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

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Version: 6 Date: 16 April 2009

Author's response to reviews: see over
Dear Editor,

MS:1736711348222800

Thank you for sending us the reviewer’s comments for our manuscript. We found the reviewer’s comments are helpful. When we checked IGF-IR antibody, we found this antibody was mouse monoclonal antibody (product code: ab16817, Cambridge, UK) and the rabbit IgG used as a control was not appropriate. Therefore we have purchased the mouse IgG (product number I 5381, Sigma, UK), carried out a further control experiment and obtained new set of data (figure 3 i and j). Similar to the rabbit IgG, the mouse IgG was also not able to inhibit IGF-I-induced caspase activation. Therefore the conclusion is the same as the previous version of the manuscript. The new data have been updated to figure 3. The IGF-IR antibody and the mouse IgG have been identified in the manuscript.

We would like to use this opportunity to thank reviewers’ comments. We believed that the manuscript has been improved and is suitable to be published.

Kind regards

Shiyu Yang

Following is our reply to reviewers’ comments:

Reviewer 1

Reviewer's report
Title: IGF-I activates caspases 3/7, 8 and 9 but does not induce cell death in colorectal cancer cells
Version: 5 Date: 25 February 2009
Reviewer: Leon A Bach

Reviewer's report:
This revision is a marked improvement on the previous versions. However, one outstanding issue needs to be resolved.
MAJOR COMPULSORY REVISIONS
1. The IGF-I receptor antibody is not identified. The source company, Abcam, list 19 antibodies raised in 4 different species. The rabbit IgG used as a
control is only appropriate if the IGF-I receptor antibody is a rabbit polyclonal antiserum.

Thanks for this very useful comment. When we checked IGF-IR antibody, we found this antibody was mouse monoclonal antibody (product code: ab16817, Cambridge, UK) and the rabbit IgG used as a control was not appropriate. Therefore we have purchased the mouse IgG (product number I 5381, Sigma, UK), carried out a further control experiment and obtained new set of data (figure 3 i and j). Similar to the rabbit IgG, the mouse IgG was also not able to inhibit IGF-I-induced caspase activation. Therefore the conclusion is the same as the previous version of the manuscript. The new data have been updated to the figure 3. The IGF-IR antibody and the mouse IgG have been identified in the manuscript.

MINOR COMPULSORY REVISIONS
1. There continue to be many instances of poor language and grammar that should be corrected.

   English and grammar has been checked and improved.

**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

Reviewer 3

**Reviewer’s report**

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

**Version:** 5  **Date:** 5 March 2009

**Reviewer:** Alexandre Arcaro

**Reviewer’s report:**

In this revised manuscript, the authors show that IGF-I activates caspases in colorectal cancer cells but does not induce apoptosis. The implications of these findings for the field are of limited interest. Also the revised manuscript lacks mechanistic data about the activation of caspases by IGF-I. A lot more work is required to describe the molecular mechanisms underlying caspase activation by IGF-I. In addition the relevance of these findings for colorectal cancer remains unclear.

We think Akt and MAPK signalling might be involved in the mechanism concerning the activation of caspases by IGF-I. We are currently carrying
more studies on them now. We believed the Akt/PI3 kinase and MAPK data could form another new paper after we obtain more new data.

**Level of interest:** An article of limited interest  
**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'