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Diverse Models: Key To Understanding Viral Diseases

Ananya Bose*

Department of Neurovirology Research, Saffron Lake University, Chandipur, India

Introduction

The study of viral diseases has been significantly advanced by the development and application of diverse animal models that recapitulate aspects of human infections. These models are indispensable for dissecting complex pathogenic mechanisms, understanding viral tropism, elucidating immune responses, and evaluating the efficacy of therapeutic interventions [1]. Traditional rodent models have long served as a cornerstone in virology research, offering a balance of genetic tractability and physiological relevance for studying a wide range of viral agents [1]. However, the limitations of these models have driven the exploration of more sophisticated systems. Genetically engineered mouse models, in particular, have revolutionized the study of specific viruses like influenza, allowing for precise manipulation of host genes to mimic human disease and immune responses, thereby providing unprecedented insights into viral entry, replication, and host immune surveillance mechanisms [2]. For highly pathogenic viruses such as Ebola and Marburg, non-human primate (NHP) models remain invaluable due to their physiological and immunological similarities to humans, making them crucial for preclinical assessment of novel therapeutics and vaccines [3]. More recently, advancements in in vitro modeling have introduced organoids and 'organ-on-a-chip' systems. These microphysiological systems offer a more physiologically relevant environment for studying viral infection and host-pathogen interactions, potentially reducing reliance on animal testing while improving translational relevance, especially for respiratory viruses like SARS-CoV-2 [4]. In the realm of veterinary virology, specific animal models are critical for understanding economically significant diseases. For instance, newborn calf models have been employed to investigate the pathogenesis of Bovine Viral Diarrhea Virus (BVDV) and assess the efficacy of novel antiviral strategies [5]. The study of arboviruses, transmitted by vectors like mosquitoes, often relies on integrated models combining insect and animal systems. Mosquitoes themselves, along with various rodent models, are used to simulate human arbovirus infection, elucidating transmission dynamics and protective immunity, which is crucial for public health interventions against diseases like Dengue and Zika [6]. The persistent challenge of chronic viral infections, such as Hepatitis B Virus (HBV), necessitates animal models that accurately recapitulate long-term disease progression. Transgenic mice and humanized mouse models are being examined for their ability to mimic viral replication, liver inflammation, and fibrosis, key aspects for assessing therapeutic efficacy in preclinical drug evaluations [7]. The COVID-19 pandemic highlighted the urgent need for robust models for emerging viral respiratory diseases. Ferret and hamster models proved instrumental in understanding SARS-CoV-2 transmission, pathogenesis, and immune response, facilitating rapid development and testing of vaccines and antiviral therapies [8]. Beyond conventional models, novel approaches are emerging. Zebrafish embryos and larvae are being utilized as a rapid and high-throughput platform for studying viral neurodevelopmental disorders, recapitulating aspects of viral pathogenesis and facilitating the screening of antiviral compounds [9]. Finally, for complex chronic infections like HIV, humanized mouse models, which involve engrafting human immune cells and tissues into immunodeficient mice, have become essential for studying viral replication, latency, immune reconstitution, and evaluating novel antiretroviral therapies and potential cures [10].

The landscape of viral disease research is continually shaped by the innovation and refinement of animal models. These models serve as critical bridges between in vitro findings and human clinical outcomes, providing essential data for understanding disease mechanisms and developing effective interventions. The comprehensive review of animal models for studying viral diseases underscores their broad utility, encompassing viral tropism, immune responses, and therapeutic interventions, while also acknowledging the importance of selecting appropriate models based on the specific viral agent and research questions [1]. Genetically engineered mouse models have been particularly transformative, offering precise genetic manipulation to study influenza virus pathogenesis and immunity. Knock-in, knock-out, and humanized mouse models have yielded unprecedented insights into viral entry, replication, and immune surveillance, proving vital for vaccine and antiviral drug development [2]. For highly virulent pathogens, non-human primate models, such as macaques and baboons, are indispensable due to their physiological parallels with humans. Their use in assessing the efficacy of countermeasures against filoviruses like Ebola and Marburg is well-established, alongside crucial considerations for animal welfare [3]. Advancements in biomimetic technologies have led to the development of organoids and 'organ-on-a-chip' systems, which offer more physiologically relevant in vitro environments. These microphysiological systems are proving valuable for studying viral infections, particularly respiratory viruses like SARS-CoV-2, and hold promise for reducing animal use while enhancing translational relevance [4]. In agricultural settings, understanding economically devastating viral diseases requires specific models. The newborn calf model has been instrumental in characterizing the pathogenesis of Bovine Viral Diarrhea Virus (BVDV) and evaluating novel antiviral treatments, providing essential data for disease control [5]. The study of arboviruses necessitates a multi-faceted approach, often employing both insect vector and animal models. Aedes aegypti mosquitoes and various rodent models are utilized to simulate human arbovirus infections, elucidating transmission dynamics and the development of protective immunity, which is vital for public health strategies against diseases like Dengue and Zika [6]. Chronic viral infections present unique challenges, and models that recapitulate long-term disease progression are essential. For Hepatitis B Virus (HBV), transgenic and humanized mouse models are being employed to mimic viral replication, liver inflammation, and fibrosis, enabling the preclinical evaluation of therapeutic agents [7]. The global response to the COVID-19 pandemic underscored the importance of rapidly deployable and relevant animal models. Ferret and hamster models played a pivotal role in understanding SARS-CoV-2 transmission, pathogenesis, and immune responses, accelerating the development and testing of vaccines and antiviral therapies [8]. Emerging model organisms are also contributing significantly to viral disease research. Zebrafish embryos and larvae offer a rapid and high-throughput platform for studying viral neurodevelopmental

