Reviewer’s report

Title: Ceramide Targets XIAP and cIAP1 to Sensitize Metastatic Colon and Breast Cancer Cells to Apoptosis Induction and Metastasis Suppression

Version: 1 Date: 18 October 2013

Reviewer: Anna ivana Scovassi

Reviewer’s report:

The manuscript by Paschall et al reports the results of a study aiming at elucidating the effect of ceramide (and analogs) on colon and breast cancer cell lines. The authors analysed the induction of apoptosis, focusing on the pathway mediated by Fas-FasL, and investigated the possible impact of IAPs on cell response, demonstrating that these apoptosis antagonists are among the targets of ceramide.

Concerning the elucidation of the properties of the drug LCL85, the comparison between different cell lines revealed that it could play a role in overcoming the resistance of metastatic cells.

The experiments are well conducted, with a panel of cellular and molecular assays; data are carefully described; the manuscript is well written.

Minor essential revisions are required:

1. Throughout the text, the authors describe the cell lines either as primary or metastatic. To avoid any misunderstanding about the exact meaning of the adjective “primary” when referred to cell lines (primary cells are cultured directly from a subject), I suggest to modify the definition “primary and metastatic human colon carcinoma cell lines” with the more appropriate “human cell lines established from primary or metastatic colon carcinoma”.

2. Is the level of IAP expression constant in the different cell lines?

3. Fig. 3, panel B can be removed.

3. Fig. 4, the calculation of data in panel B does not respond to the description. For example, for the 3 MM ceramide 30.5% (+FasL) - 17.5% (-FasL) = 13, while in the histograms is > 20%. Still for this panel: how SD of a percentage has been calculated?

Level of interest: An article of importance in its field

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.