Author's response to reviews

Title: Desmoglein 2 is a substrate of kallikrein 7 in pancreatic cancer

Authors:

Vishnu C Ramani (ramanivishnup@uams.edu)
Leah Hennings (lhennings@uams.edu)
Randy S Haun (HaunRandyS@uams.edu)

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Author's response to reviews: see over
November 7, 2008

Matt Hodgkinson BA Hons (Oxon), MSc (Cantab)
BMC Cancer Editorial Office

Re: Manuscript ID 2139552850196789
Desmoglein 2 is a substrate of kallikrein 7 in pancreatic cancer

Dear Mr. Hodgkinson:

We were pleased that our manuscript has been accepted, in principle, for publication in BMC Cancer. As you indicated in your e-mail dated October 21st, in response to the reviewers comments and your recommendations, as outlined below we have made additional revisions to the manuscript and included three supplementary figures. We hope these changes will satisfy the concerns of the reviewers and that the manuscript is accepted for publication.

The files corresponding to the revised manuscript and three supplementary figures have been submitted online. Should you have any questions concerning this revised submission, please do not hesitate to contact me.

Sincerely,

Randy S. Haun, Ph.D.
Associate Professor
Department of Pathology
4301 W. Markham St., #753
Little Rock, AR 72205 USA
Phone: +01 (501) 686-8594
FAX: +01 (501) 686-6517
E-mail: HaunRandyS@uams.edu
Response to Reviewers

Reviewer #1:

Minor essential revisions

1. Figure 3. I now accept that suitable control experiments have been carried out. I think that it is important that a sentence or two is placed in the results section explaining that negative controls with laminin and other potential substrates have been performed to make this point clear to readers of the paper. I leave it for the authors to decide whether or not to include the relevant data or leave it as ‘not shown’.

The laminin result has been mentioned in the Discussion section at the end of the paragraph discussing the in vitro degradation of Dsg1 and Dsg2. Also, as you requested, the figure has been included as Supplementary Figure 2.

2. I may be mistaken but it looks to me as if the immunohistochemical analysis of human skin with the anti-Dsg1 antibody does show staining of basal cells. The argument about the specificity of the antibody (as demonstrated in Figure 4A) would be strengthened by testing the antibody on recombinant Dsg proteins (i.e. presence of a band in the Dsg1 lane, absence in other Dsg lanes). A statement to the effect that the antibodies have been tested for specificity should be added to the text.

As you requested, the figure depicting the immunohistochemistry of normal human skin using the Dsg1 antibody has been included as Supplementary Figure 1. Also, a description of the specificity of the Dsg antibodies reported by the supplier has been included in the Methods section.

Discretionary Revisions

1. I would like to see the responses to Comment 2 (Reviewer #1) and Comment 6 (Reviewer #2) put together in a short paragraph, perhaps at the end of the discussion. This paragraph should explain that KLK7-transfected BxPC-3 cells do undergo changes in morphology and that these changes are likely to be due to loss of multiple substrates including E-cadherin (as previously published) and Dsg2 (current paper). If such a paragraph is not included it seems to me that readers of the paper will be left with unanswered questions (as were both reviewers) that will lessen the impact of the paper.

As requested by the reviewer, a paragraph has been added at the end of the Discussion section describing the change in cell morphology that results from hK7 expression and a figure depicting these changes has been included as Supplementary Figure 3.

2. Discussion. Paragraph 3. Sentence beginning ‘Initial studies....’ should be rewritten as it currently does not make sense? As suggested by the reviewer, this sentence has been rewritten.
Finally, as you requested, the reference to the hK7 immunohistochemistry in pancreatic tumors (citing our *Cancer* article) as been added to the first paragraph of the Results section.