disorders, allowing for the investigation of viral pathogenesis and the screening of antiviral compounds [9]. The complexity of human immunodeficiency virus (HIV) pathogenesis and the search for a cure have been significantly aided by humanized mouse models. These models, engrafted with human immune cells and tissues, enable the study of HIV replication, latency, and immune reconstitution, as well as the evaluation of novel antiretroviral therapies and strategies for potential cures [10].

Model Selection and Advancements in Viral Disease Research

Viral diseases continue to pose a significant threat to global health, necessitating the continuous development and refinement of research methodologies. The study of viral pathogenesis, immune responses, and the evaluation of therapeutic interventions are critically dependent on appropriate model systems. Animal models have historically played a pivotal role in advancing our understanding of viral infections, providing in vivo platforms to unravel complex biological processes that are difficult to fully replicate in vitro. A comprehensive review highlights the broad applicability of animal models in virology, emphasizing their importance in dissecting viral tropism, immune system interactions, and the efficacy of potential treatments [1]. The selection of a suitable animal model is paramount, as different viral agents and research questions necessitate tailored approaches, ranging from traditional rodent systems to more complex non-human primate models [1].

Genetically engineered mouse models have emerged as a powerful tool, particularly in the study of influenza virus. Through knock-in and knock-out strategies, as well as humanized mouse models, researchers have gained unprecedented insights into the intricate mechanisms of viral entry, replication, and host immune surveillance. These advanced models are indispensable for evaluating the effectiveness of vaccines and antiviral drugs against emergent and pandemic influenza strains [2]. For highly pathogenic viruses, such as Ebola and Marburg viruses, non-human primates (NHPs) remain the gold standard. Their physiological and immunological similarities to humans make them invaluable for preclinical studies, enabling the assessment of novel therapeutics and vaccines, while also necessitating careful consideration of ethical implications and animal welfare [3].

In recent years, there has been a significant push towards developing more human-relevant in vitro models. Organoids and 'organ-on-a-chip' systems represent a major advancement in this area. These microphysiological systems provide a more physiologically accurate environment for studying viral infections and host-pathogen interactions. They offer the potential to reduce reliance on animal testing and improve the translational relevance of research findings, particularly for respiratory viruses like SARS-CoV-2 [4]. Beyond human health applications, animal models are also crucial for understanding and managing viral diseases in livestock. The newborn calf model, for instance, has been employed to investigate the pathogenesis of Bovine Viral Diarrhea Virus (BVDV), a significant economic concern in cattle populations, and to assess the efficacy of novel antiviral strategies aimed at improving disease control measures [5].

The study of arboviruses, which are transmitted by insect vectors, often requires integrated approaches that combine both insect and animal models. Researchers utilize models such as Aedes aegypti mosquitoes and various rodent strains to simulate human arbovirus infections. This approach helps elucidate viral transmission dynamics, vector competence, and the development of protective immunity, which are critical for designing effective public health interventions against diseases like Dengue and Zika [6]. Chronic viral infections, such as Hepatitis B Virus (HBV), present unique challenges due to their long-term nature. To facilitate the preclinical evaluation of therapeutics, researchers are utilizing animal models that can accurately recapitulate chronic infection. Transgenic mice and humanized mouse models are being examined for their ability to mimic viral replication, liver inflammation, and fibrosis, key aspects for assessing drug efficacy [7].

The COVID-19 pandemic underscored the critical importance of rapid and relevant animal models for studying emerging viral respiratory diseases. Ferret and hamster models played a crucial role in understanding SARS-CoV-2 transmission, pathogenesis, and the host immune response. Their utility was instrumental in the accelerated development and testing of vaccines and antiviral therapies, providing vital data for shaping public health strategies [8]. Emerging model organisms are also contributing to the field. Zebrafish embryos and larvae are being explored as a rapid and high-throughput platform for studying viral infections, particularly in the context of neurodevelopmental disorders. This model allows for the recapitulation of viral pathogenesis, including neuronal effects, and facilitates the screening of antiviral compounds [9]. For complex chronic infections like HIV, humanized mouse models have become indispensable. These models, which involve engrafting human immune cells and tissues into immunodeficient mice, enable the study of HIV replication, viral latency, immune reconstitution, and the evaluation of novel antiretroviral therapies and potential cure strategies [10].

