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Peer Review

Review of: "Sting Pathway Activation by Orally Administered Attenuated dsRNA Vaccine Virus for Therapy of Viral Diseases"

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This review proposes an innovative and translationally ambitious concept: leveraging orally administered attenuated IBDV as a STING-activating, broad-spectrum antiviral immunotherapy that complements vaccination strategies. The manuscript effectively integrates virome biology, innate immune sensing (RIG-I/MDA5 and cGAS–STING pathways), interferon induction profiles, and a structured clinical development roadmap, which strengthens its strategic appeal. The discussion of manufacturing feasibility and affordability is also a practical advantage. However, the article would benefit from a clearer separation between hypothesis, preclinical findings, early-phase clinical observations, and robust randomized evidence. Claims of clinical efficacy across multiple viral families should be supported by concise quantitative summaries (patient numbers, trial design, endpoints, statistical significance). The autobiographical herpes zoster case, while illustrative, should be reframed as anecdotal and not mechanistic proof. Greater critical discussion of potential risks—such as chronic innate immune activation, interferon-mediated toxicity, immune dysregulation, viral persistence, and regulatory biosafety concerns—is necessary for balance. Additionally, a comparative analysis of IBDV versus synthetic STING agonists, TLR agonists, interferon therapies, and other innate immune modulators would strengthen scientific neutrality. Overall, the manuscript presents a compelling and bold therapeutic paradigm, but a more data-driven, less promotional tone and expanded safety/regulatory analysis would substantially improve its credibility and acceptance in high-impact immunology or virology journals.

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Declarations

Potential competing interests: No potential competing interests to declare.