Reviewer's report

**Title:** Viral-mediated oncolysis is the most critical factor in the late-phase of the tumor regression process upon vaccinia virus infection

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**Reviewer:** ASFAR AZMI

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The article entitled “Viral-mediated oncolysis is the most critical factor in the late-phase of the tumor regression process upon vaccinia virus infection” by Weibel et al., identifies the contribution of factors such as tumor cell specific oncolysis, destruction of the tumor vasculature or an anti-tumoral immunological response in tumor cell elimination through colonization with an attenuated vaccinia virus (VACV) in breast tumors. The authors intelligently utilize immunohistochemistry and mouse-specific expression arrays in breast xenograft model and study 6 week regression phase post VACV infection. The key findings include (a) extensive necrosis in VACV infected tumors, (b) No affect of tumor vasculature function, (c) hyper permeability and dilatation of the tumor vessels, (d) intense infiltration of MHCII-positive cells and (e) co localization of tumor vessels with MHCII+/CD31+ vascular leukocytes. Based on the above findings the authors conclude that oncolysis is the primary mechanism for tumor suppression by VACV. These studies provide strong evidence that viral based therapies are effective in breast cancer; however, they have to be optimized by enhancement of viral replication within the tumor.

The authors of this study have previously studied the role of viral colonization in human breast tumor xenografts (that leads to tumor shrinkage) and this is a logical extension of that study. While this article is a comprehensive analysis of viral oncolysis in appropriate model system, a few minor points need to be addressed would improve this manuscript prior to its acceptance and are given below:

1. Most of the studies presented in this paper utilize immunostaining procedures to verify expression patterns and localization of markers of interest. However, there is no western blot analysis supporting the data. It would benefit the article immensely if some western blot analysis is provided to show the expression of necrotic markers is presented supporting Fig 1.

2. The discussion in this article is a bit redundant, too long and can be truncated.

3. The reported statistical analysis is too vague to support the microarray analysis and should be elaborated further.

4. Minor typos should be corrected
**Level of interest:** An exceptional article

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

'I declare that I have no competing interests'