



Animal viruses: molecular biology

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In 1796, Edward Jenner developed what became a widely adopted vaccine against smallpox. This was followed by vaccination against other viral diseases—including the successful post-exposure rabies vaccine designed by Louis Pasteur in 1886. Nonetheless, the nature of viruses remained unclear to those researchers and to their colleagues. In 1898, Friedrich Loeffler and Paul Frosch reported their results on the filterability and replicative capacity of the infectious agent responsible for foot-and-mouth disease (FMD) in cattle. That same year, Martinus Willem Beijerinck published his finding that tobacco mosaic disease was caused by something smaller than a bacterium, but which was also a “filterable agent which grew in the host, and was thus not a mere toxin” (the article was indeed written in German, but the title explained the new concept with three words in Latin: *contagium vivum fluidum*). These pioneering studies laid the foundation for the new scientific discipline of virology.

Virology studies biological viruses and virus-like agents: their structure, classification and evolution, the ways in which they infect and exploit cells for reproduction, the diseases they cause, the techniques to isolate and culture them, and their potential uses in research and therapy. There are many ways in which viruses can be classified, one of them being according to the host cell they infect. In fact, an infectious agent of veterinary importance (FMD) led to the development of the specialized field of “animal virology,” which includes viruses that infect humans.

In *Animal Viruses: Molecular Biology*, the book’s editors, Thomas C. Mettenleiter and Francisco Sobrino, have entrusted an international panel of leading virologists with providing a state-of-the-art overview of the field of animal virology. The book’s focus on “veterinary” viruses serves to highlight how this group of infectious agents has contributed to our current understanding of the molecular basis of viral

infections, especially those that have had a transcending impact on our understanding of viruses as a whole and of their mechanisms of action.

The study of animal viruses is obviously important from a veterinary viewpoint since the diseases they cause are often economically devastating. But one of the main motivations for their study is that many of these viruses are also important from a human medical perspective, being responsible for infectious diseases, such as the common cold, many forms of diarrhea, hepatitis, and AIDS, and contributing to certain forms of cancer. The emergence of zoonotic diseases provides additional compelling evidence. According to Julie Gerberding, director general of the US Centers for Disease Control and Prevention (CDC; in Atlanta, Georgia), “eleven out of twelve emerging human infectious diseases in the world have arisen from animal sources.”

Overall, working with animal viruses has one important advantage over the study of viruses that only infect humans: natural virus-host systems are experimentally accessible, and multiple animal models are available to analyze infections *in vivo*. Advances in this field have helped us in understanding how viruses cause disease and have revealed the molecular basis of many types of viral infections by elucidating pathways that may be used by related viruses, including those that are pathogenic to humans. This information has provided the basis for developing prevention and intervention strategies.

Animal Viruses: Molecular Biology consists of ten review articles that offer a detailed discussion of key virus groups and their impact on the veterinary environment. The field of animal virology has benefited greatly from the methodological and conceptual advances that have emerged in several related disciplines during the past few decades. Thus, the authors have paid special attention to emphasize the role of these parallel developments in current research and to provide the reader with key references.

Chapter 1 discusses how the molecular biology of FMD has been relevant to our understanding of the viral infectious cycle, and includes an in-depth discussion of what is needed to control viral pathogenesis and disease spread. Chapter 2 deals with pestiviruses, which are responsible for diseases such as swine fever and bovine viral diarrhea, and which share many similarities at a molecular level with human hepatitis C virus. Chapter 3 is devoted to arteriviruses. No human pathogens have so far emerged from this family, but it contains important animal ones. Besides the uncertainty surrounding their “out-of-nowhere” origin, the nearly simultaneous appearance of two distantly related porcine respiratory and reproductive syndrome viruses (PRRSV) in North America and Europe continues to puzzle researchers. Chapter 4 focuses on coronavirus (CoV) replication and its

host interactions. The recent advent of the severe acute respiratory syndrome (SARS) brought worldwide attention to this viral group and highlighted the importance of animals harboring infectious agents that can be potentially transferred into human populations. At the same time, CoV-based vectors have emerged with high potential for vaccine development and, possibly, for use in gene therapy. Chapter 5 covers the Hendra and Nipah viruses, part of the diverse family of paramoxiviruses, which encompasses many important human pathogens and is considered to have one of the most extensive, but still largely unknown, natural reservoirs. The Hendra and Nipah viruses are highly virulent and contagious; they have been designated as biosafety level 4 and are the source of concern regarding their potential use as bioterrorism or biological warfare agents. Chapter 6 analyzes the avian influenza virus (AIV), its host range and the molecular mechanisms of its pathogenicity. It is well-known that certain strains of AIV are occasionally transmitted from their normal reservoir, thereby causing devastating outbreaks in domestic poultry and, in a few cases, fatal disease in humans. Chapter 7 is a molecular dissection of Bluetongue virus, responsible for serious disease in livestock (sheep, goat, cattle) and, both molecularly and structurally, one of the best understood viruses. Chapters 8 and 9 describe the molecular biology of porcine circoviruses—the smallest viruses to replicate autonomously in eukaryotic cells—and of animal herpesviruses, respectively. The latter are highly successful pathogens, infecting animals and humans. Moreover, they remain in their host for its lifetime, and are reactivated from the latent state at irregular intervals, which allows them to infect other hosts. The study of these viruses has led to a new concept in animal disease control: the use of blanket vaccination to reduce the circulation of an infectious agent. Finally,

Chapter 10 provides an overview of the African swine fever virus, which is responsible for hemorrhagic fever and is associated with high mortality in pigs.

Lethal viruses present a paradox: killing its host is obviously of no benefit to the virus, so how and why did it evolve to do so? In the book's epilogue, "Animal virology: a showcase of evolution," Esteban Domingo and Marian C. Horzineck discuss some of the considerations regarding the evolution and long-term survival of viruses as pathogens in animal populations. Since most viruses are relatively benign in their natural hosts, lethal viral diseases may arise from an "accidental" jump of the virus from a species in which it is benign to a new one that has not been previously exposed to it.

So far, despite all the available tools of modern molecular biology, it has not been possible to create effective vaccines against several of the viruses discussed. However, the more detailed our understanding of them, the higher the chances of success in the design of novel approaches towards stimulating protective immunity. Evolution is at the roots of the difficulties we encounter when trying to keep viruses at bay, but it may also unlock possibilities to design virus variants, which can be used to prevent infection and disease. Infections of animals by their authentic pathogens can provide us with detailed insight into viral invasion and its effects on host functions. A better understanding of the evolutionary mechanisms behind the viral response to host defenses should help in the design of preventive and therapeutic strategies.

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General Cell & Molecular Biology / Eukaryotic Viruses. Animal Viruses. An overview of eukaryotic viral infection is illustrated in Figure 10-1. For most animal viruses, the first step toward proliferation is attachment (or adsorption) to the surface of a host cell. This is mediated by specific proteins associated with the capsid or envelope, referred to as viral binding sites or viral attachment proteins. The attachment proteins interact with specific proteins or polysaccharides on the surface of the host cell. The proteins on the host cell are called receptors. The specificity of viral at