Author's response to reviews

Title: Nuclear hBD-1 accumulation in malignant salivary gland tumours

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Author's response to reviews: see over
Dear Mr Pueblo,

herewith I am returning the second revision of the article:” MS: 2091676334166652 - Nuclear hBD-1 accumulation in malignant salivary gland tumours.” Alterations are highlighted in the revised text as in the first revision. I did reply to all reviewers´ comments separately; my reply is in red text colour; I did not receive a comment of reviewer 1:

Mr. Yoshihirio Abiko:

2. line12, 13 in the second page of Discussion.

It is too much speculation to say that hBD-1 might play an important role in the malignant progression of salivary gland tumours. Please see above. In any case I think that there is evidence for a potential role of hBD-1 as tumour suppressor gene. I understand that hBD-1 might be a tumor suppressor gene from previous reports. This article only shows evidence that localization of hBD-1 is shifted from the cytoplasm to the nucleus of the tumour cells in malignant salivary gland tumours. How could you make this suggestion from only these two pieces of evidences?
If authors would like to say that hBD-1 might play an important role in the malignant progression of salivary gland tumours, authors should at least cite references showing that the protein can be translocated into nuclear when the cells are transformed. Otherwise, it is too much speculation.

We changed the sentences and conclusions which might be too much speculation. At present time there are no data about hBD-1 in salivary gland tumours and the contribution of hBD-1 to the malignant progression of these tumours should be seen as a hypothesis for our present investigations which include gene-expression studies. Those were impossible for this study for we did not preserve fresh frozen tissue for RNA preparation.

There have been recent reports that the hBD-1 sequence shows homology with known cationic nuclear localization signal sequences in human keratinocytes. Furthermore nuclear Localization of HBD-1 in Human Keratinocytes was described, which suggests a role for this peptide in gene expression (Bick RJ, Poindexter BJ, Buja LM, Lawyer CH, Milner SM, Bhat S.. J Burns Wounds. 2007).

C-Myc is implicated in human cancers, and overexpression of c-Myc at the protein and/or mRNA levels has been observed in virtually all types of cancers (Nesbit et al. MYC oncogenes and human neoplastic disease. Oncogene 1999, 18, 3004–3016.). HBD-1 expression is not induced by infection or inflammation but up-regulated by c-Myc expression, suggesting that c-Myc may regulate hBD-1 expression via a non-inflammatory pathway [24]. We hypothesize that an hBD-1 involving pathway might play a role in cancerogenesis.

Mr. Thomas Pufe:

Mr. Thomas Pufes´ Comments are missing.

Mr. Katsuhiro Uzawa

Because the sample of the immunohistochemistry is too small and the quantity of hBD-1 gene expression is not confirmed, this study does not achieve a criteria of the publication.

Anyway, in the revised manuscript we included a semi-quantitative analysis of the immunohistochemistry (table 2).
Mr. Geovanni Cassali

I agree with the comments made by the authors. I believe that a semi-quantitative method for immunohistochemistry analysis could improve the methodology.

You are right: as proposed, we now included a semi-quantitative analysis of the immunohistochemistry for the cellular Localization of hBD-1, -2 and -3 in malignant salivary gland tissue in comparison with healthy salivary gland tissue to the revised manuscript (table 2).

Yours sincerely

Dr. Dr. M. Wenghoefer