Reviewer’s report

Title: Retroviral expression of a kinase-defective IGF-I receptor suppresses growth and causes apoptosis of U87 PTEN-negative glioblastoma cells in-vivo.

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Reviewer: Dr Shern Chew

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after discretionary revisions

The manuscript presents interesting data showing that inhibition of IGF-IR signalling can reverse growth of a PTEN-deficient cell line (U87). The IGF-IR MK mutant functions in a dominant negative fashion to also suppress growth of CHO cells and inhibits IGF-IR and IRS phosphorylation in both cell lines. The data are substantial, convincing and the manuscript and figures are of high quality.

Discretionary revisions
1. It should be noted that it has not been shown in this work that suppression of proximal IGF-IR signalling has an effect on PIP3 levels. Thus, the distal pathway(s) for the action of IGF-IR MK are not yet known and are presumably the subject of the next body of work. I suggest revision of a sentence on p9, para 3, lines 2-4 to determine whether interruption of an upstream signal to stimulate PI-3 kinase would have the same effect as the effect on PI3 kinase by the IGF-IR MK has not been shown.

Compulsory revisions
These are all minor:
1. A reference should be supplied for the anti-IR3 antibody
2. Error on p5, last para, line 3 shown that this effect also be achieved.
3. Error on p8, para 2, line 4 overexpressing of the

Competing interests:

None declared.