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Review

Ferret models of viral pathogenesis

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ABSTRACT

Emerging and well-known viral diseases remain one the most important global public health threats. A better understanding of their pathogenesis and mechanisms of transmission requires animal models that accurately reproduce these aspects of the disease. Here we review the role of ferrets as an animal model for the pathogenesis of different respiratory viruses with an emphasis on influenza and paramyxoviruses. We will describe the anatomic and physiologic characteristics that contribute to the natural susceptibility of ferrets to these viruses, and provide an overview of the approaches available to analyze their immune responses. Recent insights gained using this model will be highlighted, including the development of new prophylactic and therapeutic approaches. To provide decision criteria for the use of this animal model, its strengths and limitations will be discussed.

Contents

Ferrets as experimental animals

Domestic ferrets (*Mustela putorius furo*) are small carnivores belonging to the *Mustelidae* family. Their closest wild relatives are wild European ferrets (*M. putorius*), European polecats (*M. furo*) and the steppe polecat (*M. eversmannii*), and interbreeding among these species produces fertile offspring, illustrating the close relationship (Lewington, 2007). Due to their relatively small size and their similarity to humans with respect to aspects of their anatomy, physiology, and metabolism, they are increasingly considered an alternative to larger animal models such as dogs and non-human primates (Clingerman et al., 1991). Ferrets are available from different commercial breeders, some of which are even offering specific pathogen free (SPF) animals. Seronegative animals, while of particular interest for the infectious disease community, are difficult to maintain due to the natural susceptibility of ferrets for human respiratory viruses. Breeders offer pre-testing of animals prior to purchase and use HEPA-filtered transport cages to minimize risk of exposure during shipping, but the serostatus of all animals has to be verified after arrival. In addition, personal

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Fig. 1. Examples of different cage types for ferret housing. Longterm free-range housing in same sex groups. Environmental enrichment like hammocks, tubes, and additional levels for climbing are provided (A, B). During ongoing experiments the animals are housed in pairs in different cage types connected by tubes or openings in separating walls (C, D).

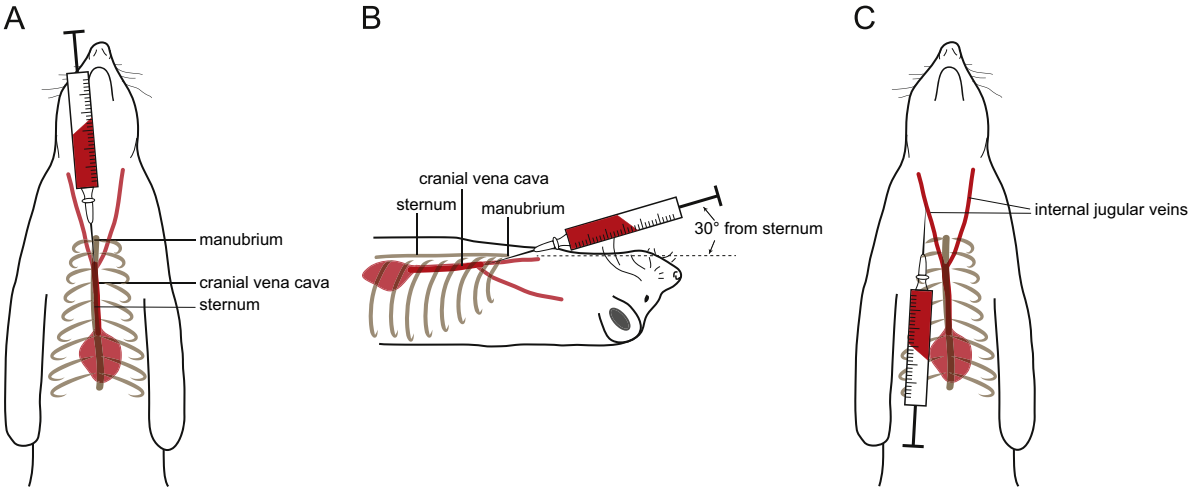

Fig. 2. Large volume blood collection sites. The anterior vena cava (A, B) and the internal jugular vein (C) allow collection of larger blood volumes.

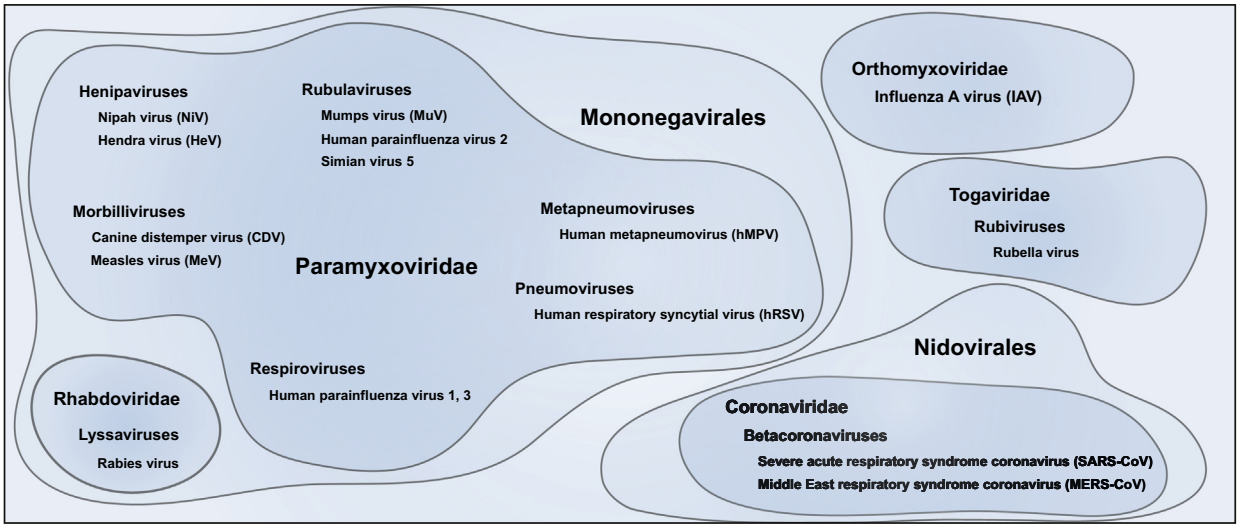

Fig. 3. Viruses investigated in ferrets. Viruses from different families discussed in this review that have been studied in ferrets.