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: 9 January 2009

Reviewer: Jack Youngren

Reviewer's report:

The authors have done an excellent job of addressing the shortcomings of their original submission. Several minor revisions in the text are necessary, mostly to correct grammatical or technical issues. The changes are as follows:

1. The abstract as well as the introduction (pg 4, line 1) describe the role of IGF-1R in apoptosis as "controversial". Actually, there is little controversy. This should be changed to state that the role of the IGF-1R is not completely understood.

2. If there is evidence that dysfunction of apoptosis directly contributes to the development of colon cancer, the authors should reference it. Otherwise, this sentence should be removed or qualified.

3. The final section in the methods (pg 7) validating the cell death assay and referencing figure 4 belongs in the results section.

4. In the last sentence of paragraph 2 on page 9 if the results, the word "various" should be changed to "varied" or an equivalent.

5. On page 12, of the discussion, the final three sentences of the first paragraph should be rewritten for clarity. It is not clear what actions of IGF-1 are partially inhibited, or what the conditions are. If the authors are referring to the serum free vs. serum conditions discussed in the final sentence, then the effects of serum are not equivalent to IGF-1 actions. Overall it is not clear what point the authors are trying to make, or why the insulin receptor is invoked.

6. The first sentence of the seconds paragraph on page 12 should read "there IS EVIDENCE indicating that caspase activation is also involved WITH PROCESSES..."

7. The final sentence of the discussion should be removed. The present studies did not address caspase inhibition. The fact that caspase activation does not lead to an overall increase in cell death is not indicate that inhibition of caspases is without effect. Thus the authors are overly, and incorrectly interpreting their results.

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 hold patents on the use of 2 classes of small molecule IGF-1R inhibitors in the treatment of cancer.