Reviewer's report

Title: Insulin-like growth factor I activates apoptotic pathways in colorectal cancer cells

Version: 2 Date: 12 November 2008

Reviewer: Alexandre Arcaro

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Major Compulsory Revisions

1) In its current state, the manuscript only relies on caspase activity measurements, which is problematic when trying to make firm conclusions on apoptosis induction. The authors need to perform additional work to firmly prove apoptosis induction in the colon cancer cells upon IGF stimulation. DNA fragmentation and PARP cleavage must be analysed to conclude that apoptosis is indeed triggered by IGF in the different cell lines under study. Moreover, a quantification of the number of cells undergoing apoptosis must be provided by performing Annexin V staining and FACS analysis. Without these data it is not possible to conclude that colon cancer cells do indeed significantly undergo apoptosis in response to IGF.

2) If IGF triggers caspase-dependent apoptosis in the cells this should also be assessed by performing cell viability assays (MTT) in the presence or absence of caspase inhibitors (ZVAD).

3) The authors have used pharmacological inhibitors of the PI3K and MAPK pathway in the caspase assays. However, they have not provided any evidence that IGF stimulates the Akt and/or the MAPK pathway under these conditions. Western blot analysis using phospho-specific antibodies must be performed to address this issue.

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'