

Retroviruses

Edited by J. Coffin, S. Hughes
& H. Varmus

Cold Spring Harbor Laboratory, \$180, 843 pp
ISBN 0-879-69497-1, 1998

REVIEWED BY HARRIET L. ROBINSON

Yerkes Primate Research Center,
954 Gatewood Drive NE
Atlanta, Georgia 30329

RETROVIRUSES stands high in the clarity and depth of its presentation of the molecular and cellular biology of retroviral infections. Chapters, authored by prominent experts, are integrated for content and edited to a common style. The first half of the book provides an *overture* of viral structure, function and replication. An *intermezzo* by the editors carries the reader from viral life cycle to viral-host interactions. The closing chapters maintain tempo, a fortissimo on endogenous viruses, retroviral vectors, pathogenesis and approaches to control. Appendices present sequence and taxonomy. Attractive artwork accentuates concepts. Encyclopedic detail is non-encumbering in well organized and referenced tables. Chapter titles head the left page and chapter topics, the right page. This book renders the detail, complexity and wonder of retroviruses accessible. It will be read, appreciated and enjoyed by students, researchers and physicians. I found it hard to put down.

The first chapter is historical, and develops five paradigm changes in the conceptualization or experimental approach to retrovirology: (i) the discovery of cancer-causing viruses (ii) the development of focus assays (iii) the discovery of reverse transcriptase (iv) the host-cell origins of retroviral oncogenes, and (v) the isolation of disease-associated human retroviruses. The next six chapters on structure/function/life style are beautifully executed. The detail of crystallographic structures, available for three structural proteins (matrix, capsid and nucleocapsid) and the three enzymes of retroviruses (protease, reverse transcriptase and integrase) is complemented by the common yet diverse features of the current nine genera of retroviruses. The canonical organization of retroviral genomes (*gag-pol-env*), the positions of auxiliary genes (mostly between *pol* and *env* or after *env*), and the beehive of host cell factors regulating transcriptional ac-

tivity, are lucidly detailed. The emerging molecular and cellular biology for assembly of virions at the plasma membrane (C-type viruses), in the endoplasmic reticulum (A-type particles) or in the cytoplasm (B- and D-type viruses) and the active and passive incorporation of cellular proteins set the frontiers for future work. The power of proteins functioning as oligomers and the changing functions of Gag-pol and Env polyproteins, pre- and post-proteolytic processing, are laid out in the multiple contributions to the robustness of viruses that require but 10 kb of genetic information and a host for life. This is comprehensive, interesting reading.

The *intermezzo* begins with an overview of the lifestyles of simple versus complex retroviruses (those with auxiliary genes) and moves to the myriad interactions in which retroviruses depend on host cell functions to support their entry, multiplication and exit from cells. A discussion of replication, differentiation and the cell cycle highlights differences in the actively growing cultures used for research and the largely quiescent and post-mitotic cells that make up multicellular organisms. The ability of retroviruses to both activate and arrest the cell cycle is discussed. The *intermezzo* considers the mostly benign life-long infections established by typical retroviruses. Unlike highly infectious RNA viruses such as influenza or measles, for which pathogenesis aids transmission, the transmission of retroviruses is by healthy hosts. For HIV-1 in humans (a recently acquired infection) an intermediate scenario is seen: an inexorable progression to death yet sufficient time for transmission by seemingly healthy carriers. In the broader scheme, simple retroviruses tend to be transmitted early by congenital infection, with the virus being treated as "self" by the immune system—a phenomenon assisted by the presence of endogenous viruses. By contrast, complex retroviruses mainly transmit through immune-competent hosts with auxiliary genes functioning in part to sustain infection in the face of immune responses. The *intermezzo* ends with a look at insertional mutagenesis as an agent of genetic change, and the promise of retroviral vectors for therapeutic genetic change.

The closing chapters on viral host interactions address far more complex and less poorly understood issues than the opening chapters on structure/function. Outstanding among these is the chapter detailing eight different retroelements that reside in chromosomal DNA—elements that do and do not encode a reverse transcriptase; that do and do not require infection; and elements that reside in either chromosomal or mitochondrial DNA.

Chapter X, "Pathogenesis", sports a six page table listing and referencing host cell loci associated with cancer-causing insertional mutations. These include targets affecting transcription factors, growth factors, growth factor receptors, G

kinases, cyclins and tumor suppressors. Interestingly, we learn that the first identified target for insertional mutagenesis, *c-myc*, also may be the most permissive—cancer-inducing insertions in *c-myc* are associated with 12 different retroelements. The chapter on the pathogenesis of SIV and HIV competently orchestrates etiology, epidemiology, clinical latency, viral load, immunopathogenesis, opportunistic infections and AIDS-associated cancers. The final chapter, "Immunological and Pharmacological Approaches to the Control of Infections", was the one chapter I found disappointing. Perhaps virologists should not attempt an overview of immunology (sure "danger"). Also the longest listing of phenomena without summarizing Figures or Tables are in this chapter.

RETROVIRUSES is the third in a series of books on RNA tumor viruses from the Cold Spring Harbor Press. The first, published in 1973, was edited by John Tooze. This classic volume, which I still use, addressed both RNA and DNA tumor viruses. By 1982, when the next volume appeared (with a supplement in 1984), RNA tumor viruses were considered separately from DNA tumor viruses. At that time, retroviruses were discovery engines for the emerging genetics of cancer. Now sixteen years later, retrovirologists are responding to the need to control a major human epidemic, HIV-1 induced AIDS. Hopefully, the next volume will be graced with the erudition and elegance of this edition as well as a requiem for AIDS.

