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At the beginning of last century, scientific observations founded viral oncology. These observations defined transmissibility of avian leukemia in 1908 by Danish researchers Ellermann and Bang and soon afterwards of an avian sarcoma in chickens in 1911 by Peyton Rous in New York. These important discoveries were not appreciated at the time, and their impact on virology and medicine was not recognized for decades. Happily, Rous lived to be awarded the Nobel Prize in 1966, as the first nonagenarian to receive this honor, 55 years after his great discovery. This reflects the span of time that was needed to appreciate the full significance of Rous’ findings and to accept the idea of viruses as causative agents in cancer by medical research community.

It has been 36 years since the isolation of Epstein-Barr virus (EBV), the first virus to be associated with a human tumor. The most recent human tumor virus isolated is another herpesvirus, human herpesvirus 8, which in 1994 was recognized to be associated with Kaposi’s sarcoma. It is now clear that five virus types are involved in the causation of human cancer: papillomaviruses, retroviruses, herpesviruses, hepadnaviruses and flaviviruses. Approximately 15% of human cancer incidence can be attributed to virus infection, i.e., viruses represent the second most important risk factor (after tobacco consumption) for cancer development in humans. Only two RNA viruses (human T-cell lymphotrophic virus type I and hepatitis C) are considered as causative agents for human malignancies while most virus-induced tumors are attributed to infection with DNA viruses. Eighty percent of virus-induced malignancies are sequelae of infection by two DNA viruses, hepatitis B and human papillomavirus. Interestingly, there is a growing number of neoplasms ascribed to infection with another herpesvirus, EBV.

One of the major problems in proving that the association is causal or casual in human cancer is the high rate of infection in the general population,
given that there are geographical variations in infection rates. Several DNA viruses have been associated with human cancers and possessed transforming potential when tested in experimental models; however, a recent detailed epidemiologic observation failed to provide evidence for a causative role in human cancers. It is possible that these viruses may be important in a modulation of cellular pathways of already transformed cells by inducing/increasing their malignant potential. This may explain aggressive tumor growth observed in patients infected with herpesviruses such as human cytomegalovirus or herpes simplex virus type 2.

This book describes molecular mechanisms of cellular transformation of DNA viruses. Although a relevance of some viruses for human cancer remains elusive, the different DNA viruses utilize common strategies which may be important for development of tumors. The effector pathways, at least in part due to shared function of viral oncoproteins, are common not only to small oncogenic DNA viruses such as polyomaviruses and papillomaviruses, but also to large DNA viruses such as herpesviruses. These events may include activation of mitogen-activated protein kinases pathways, interaction of viral proteins with cellular tumor suppressor genes and effects on cell cycle progression or apoptosis. In the past, tumor virology, using model systems, has been the source of much of our fundamental knowledge of oncogenesis and basic cellular mechanisms (e.g. oncogenes were discovered in avian retroviruses; mRNA splicing was first described in human adenoviruses). Some of the novel findings introduced in this book confirm that tumor viruses retain their promise as tools for studying the basic mechanisms underlying neoplastic changes. On the other hand, special mechanisms of some viruses such as EBV, human herpesvirus 8 or human papillomavirus with a well-documented role in tumorigenesis are also considered in depth in the chapters which follow. From a medical point of view, the understanding of molecular mechanisms of virus-induced cellular transformation is an essential step for development of strategies for prevention and treatment of virus-associated tumors. In the absence of virus infection, the virus-induced cancers would be reduced by 95% with a significant reduction in morbidity and mortality.

There is still much to be learned. It is hoped that the contents of this book will give further help in understanding the mechanisms of DNA tumor virus transformation with special attention to virus/host cell interactions.

J. Cinatl, Jr.
H.W. Doerr