Reviewer’s report

Title: TMEM45A as a new biomarker of chemoresistance in cancer cells

Version: 2 Date: 19 July 2012

Reviewer: Laki Buluwela

Reviewer’s report:

Experimental and clinical studies have long suggested that tumour cell adaptation to hypoxia contributes to the development of chemoresistance and is associated with malignant progression. In this context, it is commonly believed that chemotherapy stimulates cancer cells to undergo apoptosis, inhibition of which allows the development of chemoresistance. This has led to several published studies investigating the link between hypoxia and apoptosis in tumours and is the area the paper by Flamant et al addresses. Specifically, the study uses the estrogen receptor negative, metastatic breast cancer cell line MDA-MB-231 to assess the effects of hypoxia on apoptosis mediated by paclitaxel and epirubicin and further characterise the mechanism of paclitaxel-induced apoptosis in these cells under hypoxic conditions. In doing this, a comparison is made to etoposide induced apoptosis in the HepG2 hepatocellular carcinoma cells.

Specific comments:

The manuscript by Flamant et al uses the MDA-MB-231 cell line with gene expression microarray analysis to investigate responses to epirubicin (epi) and paclitaxel (tax) under normoxia and hypoxia conditions. This has led to the finding that the TMEM45A gene is regulated by hypoxia and involved in the epirubicin response in MDA-MB-231 cells and is also involved in the response to the DNA damaging agent etoposide in the HepG2 hepatocellular carcinoma cell line. The revisions the authors have made have addressed all of the points raised in my first round of review, with the exception of my points 5 and 6, which have also been noted by the other reviewers. The authors’ rebuttal for the lack of protein expression data to demonstrate successful siRNA mediated knockdown of TMEM45A is made on the basis of the antibody used. It is not clear if the supporting data relating to this, as provided in the letter of rebuttal, will now be included as supplementary data and appropriately commented on in the manuscript.

Major Compulsory Revisions:

The revised text needs to be carefully proof read and corrected accordingly.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: In addition to proof reading, the manuscript could benefit from minor revisions in the use of English.

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

**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.

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