Reviewer’s report

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

Version: 1 Date: 22 May 2008

Reviewer: James K Wahl III

Reviewer’s report:

The manuscript titled “Desmoglein 2 is a novel substrate of kallikrein 7 in pancreatic cancer” by Ramani et al. describes a preliminary set of experiments that suggest that kallikrein 7 may play a role in desmosome turn over in the pancreas. While the data are interesting and present a new mechanism for desmosome turnover, the manuscript in the present form is too preliminary and not suitable for publication at this time. Several major points are described below.

1. Figure 1 and 2 present data showing reduced desmoglein expression in pancreatic adenocarcinoma compared to normal pancreas and pancreatitis samples. It would be helpful if serial sections were also stained with anti kallikrein 7 to show increased expression of the protease.

2. The authors present data that suggests that desmoglein expression is reduced in pancreatic adenocarcinoma while expression is high in chronic pancreatitis and normal pancreas tissue. While desmoglein 2 expression has been reported to be widespread, it is surprising that desmoglein 1 expression was found in normal pancreas. Desmoglein 1 expression is thought to be restricted to squamous epithelial cells. This raises the possibility that the anti Dsg1 reagent may not be specific for Dsg1 and may also recognize desmoglein 2. The authors should present data supporting the specificity of the antibody reagents. In addition, control slides stained without the addition of primary antibody would be helpful in figure 1 and figure 2.

3. Figure 3 shows in vitro digestion of recombinant Dsg by hK7. Please include a negative control. Does Kallikrein7 digest all exogenous substrates?

4. Desmosomal cadherins are not particularly soluble in buffers containing non-ionic detergents. Figure 4 presents immunoblots of various desmogleins in M-PER extraction buffer and these samples are likely to contain only a small fraction of the total cellular desmoglein. SDS or Urea extracts should be examined.

5. Please compare Dsg localization in cells expressing kallikrein7 and control cells using anti Dsg2 directed against the extracellular epitope as well as an intracellular epitope.

6. The authors do not discuss the possibility that effects on desmoglein degradation may be due to general cell adhesion changes. Previous work from Dr. Haun’s lab has shown E-cadherin to be a substrate of kallikrein 7 and desmosome assembly and turnover depend on adherens junction assembly. Digestion of Dsg may be a secondary effect to alteration of the adherens junction.
and removal of E-cadherin from the cell surface.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**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