

COMMENTS TO AUTHORS

Dr. Moschovis and co investigators, in a comprehensive review, describe mucin expression in neoplasms of the pancreas, the ampulla of Vater and the biliary system. The review is important, interesting and well-written and should be published after a minor revision.

We thank the reviewer for his/her positive review and constructive comments. We provide a point-by-point reply below.

Comments:

1. Please explain how literature search has been conducted.

2. Please explain what were the inclusion and exclusion criteria for choosing papers to be included in the review.

Reply: We have searched the Pubmed database for articles that were published after 1990 by using the search terms “mucins” and [“pancreatic” or “biliary” or “ampulla of Vater” or “pancreatic ductal adenocarcinoma” or “pancreatic intraepithelial neoplasia” or “intraductal papillary mucinous neoplasms” or “mucinous cystic neoplasms” or “intraductal tubulopapillary neoplasms” or “biliary intraepithelial neoplasia” or “intraductal papillary neoplasm of the bile ducts” or “intrahepatic cholangiocarcinoma” or “bile duct cystadenocarcinoma” or “extrahepatic bile ducts carcinoma” or “carcinoma of ampulla of Vater”]. The relevant articles were reviewed by the authors for scientific significance and those that considered suitable were reviewed in depth and included in this review.

3. BillN = biliary intraepithelial neoplasm?

Reply: It is our understanding from the literature review that the acronym BillN is used most often for biliary intraepithelial neoplasia

4. "associated with invasive capacity" – "associated with invasive potential"

Reply: We have modified the text accordingly.

5. Mucins are distinguished from proteoglycans not only by the lack of uronic acid and xylose , but also by the O-glycosidic links.

Reply: We have modified the text accordingly.

6. MUC1-21.

Reply: We have corrected the text

7. Associated with the membrane = membrane-bound

Reply: We have replaced “Associated with the membrane” with “ membrane-bound”

8. Not only secreted mucins have tandem repeats.

Reply: We have modified the text accordingly.

9. Close the bracelets (DF3, MUSE11 and 139H2....

Reply: We have corrected the text.

10. What is mesothelin?

Reply: We have added appropriate information in the text.

11. What is HIF-dependent manner?

12. What is HIF1-a?

Reply: We have explained the acronym in the text.

13. PDGFA or PDGF-A?

Reply: We have corrected the text.

14. "is primarily located in the main...."

Reply: We have corrected the text.

15. What is BTC?

Reply: We apologize for not explaining the acronym. BTC stand for biliary tract cancer. We have explained the acronym in the text.

16. "...detection of MUC5AC in cholangiocarcinoma was associated with larger-sized....." – what is the cause and what is the effect?

Reply: To our knowledge there is inadequate evidence in the literature to support one possibility over the other.

17. For every MUC the discussion should be separated for association (marker for diagnosis) and prognostic factor.

Reply: We thank the reviewer for his comment. Nevertheless, we felt that the overlap between expression patterns and prognostic significance of mucin expression is so high that by trying to separate them in our manuscript it would lead to extensive repetition of the data.