

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

Rupal Ojha¹

1 Washington University, Saint Louis, United States

Potential competing interests: No potential competing interests to declare.

This is a nice piece of work by Holmes et al., addressing a significant need in pandemic preparedness, particularly considering vaccine hesitancy and the increasing threat of zoonotic diseases. However, there are several key areas where additional clarification and detail could strengthen it. Specifically, the authors could enhance the discussion by addressing 1. the mechanism of action of R903/78, such as how it acts against the viruses. This would be crucial to understand why it might be effective as an antiviral treatment in both herpes zoster and potentially against other viruses like COVID-19/influenza. 2. Detailing about the reverse engineering is not clearly mentioned. How this makes the virus safe or enhances its efficacy. 3. Also, the number of ongoing clinical trials and their outcomes is lacking. 4. Shed some more light on the proposed combination therapies. The authors mention that combining R903/78 with other drugs like acyclovir for herpes zoster and with immunotherapy drugs (ipilimumab plus nivolumab) for hepatitis B. Explain the theoretical basis or evidence behind these combinations.

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