

Survey on Biological Adenoviruses Utilising Rat Model

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Introduction

Numerous aspects of human diseases and disorders are studied using various animal models. They are also crucial for the preclinical testing of drugs and vaccines. Human adenovirus infections are typically self-limiting and can result in minor respiratory symptoms with fever, eye infections, or gastrointestinal symptoms. However, there have been a few instances of localised outbreaks with severe disease courses that have been documented [1]. Adenovirus infections also pose a serious risk to kids and people with compromised immune systems. Beginning in the 1950s, studies of human adenovirus-induced disease and tumour development were conducted using animal models. Since then, a number of animal species have been examined for their vulnerability to human adenovirus infection, and some have been found to mimic important aspects of the human infection, including persistent infection. Additionally, a few rodent species particularly in immunocompromised people, human adenovirus (HAdV) infections can result in a wide range of clinical symptoms, from mild upper respiratory tract illness to fatal outcomes. There are currently no effective treatments for HAdV infections, neither approved antiadenoviral drugs nor widely accessible vaccines. Therefore, there is a need for standardizable in vitro systems and animal models that are appropriate for the development of HAdV therapeutics and/or vaccines, preclinical evaluation of those therapeutics and/or vaccines, and a thorough understanding of HAdV-induced disease.

Rodents like Syrian hamsters, mice, cotton rats, and rabbits are currently used as HAdV pathogenesis, persistence, and tumorigenesis animal models. Additionally, a few recent studies on different species, like pigs and tree shrews, provided encouraging results. These simulations replicate (some of the) pathological effects of HAdV. The use of animal models in basic and applied research is crucial for the expansion and validation of in vitro results as well as the physiological study of diseases and treatments. They made fundamental contributions to the study of the pathogenesis of infectious diseases and are crucial for determining the mechanisms of action and therapeutic efficacies of anti-infectives and preventative measures. An ideal animal model replicates the key phenotypic, pathophysiological, and histopathological features of a specific disease or condition in a non-human organism, as well as the response to treatment. Our understanding of the progression of viral infections, including disease, associated pathology, persistence, and viral transformation in human adenovirus (HAdV) infections, has greatly improved thanks to animal models. Additionally, data are necessary for the preclinical evaluation of anti-adenoviral therapies, adenovirus-based therapeutics, and vaccines. As is currently the case with COVID-19 vaccines, from studies in pertinent in vivo settings [2].

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Description

In addition to COVID-19, various HAdV types and simian adenoviruses can be used as effective vaccine vectors to combat zoonotic diseases like AIDS, malaria, and Ebola. There has been a thorough review of in vivo research on adenoviral vectors in general and their application to gene and vaccine therapy in particular. The same holds true for oncolytic adenoviruses in animal models, which are not included in this work but have recently been reviewed by others. This review summarises the current understanding of the HAdV susceptibility of various animal models, highlighting salient characteristics, advantages, and disadvantages. The majority of the studies we focused on describe adenovirus pathogenesis and adenovirus-induced cell transformation. In the virus family Adenoviridae, the genus Mastadenovirus contains HAdVs. Based on viral sequences and serological information, they are divided into various species and subsequently classified into more than 100 different types. Human HAdV infections are widespread and have high seroprevalences. The genome sizes of these non-enveloped, double-stranded DNA viruses range from 24 to 48 kb, depending on the type [3]. There are currently neither widely accessible vaccines nor approved specific antiadenoviral compounds available to prevent and treat HAdV infections.

Clinical symptoms in infected individuals vary. Immunocompetent people experience relatively mild symptoms, whereas immunocompromised or paediatric patients can experience severe and occasionally fatal illness from infections. Additionally, various HAdV strains have unique tissue tropisms and can cause infections of the respiratory, gastrointestinal, and urinary tracts. As the eyes, it has been said. The tissue tropism largely correlates with clinical symptoms in humans, which can include gastroenteritis of various severity levels, conjunctivitis, and respiratory diseases. As thoroughly reviewed elsewhere, some types are also considered to be risk factors for obesity. Researchers have been looking for suitable animal models that phenocopy human HAdV infection for about 70 years in order to understand HAdV pathogenesis and infection-related consequences. Various rodents, including xenotransplanted and genetically modified transgenic mice and hamsters, pigs, non-human primates, and other species, were used as models. These models are all used to simulate various aspects of the human disease and to varying degrees enable HAdV replication and the induction of HAdV disease symptoms. However, a perfect model that replicates the illness in humans has not yet been developed. The 1950s and 1960s saw the earliest experimental HAdV infections on animals. All of these studies supported the findings of Rowe and colleagues, who found that experimentally, infected rabbits, mice, hamsters, Guinea pigs, cats, ferrets, rats, and even non-human primates did not exhibit any clinical disease symptoms. Another follow-up study revealed rabbits with persistent infection that had no symptoms. By re-isolating the virus from spleen homogenates, they discovered persistent HAdV-C5 in experimentally infected adult rabbits at 8 weeks post-inoculation. Later methods assessed the susceptibility of dogs and even pigs to various HAdV types using various infectious doses, as well as HAdV-induced tumours in rodents as described below, but none of these animals proved to be suitable for studying HAdV infection. Recent research by Radke and colleagues revealed that HAdV-B14 and a newly discovered variant, B14p1, cause severe lung pathogenesis in Syrian hamsters that is characterised by localised infiltrations of inflammatory cells that progress to bronchopneumonia. However, despite the fact that the authors did not mention any overt symptoms of the disease, these studies, along with those carried out in Syrian hamsters by Tollefson and colleagues, allowed for comparisons of the pathogenicity of various HAdVs and evaluation of corresponding immune responses.

The Syrian hamster model was first used by Toth and colleagues in.

These STAT2 knockout animals exhibit reduced interferon signalling, which, upon intravenous infection, promotes higher HAdV-C5 replication, more severe liver pathology, and increased mortality when compared to wild type Syrian hamsters, and thus resembles HAdV infection in immunocompromised individuals. Infected STAT2 knockout hamsters also displayed a dysregulated interferon immune response. Hamsters of both the wild type and those modified genetically have been found to be useful for studies on the effectiveness of HAdV therapeutics and vaccines as well as the development of vectors [4]. Small rodents called cotton rats are vulnerable to a number of human pathogens, particularly upper respiratory tract infections, to which mice and rats are typically more resistant. Using moderate HAdV-C5 titers to infect one-month-old animals, Pacini and colleagues published the first study using hispid cotton rats (*Sigmodon hispidus*) as a HAdV animal model in 1984. They found viral titers in the lungs and nasal mucosa and seroconversion as early as six days after infection. Lung samples from infected cotton rats were examined histopathologically, and the results showed transient peribronchial immune cell infiltration and other subtle pneumonial symptoms. Pacini and colleagues did not notice any clinical symptoms, but a follow-up study revealed that high HAdV-C5 doses resulted in more severe lung symptoms. Animals perished in the first week following infection [5].

Conclusion

The adenovirus-induced eye disease keratoconjunctivitis is also studied in cotton rats as an animal model (EKC). EKC is a highly contagious disease that frequently causes outbreaks and is characterised by eye inflammation and vision problems brought on by corneal opacities. Cotton rats that had been infected with ocular HAdV-C5 and D8 displayed symptoms similar to those of human disease, including virus replication and the emergence of the aforementioned sub epithelial corneal opacities. This HAdV-animal model

can become infected with HAdV and even exhibits EKC-like characteristics in humans. As a result, cotton rats have been employed in a number of methods to test therapeutic interventions and research oncolytic adenoviruses.

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Conflict of Interest

There is no conflict of interest by author.

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