Reviewer's report

Title: A comparative study between mixed-type tumours from human salivary and canine mammary glands

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Reviewer: David Sargan

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General: Canine mammary neoplasias are commonly occurring tumours that could be extremely useful in modelling human tumours. The authors are to be commended for attempting to bring a potential model for an important group of human tumours to the attention of readers. This M/S describes a small histological and immunohistological study comparing human salivary pleiomorphic adenomas and carcinomas-exPA with canine mammary benign and malignant mixed tumours. The study points up some similarities in the tumours but the discussion overstates some points in a manner not justified by the data, whilst some results are poorly explained.

All of the antigens studied in this M/S have received previous attention in canine mammary neoplasias, although perhaps not in all cases in mixed tumours, and not in a comparative context. The histochemical and immunohistochemical figures that constitute the majority of work in the M/S are for the most part clear and adequate although the findings are unremarkable (and see minor revisions below).

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The most contentious points in this manuscript are the attempts to compare age structure and gender of the tumour groups. The age structure comparison relies on one of the oldest of a number of comparative age scales in the literature. None of these scales have much validity without knowing about the breed structure of the group one is comparing, as different breeds have life expectancies which differ by up to two fold. Even then such scales have limited utility, and the inter-species statistical comparisons presented here are quite meaningless. This would be best tackled by comparing the real ages of human PA and Ca-exPA separately and then doing the same for the dogs, whilst noting that in both species these represented groups of middle aged to mature adults in both species.

2. With regard to gender, the conclusion that canine mammary tumours have a different distribution to salivary gland tumours is undoubtedly valid but seems to me wholly unremarkable, given that it has long been known that estrogens are required for mammary ductal development and that neither male dogs nor females that have not undergone oestrus develop any substantial number of mammary gland tumours. This study adds nothing to what was already known. With regard to oestrogen receptor status, the results are again simply a reiteration of what has already been published for both tumour groups. It is not correct to suggest that salivary tumours are “not very responsive to the hormonal environment”, when the results apply only to the ability to respond directly to estrogens, and no other hormones have been measured. A more straightforward discussion could briefly explain the differences seen.

3. A study of gland sizes is described in the methods, and three size categories are described in table 5: but there are no measurements provided to allow the reader to compare these size differences, (oddly, given the description of a method on page 5). The evidence which is provided to back up the statements about tumour distribution and gland size is strictly limited to a reference to a single published study for the human case, whilst the evidence in reference 27 is not available for scrutiny by most readers and the observations referred to are controversial. Figure 1 appears to compare locations of tumours by size of gland, but this figure seems not to be referred to in the text, and the sources and numbers of these tumours are not clear. If, as seems possible, one is looking at the 40 tumours in total used elsewhere in the study, then the numbers are very small and findings as shown will not support statistical analysis. Furthermore, if taken at face value they appear to directly contradict the authors claim that “the frequency[…] is inversely proportional to the size of the affected gland”. (p4, first paragraph, my italics). I am aware that the figure looks at total rather than malignant tumours, but the sample size is too small for further division. In the absence of further data, the sections of the introduction and methods, the few words in the discussion and table 5 and Figure 1 dealing with gland size should all be removed. This study if performed well would add a good deal to the M/S, but a sound study will require much further work.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

4. The download that I have of figure 4, (attempted twice), suggests that the bottom part of this figure is incomplete. This was not needed to make a judgement, as part of each micrograph was present, but obviously it should be put right if the M/S is to be published

5. There are remaining errors in the English, some of which considerably alter or obscure the authors’ meaning. (e.g. paragraph 2 “there is a well-known relationship between the incidence of human mammary and salivary glands.” Presumably the authors intend to refer to tumours somewhere in that sentence. In the Abstract Line 8 (“Ten samples of each human pleiomorphic adenoma…” implies that every individual tumour was sampled 10 times: I suspect the authors mean “Ten examples of each of the tumour types human pleiomorphic adenoma [etc.] were examined.”) There are more minor errors in several places (e.g. in the methods para 1 line 8, the omission of a noun after “clinical” - such as “features”). The authors should ask a native or highly proficient English speaker to iron out the remaining problems with them.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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.

Declaration of competing interests:

I declare that I have no competing interests.