

Preface

For many years the pathogenic and functional properties of retroviruses have been the focus of intense dedicated research. The developments and advances in the field have not only attracted the attention of other virologists but have also significantly enriched our knowledge and the scope of molecular biology, oncology, gene delivery, vaccinology, immunology and evolutionary biology. The discovery of a transmissible agent causing sarcomas in domestic birds by Peyton Rous in 1911 led researchers in the ensuing decades to focus on the oncogenic effects of avian, murine and human retroviruses. However, research efforts shifted dramatically and were strongly intensified with the discovery of a new retrovirus in the early 1980s. The human immunodeficiency virus (HIV), the causative agent of acquired immunodeficiency syndrome (AIDS), slowly erodes the human immune system and without treatment almost inevitably results in death by opportunistic infections or rare forms of tumors. The accumulated knowledge of retroviruses has facilitated the development of effective antiretroviral drugs and therapeutic intervention strategies within a relatively short period of time. Indeed, the first drugs to be licensed in the late 1980s targeted HIV's reverse transcriptase, a fundamental enzyme from which retroviruses get their name, which transcribes the viral genomic RNA into DNA to allow integration into the chromosomal DNA of the host cell.

— Retroviruses share a common ancestry with a wide variety of retroelements, a superfamily of more or less mobile genetic sequences

that transpose via an RNA intermediate and include retrotransposons and related reverse transcriptase-utilizing entities (see chapter 1 for details). The genetic material of vertebrates is surprisingly rich in retroelements, comprising for example about 42% of the human genome, 8% of which consists of sequences from ancient retroviruses. These so-called endogenous retroviruses are fossils of inherited germ line infections that resulted in vertical transmission from parents to offspring.

Infectious retroviruses are distinct from these retroelements in that their amplification is not confined to those cells already harbouring the integrated proviral element but extends to neighbouring cells and other individuals. The origin of vertebrate retroviruses is yet to be systematically investigated, but due to their similarity in genomic structure and sequences, it is likely that they evolved from Ty3/Gypsy LTR retroelements (see chapter 1 for details). This group of retrotransposons and retrovirus-related elements still exists in plants, fungi and invertebrates.

Retroelements themselves appear to be very ancient and might even have played a role during the switch from the RNA into the DNA world. Retroviruses code for proteins and protein domains that are often homologous to those of eukaryotic cells, some plant and animal DNA viruses and even fungal mitochondria. Although it is well known that retroviruses pick up genetic material from their host cells, the historical origins of retroviruses can nevertheless be traced back to events coincident with the prokaryotic

invasion of primitive eukaryotes. In this regard, endogenous retroviruses represent a rich archive of former retroviral infections. The ongoing sequencing of entire species genomes and the use of sophisticated bioinformatic approaches to recognize and compare retroviral sequences will be instrumental in constructing an overall phylogeny that chronicles major aspects of the history and relationships of retroviruses.

Although a comprehensive and rational taxonomy that includes both endogenous and exogenous retroviruses is presently not available, endogenous and exogenous retroviruses of all vertebrates can be grouped into three major classes designated I, II and III based on aspects of homology. This classification is complementary to the latest International Committee on Taxonomy of Viruses (ICTV) grouping of exogenous retroviruses, as class I comprises the genera gamma- and epsilonretroviruses; class II includes lentiviruses, alpha- and betaretroviruses; and class III contains spumaviruses. The taxonomic family *Retroviridae* is presently divided into two subfamilies: orthoretrovirinae and spumavirinae. The spumaretrovirinae contain the genus spumavirus, whereas the orthoretrovirinae comprises the other six genera (Fig. 1).

Although several chapters of the book focus on a single or a limited number of retroviral genera, taxonomy alone is not the basis for the overall structure of this book that consists of 16 chapters. The book begins with chapters reviewing

retroelements, endogenous retroviruses and the basic features of retroviruses. Important characteristics of the life cycle of exogenous retroviruses are covered next, followed by aspects of transmission, epidemiology, pathogenesis, host restriction factors and vaccination strategies. Selected retrovirus genera including gammaretroviruses and lentiviruses and their use as gene delivery tools are then discussed. In the final two chapters the focus shifts to simian and human (HTLV and HIV) retroviruses with a discussion of their medical implications.

The book has been written by scientists internationally recognized to be authorities in their fields of research. They provide comprehensive and focused overviews of their respective topics, emphasizing recent advances and future research directions while keeping the content as coherent and plain as possible.

The editors have taken care that this book would not become a compilation of separate chapters but, instead, would offer a broad and consistent overview of the present knowledge of the molecular biology, genomics and pathogenesis of retroviruses. However, each chapter can easily be read and understood independently of the others although this intention inevitably necessitated some degree of redundancy for the sake of clarity. The structure of each chapter is consistent, each having an abstract to explain the concept of the chapter, a conclusion reiterating the most important points, a number of illustrations and tables,

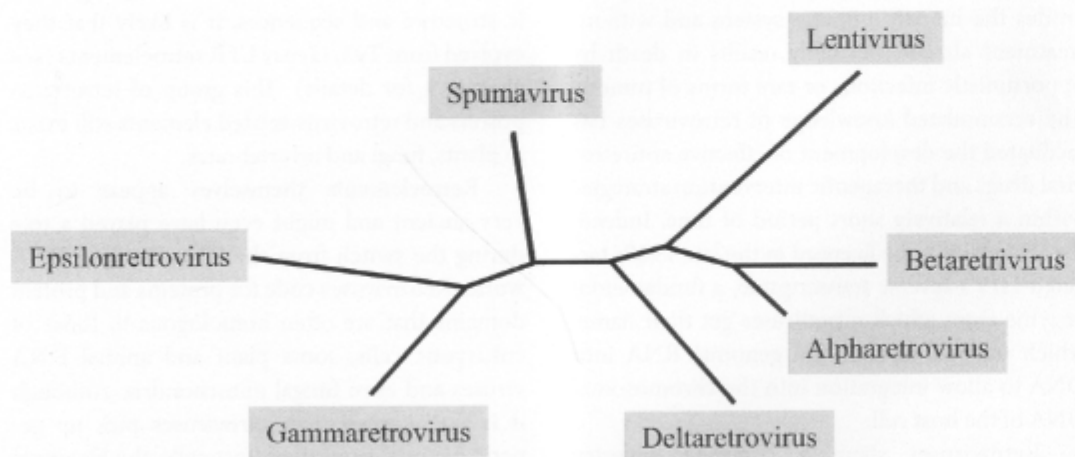


Figure 1 Schematic presentation of the phylogenetic relationships of the *Retroviridae* based on conserved sequences in the polymerase gene.

and finally a selected list of references for further reading. However, despite the extensive bibliography we almost certainly missed a number of publications that other colleagues may consider to be essential and we apologize in advance for such oversights.

We are convinced that this book will help introduce interested students, clinicians, veterinary scientists and virologists to the field and will serve

professional retrovirologists as a source of valuable supplementary information and overview.

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