

## Preface

*Latency* is a most remarkable property of herpesviruses that ensures the maintenance of their genetic information in their hosts for an extended period in the absence of productive replication. Members of all three herpesvirus subfamilies infecting a wide variety of target cells are able to establish latent infection, which is associated with a restricted expression of the viral genome. Latency-associated transcription is either confined to protein noncoding RNAs and/or protein coding RNAs not translated in the latently infected cells or may include transcripts for viral oncoproteins that alter host cell behavior (*immortalization, malignant transformation, tumorigenesis*). In this book, we wished to review the intriguing latency strategies developed during the estimated 200-million-years-long coevolution (McGeoch and Davison, 1999) of *Alpha*-, *Beta*-, and *Gammaherpesvirinae* and their host species. We put the main emphasis on herpesviruses infecting humans, but we discuss relevant cases of herpesviruses infecting animals as well. We wished to highlight immune evasion tactics used by these viruses as well as the molecular mechanisms regulating the latent promoters of their genomes and signals and molecular pathways resulting in *reactivation* of latent viral genomes. We gave special attention to *epigenetic mechanisms* (DNA methylation, histone modifications, chromatin structure) involved in cell-type-specific expression of growth transformation-associated gammaherpesvirus genes.

The goal of this book is to bring together recent results of herpesvirus research with special attention to latent infections. Although the chapters follow the classical scheme with three subfamilies (*Alpha*-, *Beta*-, and *Gammaherpesvirinae*), we also included special chapters dealing with important aspects of herpesvirus latency, like the modulation of apoptotic pathways and the maintenance of latent, episomal DNA genomes. In the first chapter, Tibor Valyi-Nagy, Deepak Shukla, Herbert H. Engelhard, Jerry Kavouras, and Perry Scanlan describe how alphaherpesviruses (herpes simplex virus and varicella-zoster virus) hide in neurons, giving utmost care to the mechanisms of immune evasion and the molecular biological background (including an epigenetic regulatory mechanism, histone modification) ensuring the almost complete transcriptional silence of the latent genomes. Next, in a special chapter, Klára Megyeri gives a detailed picture of apoptotic pathways modulated by herpes simplex viruses. In the third chapter, Katalin Burian and Eva Gonczol deal with the latency strategies of human cytomegalovirus (HCMV, a betaherpesvirus) discussing the models of differentiation-dependent expression of lytic viral genes and the molecular mechanisms

preventing virus production in undifferentiated cells. They give a detailed overview of how HCMV evades innate and adaptive immune responses, too. In Chapter 4, Béla Taródi summarizes the current knowledge on human herpesvirus 6 and 7 latency, highlighting the unique features of the latency-associated transcripts. He pinpoints that one of these betaherpesviruses, HHV-6, can be transmitted in infrequent cases *via* the germline. In addition to viruses of medical interest, certain herpesviruses infecting animals are also described in this book. In Chapter 5, Julius Rajčáni and Marcela Kúdelová give a detailed description of murid herpesvirus 4, which provides an important animal model for human gammaherpesvirus research. Much less knowledge has accumulated on equine alpha- and gammaherpesviruses: Laszlo Egyed compares the available data on their latency in Chapter 6. Turning to human gammaherpesviruses, Christopher M. Collins and Peter G. Medveczky focus on LANA1 (latency-associated nuclear antigen 1), a multifunctional nuclear antigen of Kaposi's sarcoma-associated herpesvirus (Chapter 7). This sequence-specific DNA binding protein plays a crucial role in the replication and maintenance of the latent, episomal viral genomes and mediates their segregation during cell division. It is also involved in the alteration of cellular behavior (malignant transformation). The properties of LANA1 homologues encoded by *Herpesvirus saimiri* and murine gammaherpesvirus 68 are also discussed here. In the final chapter, Hans Helmut Niller, Hans Wolf, and Janos Minarovits review the latency strategies of Epstein-Barr virus (EBV). EBV, a *Lymphocryptovirus*, hides in memory B lymphocytes and contributes to the development of a wide variety of neoplasms. They describe how the expression of latent EBV genes is regulated by DNA (CpG) methylation and how the cell-type-specific usage of latency promoters is reflected in cell-type-specific methylation patterns of the viral genomes (epigenotypes). They also discuss how other epigenetic mechanisms (binding of regulatory proteins, histone modifications) leave their marks on the locus control region (LCR) of the latent viral episome, which persists like an independent chromosomal domain.

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