Reviewer’s report

Title: Expression of RNA interference triggers from an oncolytic herpes simplex virus results in specific silencing in tumour cells in vitro and tumours in vivo.

Version: 1 Date: 15 February 2010

Reviewer: John C Bell

Reviewer’s report:

This is an interesting study that shows for the first time the ability to program an oncolytic vector so that it can express an RNAi molecule to manipulate the infected cell and facilitate productive virus infection. In principle I like the study but I think it could be improved with some modifications.

(1) Page 7….xenograph should be xenograft

(2) The authors argue that this strategy could be used to enhance the replication of an OV in target cells. What sort of targets are they contemplating? How would this type of genetic manipulation maintain tumour specific replication? For instance if the vector was engineered to dampen the anti-viral response would the resultant virus have enhanced virulence? This should be discussed.

(3) I like the idea that the vector could be programmed to down regulate factors secreted normally by tumours to dampen anti-tumour immune responses. Can the authors expand on this concept?

(4) Figure 2C is not very compelling,…it is not clear from the manuscript nor the figures, the extent of virus infection in vivo. The B-gal assays suggest that the RNAi treatment reduces enzyme expression by about 20% and thus perhaps it is not surprising that the western blots are unconvincing. Was any quantitation of the WBs attempted? The authors should section infected tumors and show that the virus expression co-localizes with decreased B gal activity or expression.

(5) Figure 2B is confusing to me. The higher the MOI the less efficient the silencing. The authors argue that higher MOI means more cytotoxicity and therefore the effect on B gal expression is less obvious. However they also argue that this cell line is somewhat refractory to virus infection and thus one would expect that increased MOI should lead to more silencing. At an MOI of 1 at the time of the assay would all cells be infected…figure 2A suggests not. This same experiment should have been done at an MOI of 5. What is the viability of the cell culture at the two MOIs. Does the higher MOI lead to more cell death at the time of the assay?

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.

Declaration of competing interests:
I declare that I have no competing interests