Reviewer's report

Title: Integrated microarray and multiplex cytokine analyses of Kaposi's Sarcoma Associated Herpesvirus viral FLICE Inhibitory Protein K13 affected genes and cytokines in human blood vascular endothelial cells

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Reviewer: S.-J. Gao

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In this study, Punj and colleagues present comprehensive data on KSHV vFLIP regulation of cytokines in endothelial cells using microarray, Luminex and PCR assays. Similar results have also been reported by other groups on vFLIP and KSHV in various types of endothelial cells including HUVEC used in this study. The results presented here have confirmed previous findings and offered some any additional new insights into the functions of vFLIP, and pathogenesis of KSHV-induced malignancies. A number of other issues should also be addressed, which are listed below:

1. A number of published studies have examined vFLIP and/or KSHV regulation of cellular gene expression in endothelial cells with some exclusively focusing on cytokines. The authors should compare their results with these studies, particularly for those that are different from their observations. To the minimum, these highly relevant published papers should be cited.

2. The authors state that the vFLIP HUVEC cannot be permanently maintained. How long were these cells infected. The expression of vFLIP was only induced for 48 h. Could the cells be still in transient state rather than static state as should be expected for latent KSHV-infected cells?

3. No information on the KSHV-infected cells was provided. How long they were infected? What was the latent vs lytic status of the virus? This is very information that should be included since a number of viral lytic genes also regulate cellular cytokines.

4. The failure to observe lymphatic conversion is interesting. Some commercial endothelial cells are not pure, which had confounded some of the previous KSHV studies. Have the authors tested the purity of their cells? Contamination with mixed cells could pose problem for this type of study. Were the authors able to observe lymphatic conversion in KSHV-infected cells as reported by others? These data can serve as positive controls for their experiments.

5. vFLIP regulation of SOD2 has recently been reported (J Virol. 2009 Jan;83(2):598-611). The author should discuss and cite the paper.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.