Reviewer's report

Title: IGF-I activates caspases 3/7, 8 and 9 but does not induce cell death in colorectal cancer cells

Version: 3 Date: 23 December 2008

Reviewer: Leon A Bach

Reviewer's report:

The authors have revised the manuscript according to reviewers’ comments but a number of issues remain before the manuscript is acceptable for publication.

MAJOR COMPULSORY REVISIONS
1. Although they provide a direct response to reviewers’ comments, some of the responses have not been incorporated into the manuscript, e.g. the statistical method for multiple comparisons.
2. The authors have measured apoptosis using a single assay. It has not been directly validated against other measures of apoptosis and the ‘validation’ provided shows an extremely modest response to high concentrations of 5FU (<25% increase in apoptosis). The results would be more convincing if a more potent apoptosis inducer was used and apoptosis was demonstrated in various ways.
3. IGF-I did not stimulate apoptosis despite increasing caspase activity, but the introduction and discussion still largely focus on apoptosis rather than the interesting discrepancy between these observations.
4. The authors must describe the cell viability assay.
5. In their response, the authors allude to a proliferation assay but no data are shown in the manuscript.
6. It would appear that no isotype-matched control was used for the IGF-IR antibody experiments, raising the possibility that the observed effect was non-specific. This possibility should be mentioned if not rectified.

MINOR COMPULSORY REVISIONS
There continue to be many instances of imprecise language and typographical errors that should be corrected.

The figure legends and text refer to ** as p<0.001, whereas the methods state that this symbol represents p<0.01.

DISCRETIONARY REVIEWS

Were caspase 8 and 9 measured in SW and C2 cells and not elevated by IGF-I or were they not measured?
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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