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Peer Review

Review of: "Can a Mosquito-Borne Virus Become a Cancer Therapy? Rethinking Getah Virus Through the Lens of Oncolytic Virotherapy"

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This article summarizes the biology of the arbovirus Getah virus (GetV), focusing on its roles as 1) a veterinary pathogen, and 2) a potential oncolytic virus for cancer therapy. The article is succinct and shows that different strains of the virus exhibit distinct biological features; whereas MM2021 has features consistent with an environmental mosquito-borne pathogen, M1 has a clear selectivity for tumor cells.

The article could be improved by adding a few details.

1. Although the authors mention GetV as a veterinary pathogen, it would be helpful to add a few sentences describing natural infection with GetV for those not familiar. What is the impact of GetV infection on livestock and/or wild vertebrate populations? Is it frequently lethal in animals?
2. The authors suggest that M1 has a tropism for tumor cells. Does M1 infect all tumor cells tested or only a portion? Which types of cancer have been tested? How effective has M1 been in xenograft models?
3. In Figure 2, the text suggests that M1 preferentially infects tumor cells due to defective interferon signaling and ZAP deficiency. However, the image shows an arrow from ZAP to a lysed tumor cell, suggesting that ZAP is playing an active role. It might be helpful to show in healthy cells how interferon signaling and ZAP control M1 infection in order to highlight how their loss leads to permissiveness in tumor cells.
4. Figure 3 shows several features of both strains of GetV that are not really developed in the text (MM2021: vaccine development; M1: immune activation and combination therapy). If there are data

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developed regarding these, those data would be worth discussing. If not, it is probably best to clarify in the figure that these are possible areas of future investigation.

Declarations

Potential competing interests: Institutional research support from Alkermes, Bristol-Myers Squibb, Genentech, Merck, nFerence, Perspective Therapeutics, Pharmacyclics, Regeneron, Sorrento, TILT Biotherapeutics, and Transgene. None are closely related to the work under review.