

Peer Review

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

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The commentary explores the potential use of the infectious bursal disease virus (IBDV) strain R903/78 as a broad-spectrum antiviral therapy to complement existing vaccines in the control of viral infections.

Strengths

1. The concept of repurposing a non-pathogenic virus like IBDV for viral control is innovative and promising. This approach challenges conventional antiviral treatments, offering an alternative strategy in the fight against viral infections.
2. The commentary does a commendable job of explaining the mechanism of action of IBDV, particularly how it triggers interferon responses and activates innate immunity through Toll-like receptors (TLRs). The authors successfully describe the safety profile of IBDV in mammalian systems and its lack of lytic effects, which enhances its therapeutic potential.
3. The commentary addresses urgent global concerns regarding zoonotic diseases, influenza pandemics, and the limitations of current vaccine strategies. The link to the One Health approach, which connects human, animal, and environmental health, is an important contribution, underscoring the growing need for innovative antiviral strategies.
4. The article appropriately references previous studies that support the notion of using live attenuated vaccines for non-specific protection against unrelated infections, including the historical evidence from poliovirus and herpes simplex virus. This strengthens the overall argument for exploring IBDV in antiviral therapy.

Suggestions

1. While the authors present a compelling idea, the argument could be more tightly structured. The potential benefits of IBDV therapy (broad-spectrum antiviral action, safety, and ease of use) should be clearly distinguished from the limitations and challenges of implementation. In particular, more discussion on the potential risks of using IBDV, even in attenuated forms, would provide a more balanced view.
2. The article references a number of studies that show IBDV's potential in treating viral infections like hepatitis and herpes zoster, but the data provided is somewhat scattered. A more in-depth discussion of the specific outcomes of these studies, including quantitative results (e.g., reduction in viral load, clinical improvements, adverse events), would significantly strengthen the case for IBDV as a therapeutic candidate. Additionally, more recent or ongoing clinical trial data could be included to provide a clearer picture of its current status.
3. The authors mention the use of reverse genetics to generate the R903/78 strain, but the commentary would benefit from a more detailed explanation of the methods used to evaluate the safety and efficacy of this virus in humans. For example, a clearer description of the Phase I/II trials with herpes zoster patients, including endpoints and duration of follow-up, would help contextualize the potential impact of this therapy.
4. The authors mention the idea of combining IBDV with other treatments (e.g., acyclovir for herpes zoster), which is a valuable point. However, more discussion on the potential for IBDV to be used in combination with other antiviral strategies, particularly for emerging RNA viruses like SARS-CoV-2 or future influenza strains, would provide more depth. The authors could elaborate on possible synergistic effects, potential dosing schedules, and how such combination therapies could be integrated into existing clinical practices.
5. The article rightly points out that vaccine hesitancy may limit the effectiveness of future pandemic responses. While the use of IBDV as an alternative is presented as a solution, further evidence or examples of how such an antiviral could be distributed or administered effectively in a global context would be valuable. The commentary could expand on the practicality of using IBDV in resource-limited settings or in populations with high vaccine hesitancy.

This commentary offers a novel perspective on utilizing non-pathogenic viruses as therapeutic agents for controlling viral infections. It provides an intriguing case for the development of IBDV as a stockpiled antiviral drug for pandemic preparedness. However, to strengthen the argument, the authors could clarify certain aspects of their proposal, particularly in terms of safety, efficacy, and the

regulatory pathway. Additionally, providing more concrete data and addressing potential risks and limitations would enhance the impact of the paper. The overall tone is constructive, and the work presents a clear, well-supported hypothesis that has the potential to contribute meaningfully to the fields of virology, immunology, and public health.

Declarations

Potential competing interests: No potential competing interests to declare.