Author’s response to reviews

Title: Expression analysis of the mouse S100A7/psoriasin gene in skin inflammation and mammary tumorigenesis.

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Author’s response to reviews: see over
27th January, 2005

To the Editor-in-Chief
BMC Cancer

Please find enclosed the revision of manuscript # 7536728244999182. The manuscript was originally entitled “Identification of the murine ortholog of the human S100A7 (psoriasin) gene” by Meghan Webb, Ethan Emberley, Michael Lizardo, Salem Alowami, Gefei Qing, Abdullah Alfia'ar, Linda Snell-Curtis, Yulian Niu, Alberto Civetta, Yvonne Myal, Robert Shiu, Leigh Murphy, and Peter Watson. As recommended by one of the reviewers the title of the revised manuscript has been changed and is now “Expression analysis of the mouse S100A7/psoriasin gene in skin inflammation and mammary tumorigenesis”. The authorship has NOT changed.
We have revised the manuscript taking into account the comments and criticisms of the two reviewers. We thank the reviewers for their time and effort in reviewing our manuscript. We feel that revision of the manuscript taking into account the reviewers comments, has strengthened the manuscript. A point by point response to the reviewers comments is attached to this cover letter. Changes in the manuscript except for those to the reformatted reference list, are underlined.

We hope that our manuscript is now suitable for publication on BMC Cancer.

Yours sincerely

Leigh Murphy PhD
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Responses to Reviewers:
Re Ms # 7536728244999182 ‘Identification of the murine ortholog of the human S100A7 (psoriasin) gene,’ by Webb et al.,

Please note that all changes have been underlined in the revised manuscript

Reviewer 1 – J Kulski

1. We thank the reviewer for bringing this paper to our attention. We became aware of this paper after we had submitted the current manuscript. We have changed the title of the manuscript along the lines suggested by this reviewer. The title is now ‘Expression analysis of the mouse S100A7/psoriasin gene in skin inflammation and mammary tumorigenesis’. As a consequence we have also changed the background in the abstract.

2. The Marenholz et al., 2004 reference has now been added see reference #9. As well the Introduction (page 4, line 17-24) and Discussion (page 14, line 7-8) have been altered to refer to and reflect the information contained in Marenholz et al., 2004.

3. We have followed the suggestion of Marenholz et al., 2004 with respect to the nomenclature of the mouse S100A7 homolog. And have altered mouse S100A15/psoriasin -> mouse S100A7/psoriasin. The changes have been underlined in the text of the revised manuscript. Also the Discussion has been modified to reflect this change see Discussion (page 14, line 7-8).

4. undertaken -> undertaken (page 4, line 16) psoriasin -> psoriasin multiple times, underlined in revised manuscript. Time groups and time points -> time-groups and time-points, page 5 ‘anonymized -> “….coded and therefore anonymous…” page 5, line 14.

Page 8-Phylogenetic analysis- the mouse sequence accession numbers, are immediately following the human ones, page 8, lines 25-29.

The antibody used for IHC would not distinguish between human S100A7 and human S100A15. But often except in the case of psoriasis, it is S100A7 and not S100A15 that is upregulated in neoplastic disease situations. See under Discussion page 14, paragraph 2 and page 15, paragraph 1 and 2. However, we cannot exclude unequivocally that S100A15 is not expressed in human lung and cervical tumors.

References 7 and 8- these are the only published reference to these data. We have a manuscript entitled ‘the S100A7-Jab1 pathway enhances pro-survival pathways in breast cancer’, by Ethan D. Emberley, Yulian Niu, Linda Curtis, Sandra
Troup, Sanat K. Mandal, Jeffery N. Myers, Spencer B. Gibson, Leigh C. Murphy, Peter H. Watson, which is submitted, and which contains the results presented in these two abstracts.

Reference 16, which is reference 18 in the revised manuscript, is corrected.

The formatting and typos in reference list have been corrected.

Inflammation at the bottom of Table 2, has been deleted.

Fig 3 has been corrected XM356221 -> XM_356221. In the original manuscript submitted, the ORFs of all the sequences had been truncated, and the error was not picked up at that stage. We have corrected this error as well in the new figure 3.

Reviewer 2 – J Schalkwijk

Minor revisions only;

1. ER = estrogen receptor. This abbreviation has been defined in the text (page 6, line15) where it first appears
   Jab1 = Jun activation domain-binding protein 1. This abbreviation has been defined in the text (see page 4, line 12) where it first appears.

2. A section in which there is reference to Jab1’s possible function(s) has been included. This is underlined in the text. See page 10, third paragraph under “Presence of putative jab1 binding motif in mouse S100A7/psoriasin.”, line 5-8, page 11, lines 1-2 and three additional references.- 21, 22, 23.

3. Page 6, second paragraph- there is nothing wrong with our copy, it is possibly due to some compatibility problem between systems since the manuscript was prepared mainly on a Mac G5 (OS 10.2) and converted to pdf, and then uploaded to the web.

Discretionary revisions-
“although oncology is not my field….”

To discuss the comments above of this reviewer, differentiation as a morphological entity in tumors is poorly understood, but categories of differentiation along specific cell lineages should not be confused with categories of pathological grading (assessment of 'differentiation'). In many organ systems where tumors arise from squamous epithelium (eg skin, esophagus, cervix), most of these tumors manifest squamous differentiation,
but the extent of these morphological features within these tumors is assessed by pathologists and used to classify these tumors (grading) into well, moderate or poorly differentiated tumors. In other organ systems, like lung, squamous tumors are one of several major subtypes arising from the same epithelium, and can be graded, but squamous tumors are not different in overall malignancy from an adenocarcinoma of the same bronchial epithelium. In human breast, squamous differentiation can rarely occur in malignant and benign tumors, and does not confer or associate with increased progression or malignancy. In murine breast tumors squamous differentiation is common but can also occur as a component in low and high grade invasive tumors.

Therefore, the association of psoriasin with squamous differentiation in tumor types does not equate with a negative correlation with malignancy but may illuminate its role in a specific cell program (that is also associated with what we recognize as a squamous cell). We would agree that the conclusion that the literature and our current data suggest mostly is that psoriasin is expressed in and exerts its role in only in the context of certain cell types, and this cell type coincides with what we recognize morphologically as abnormal squamous differentiation in many organs or as high grade ER-ve cells as an equivalent cell type in human breast.