Reviewer's report

Title: Mast Cell Regulation of Na-Glutamine Co-Transporters B0AT1 in Villus and SN2 in Crypt Cells during Chronic Intestinal Inflammation.

Version: 2  Date: 20 November 2014

Reviewer: Lori A Coburn

Reviewer's report:

Major Revisions:
1. In the statistical analysis section, the authors describe using the unpaired Student’s t-test. This is used for directly comparing 2 groups of data, however, there are 4 groups of data (normal, inflamed, normal + ketotifen, and inflamed + ketotifen). They need to take into account all of the experimental and control groups and control for multiple comparisons by first using a statistical test such as an ANOVA and if the overall ANOVA is significant, then they could use a t-test or Student Newman Keuls for example. This should be redone for the entire paper and can be performed in the Graphpad program.

2. Why are only 3 groups presented in Tables 1 and 2? It would be useful to compare what happens in the normal + ketotifen group. If this control group was not done, the reason should be addressed. Again, as there are at least 3 groups, an overall ANOVA should be done prior to doing a t-test as in point 1 above.

3. Fig 5, shows a western blot for B0AT1 along with that for Ezrin as a loading control. Why is there not a similar film for Ezrin as a loading control in Fig 6?

Minor Essential:
1. In all of the figure/table legends, it is not clearly defined what the significance symbols are referring to. i.e. *p<0.05 is stated but not between which groups.
   - specific example: Fig 1. On the figure *p<0.01 above inflamed – seems likely that this is compared with normal tissue. However, **p<0.01 above inflamed + KT - is this compared to normal tissue or normal + KT?
   
   This should be clarified in each figure/table legend.

2. Fig 4 A and B – the figure and text do not match in the definition of the symbols – in figure *p<0.05 but in the text lines (226-230) *p<0.01 – need to correct this error depending on which is correct.

3. In lines 195-210 (Fig 2), the authors state that these data show that ketotifen reverses the inhibition of B0AT1 activity seen in villus of inflamed tissue and reverses the stimulation of SN2/SNAT5 activity seen in the crypts of inflamed tissue. However, the data in Fig 2 really only show that the alterations in glutamine uptake are reversed with the ketotifen. It is not until we see the actual transporter kinetics (Tables 1 and 2) that it can be said that the ketotifen is
directly affecting the transporters. Need revise this area. Once kinetic results are presented you will be able to make this statement.

4. In lines 231-233 – the data in Fig 4 really only show that the alterations in glutamine uptake are reversed with the ketotifen. It is not until we see the actual transporter kinetics (Tables 1 and 2) that it can be said that the ketotifen is directly affecting the transporters.

(Lines 261-264 are supported after showing all the preceding data)

Discretionary:
1. As there are only 4 mice in each group, would consider showing the actual data points instead of bar graphs to allow reader to see each data point.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**
I declare that I have no competing interests