Reviewer’s report

Title: Matrix Association Region/Scaffold Attachment Region: The Crucial Player in Defining the Positions of Chromosome Breaks Mediated by Bile Acid-Induced Apoptosis in Nasopharyngeal Epithelial Cells

Version: 0 Date: 12 Sep 2018

Reviewer: Reviewer 2

Reviewer’s report:

PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWSER COMMENTS FROM REPORT: Nasopharyngeal carcinoma (NPC) is caused by gastric refluxes, which contain bile acid, a proponent of apoptosis and carcinoma driver. The authors hyposthesise that bile acid induces chromosomal breaks at hotspot regions.

Using normal nasopharyngeal epithelial cells, the authors investigated one of these chromosomal breakage hotspot (AF9) and found that bile acid did induce chromosomal rearrangements at the AF9 loci, which is rearranged in ALL leukemia patients.

Although long, the Introduction is well written and informative.

The Bibliography seems to be outdated with very few recent research articles.

The Methods section is well detailed. However, the source of normal cell lines being other academics, how did the authors validate the authenticity of the cells? What was the passage number? For how many passages the cells kept in culture?

Also, catalogue numbers for reagents could be useful.

The Authors have thoroughly investigated the effect of bile acid on the breakage of AF9 loci.

REQUESTED REVISIONS:

A few typos and corrections (highlighted in CAPITAL):

- Page 4, around line 25 in PDF file: The typical GORD symptoms such as heartburn and acid regurgitation may not BE present in half of these patients [20].

- Page 5, around lines 20-27: In addition, BA has also been shown to have the carcinogenic effect in human hypopharyngeal squamous carcinoma FaDu cells through epithelial-
mesenchymal transition (EMT) [REF 60?]. EMT is a major pathway related to cancer invasion and metastasis [60 A RECENT REVIEW ON EMT AND CANCER SHOULD BE INCLUDED].

- Page 5, from line 34, there are many "MAY". It makes the NF-kappaB area seem very hypothetical while NF-kappaB is known to play a central role in inflammatory responses. A review (such as PMID 22257950) could be referenced.

- Page 14, line 45, "intron 4 (MAR/SARs 22-26 in Table 1) WERE found to contain five MAR/SAR sites" and line 53, "(MAR/SAR 29 in Table 1) WERE found to contain one MAR/SAR site"

- Page 9, lines 46-58 are not necessary. Could mention something briefly about it in the Discussion if useful.

- Page 10, lines 34-44. Although there is a reference, the amount (μM or mM) for each component should be specified.

A suggestion to increase impact and broaden interest would be to perform next-generation sequencing (NGS) of bile acid-treated cells to identify breakage points genome-wide.

**Are the methods appropriate and well described?**  
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**  
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**  
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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