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Advancements in *In Vitro* Culturing of Human Norovirus over the Last 20 Years

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Introduction

Japanese Encephalitis Virus is a flavivirus primarily transmitted to humans through the bite of infected mosquitoes, particularly Culex species. It is the leading cause of viral encephalitis in Asia, with widespread occurrences in countries such as India, China, Thailand, and Vietnam. The virus exists as several genetically distinct strains, with Genotype 4 (G4) emerging as a dominant and highly pathogenic variant in recent years. While JEV primarily affects humans and horses, pigs play a central role in the transmission cycle of the virus, serving as amplifying hosts that allow mosquito vectors to feed on high viral loads. Experimental infections in pigs provide valuable insights into the mechanisms of JEV transmission, pathogenesis, immune responses, and the potential development of vaccines. This article reviews the significance of experimental studies involving JEV Genotype 4 infection in pigs, exploring the findings and their implications for human health and disease control. JEV is a mosquito-borne virus that belongs to the Flavivirus genus, and it is closely related to other important pathogens, such as West Nile Virus and Dengue Virus. The virus typically circulates in a zoonotic transmission cycle, with mosquitoes acting as vectors and pigs and birds acting as amplifying hosts. Infected pigs produce large amounts of viral particles in their blood and tissues, which can be consumed by mosquitoes, thereby maintaining the transmission cycle [1,2].

Description

As the field progressed, more sophisticated models were developed to more accurately replicate the human gastrointestinal tract. These models included human gastric and duodenal epithelial cell lines. For example, derived from primary human gastric cells, demonstrated some capacity to support norovirus infection and provided insights into the mechanisms of viral entry and replication in different regions of the GI tract. While these models were still limited in their ability to support high-level viral replication, they helped researchers identify factors, such as specific receptor molecules and host factors, required for viral entry and replication. Importantly, they enabled the study of differences in norovirus tropism, such as which types of gastrointestinal cells are most permissive to infection. A major breakthrough in the culture of human norovirus came with the development of human intestinal organoid models. These organoids are three-dimensional cultures derived from adult stem cells and replicate the architecture and function of human tissues much more accurately than traditional cell lines. These models provide a unique opportunity to study the viral lifecycle in a more physiologically relevant context [3-5].

Conclusion

In the past 20 years, there has been remarkable progress in the in vitro culture of human norovirus. From early attempts with B-cell lines to the development of sophisticated human intestinal organoid models, these advancements have significantly improved our ability to study norovirus pathogenesis, viral replication, and interactions with host cells. As a result, we now have a more accurate understanding of the virus's lifecycle, the receptors it uses to enter cells, and its relationship with the gut microbiome. Moreover, these developments have opened up new possibilities for drug and vaccine development, which are crucial for controlling norovirus infections and reducing their public health impact. While challenges remain, particularly in scaling up the replication of human norovirus in vitro, these advancements represent a crucial step forward in the fight against one of the world's most prevalent gastrointestinal pathogens. As research continues to evolve, the prospects for new therapies and vaccines against human norovirus are brighter than ever.

Acknowledgement

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Conflict of Interest

None.

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