Reviewer's report

Title: Deoxycholic Acid Induces MUC2 Intestinal Mucin Overexpression via NF-kappaB Through PKC in Human Esophageal Adenocarcinoma Cells

Version: 1 Date: 24 August 2008

Reviewer: Jeffrey Peters

Reviewer's report:

The authors report an in-vitro study of the effects of bile salt stimulation on MUC2 transcription and protein expression in SEG-1 cells. The potential role of NFKB was assessed using a luciferase reporter construct. Bile acid stimulation resulted in a 4-5 fold increase in both MUC2 transcription and protein expression in a time and dose dependent manner. Deoxycholic acid had the strongest effect at 50-300uM for 18 hrs. Similarly 300uM DCA and other bile acid stimulation resulted in 4-5 fold increases in NFKB protein expression and transcriptional activity of the NFKB promoter. The authors next tested the requirement for NFKB using CAPE inhibitor of NFKB activity and siRNA inhibition of NFKB p65 activity. CAPE inhibition of NFKB completely blocked MUC2 induction, as did siRNA inhibition of the p65 subunit of NFKB. Aspirin also inhibited DCA induced changes in MUC2 and NFKB. Finally the authors tested the involvement of PKC and MAPK signaling via specific inhibitors. Inhibition of PKC nearly completely eliminated DCA induced MUC2 and NFKB transcription and protein expression. DCA stimulation was not dependent on MAPK.

The molecular events involved in esophageal carcinogenesis and the effects of bile salts are a significant topic of recent interest. An understanding of these events is slowing beginning to emerge. The authors provide an excellent series of experiments which confirms and extends those already published. The methodologies are appropriate, and both transcriptional activity and protein expression were studied in several points along the putative signaling pathway.

COMMENTS:

1) Based on array genotyping SEG-1 cells were recently discovered to be of likely lung epithelial origin rather than esophageal. The authors should Contact Dr. David Beer of the University of Michigan for more information. As such the title should be changed and the new information regarding the cell line reported in the methods section of the paper.

2) The aspirin experiment is interesting but seems a bit out of place. No data regarding the potential mechanism nor discussion of the findings are given.

3) The authors should more clearly review and acknowledge similar work by other investigators in the discussion.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: I have done similar work otherwise I have no competing interests