Review of: "A Harmless Avian Vaccine Virus Could Be Developed into an Off-the-Shelf “Antibiotic” for Viruses"

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Potential competing interests: No potential competing interests to declare.

Introduction

The article by Holmes et al. delves into an intriguing approach to antiviral therapy: leveraging viral competition, specifically viral interference, as a means to combat viral infections. This paper outlines the theoretical and practical foundations of using the Infectious Bursal Disease Virus (IBDV) strain R903/78 as a broad-spectrum antiviral. Given the recent surge in zoonotic infections and global pandemic risks, this paper is timely and attempts to bridge the gap between traditional vaccination and innovative antiviral therapies. The authors argue convincingly that IBDV offers a promising tool for pandemic preparedness, particularly in an era marked by vaccine hesitancy.

Strengths of the Article

Novelty of Concept: The article champions a paradigm shift by introducing viral interference as a potential antiviral strategy. The idea of "fighting fire with fire," using non-pathogenic viruses to control more virulent strains, is both innovative and underexplored in current antiviral therapies. The authors effectively contextualize IBDV within this novel framework, emphasizing its unique ability to modulate host immunity without high inflammatory side effects.

Clear Argumentation and Relevance: The authors build a logical argument connecting the prevalence of zoonotic diseases and pandemic preparedness with the need for alternative antiviral approaches. By highlighting the limitations of traditional vaccinations, especially given current trends of vaccine skepticism, they position IBDV as a valuable complementary tool. Their discussion around zoonotic spillovers, particularly involving livestock, effectively underscores the urgency of developing additional therapeutic options.

Comprehensive Evidence Base: The paper references a broad array of studies, including historical and recent findings, to substantiate the potential of IBDV in controlling viral infections. The documentation of IBDV’s safety profile and efficacy across various viral infections, such as hepatitis and SARS-CoV-2, adds credibility to its potential as an antiviral candidate.

Focus on Practical Implications: The authors’ proposal for IBDV as a stockpiled antiviral drug for rapid deployment is particularly relevant to current health crisis management. Their vision aligns well with the need for scalable, rapidly deployable solutions in pandemic scenarios, making it a strong addition to the discourse on public health preparedness.

Opportunities for Improvement

Lack of Clinical Trial Data: While the paper presents promising evidence from studies on animals and a small number of patients, the transition from preclinical to large-scale clinical trials is critical. Expanding on any ongoing or planned clinical trials for IBDV in humans, including specific timelines and expected challenges, would strengthen the argument for its feasibility as a human antiviral therapy.

Potential Risks of Viral Interference: While the authors extol the benefits of IBDV, they do not fully explore the risks associated with viral interference, particularly if the therapy were to misfire or trigger unexpected immune responses. A more balanced discussion of risks, including the potential for autoimmune reactions or unintended interactions with existing viral infections, would provide a more comprehensive view of the therapy's limitations.

Regulatory Challenges: The paper briefly touches on regulatory concerns, such as the risk of zoonosis from attenuated avian viruses, but lacks a thorough examination of the regulatory landscape. Regulatory hurdles are likely to be a major bottleneck for IBDV, and the authors could enhance their argument by proposing specific strategies to navigate these challenges, such as collaborations with regulatory bodies or case studies of similar therapies.

Economic and Logistical Considerations: The authors advocate for IBDV as a stockpiled treatment but offer limited details on the financial and logistical aspects of its development, production, and distribution. A more detailed analysis of the costs, potential funding sources, and logistical challenges of producing and stockpiling IBDV at a global scale would strengthen the practicality of the proposal.

Limited Mechanistic Insight: Although the article explains the immune-modulating mechanism of IBDV through Toll-like receptor activation, it lacks a deeper mechanistic exploration, particularly around the virus's interaction with specific immune cells. More detailed information about how IBDV selectively induces IFN-β and IFN-λ, while sparing IFN-γ, could offer valuable insights into its unique immune modulation properties.

Conclusion

Holmes et al. present a compelling case for IBDV as a broad-spectrum antiviral candidate, filling a gap in pandemic preparedness by addressing the limitations of vaccination alone. Their advocacy for viral interference is both innovative and grounded in empirical evidence, though future iterations of this work would benefit from a more balanced discussion of risks, regulatory challenges, and logistical considerations. Overall, this paper is a significant contribution to antiviral research and opens new avenues for investigating viral competition as a viable therapeutic strategy.