The continued innovation in animal and in vitro modeling is essential for addressing the persistent and emerging threats posed by viral diseases. Each model system offers unique advantages and limitations, underscoring the need for judicious selection and integration of these tools to advance our understanding and combat viral pathogens effectively.

Description

The fundamental role of animal models in unraveling the pathogenesis of viral diseases is widely acknowledged, encompassing their application in understanding viral tropism, immune responses, and therapeutic interventions. These models provide a crucial in vivo platform for research, and the choice of model is highly dependent on the specific viral agent and the research question at hand, ranging from traditional rodent systems to more complex non-human primate and ex vivo models [1].

Genetically engineered mouse models have significantly advanced the study of influenza virus pathogenesis and immunity. Through sophisticated genetic manipulation techniques such as knock-in and knock-out strategies, alongside the development of humanized mouse models, researchers have gained unprecedented insights into viral entry, replication, and host immune surveillance mechanisms. This progress is critical for evaluating vaccine efficacy and guiding the development of antiviral drugs against emerging and pandemic influenza strains [2].

For highly pathogenic viruses, particularly filoviruses like Ebola virus and Marburg virus, non-human primate (NHP) models remain indispensable. Macaques and baboons, due to their physiological similarities to humans, are utilized in preclinical studies to assess the efficacy of novel therapeutics and vaccines. This research also necessitates careful consideration of ethical aspects and the paramount importance of animal welfare [3].

Advancements in in vitro modeling have introduced organoids and 'organ-on-a-chip' systems, representing a significant step forward in viral disease research. These microphysiological systems offer a more physiologically relevant environment for studying viral infection and host-pathogen interactions. They hold promise for reducing the reliance on animal testing while improving the translational relevance of research findings, especially for respiratory viruses like SARS-CoV-2 [4].

In the context of veterinary medicine, understanding and controlling economically significant viral diseases is crucial. The newborn calf model has been employed to investigate the pathogenesis of Bovine Viral Diarrhea Virus (BVDV) and to assess the efficacy of novel antiviral strategies. This research provides valuable data for developing improved control measures against this economically impactful disease [5].

The study of arboviruses, such as Dengue and Zika viruses, often requires a combination of insect and animal models to fully elucidate transmission dynamics and pathogenesis. Aedes aegypti mosquitoes and various rodent models are used to simulate human arbovirus infection, helping to understand viral transmission, vector competence, and the development of protective immunity, which is vital for public health interventions [6].

Chronic viral infections, such as Hepatitis B Virus (HBV), pose long-term health challenges that necessitate animal models capable of recapitulating chronic disease states. Transgenic mice and humanized mouse models are being developed and utilized for preclinical drug evaluation, focusing on their ability to mimic viral replication, liver inflammation, and fibrosis, key aspects for assessing therapeutic efficacy [7].

The COVID-19 pandemic underscored the critical need for robust animal models to study emerging viral respiratory diseases. Ferret and hamster models have made significant contributions to understanding SARS-CoV-2 transmission, pathogenesis, and the immune response. These models were instrumental in the rapid development and testing of vaccines and antiviral therapies, providing crucial data for public health strategies [8].

Emerging model organisms are also offering new avenues for viral disease research. Zebrafish embryos and larvae are being utilized as a rapid and high-throughput platform for studying viral infections, particularly in the context of neurodevelopmental disorders. This model allows for the recapitulation of viral pathogenesis, including neuronal effects, and facilitates the screening of antiviral compounds [9].

For complex chronic infections like HIV, the development and application of humanized mouse models have been essential. These models, created by engrafting human immune cells and tissues into immunodeficient mice, allow for the study of HIV replication, viral latency, immune reconstitution, and the evaluation of novel antiretroviral therapies and potential cure strategies [10].

Conclusion

This collection of research highlights the critical role of diverse animal and in vitro models in understanding viral diseases. From traditional rodent and non-human primate models to advanced genetically engineered mice, organoids, and 'organ-on-a-chip' systems, these tools are essential for dissecting viral pathogenesis, immune responses, and evaluating therapeutics. Specific models are employed for viruses like influenza, Ebola, SARS-CoV-2, BVDV, arboviruses, HBV, and HIV. The ongoing development of these models, including zebrafish and humanized mice, continues to advance our ability to combat viral threats and improve public health strategies.

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Conflict of Interest

None.

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Address for Correspondence: Ananya, Bose, Department of Neurovirology Research, Saffron Lake University, Chandipur, India , E-mail: a.bose@saffronlake.edu

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