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:** 5 December 2014

**Reviewer:** Pradeep Dudeja

**Reviewer’s report:**

This manuscript presents novel data pertaining to the role of mast cells in mediating differential regulation of intestinal epithelial Na-glutamine transporters in villus and crypt regions of the inflamed intestine. The studies in general are straight-forward, the analysis and interpretation of the data is reasonable. Authors need to address the following concerns to strengthen the manuscript.

1. It is mentioned at many places that enterocyte hexosaminidase was measured as an index of mast cell degranulation. Mast cell hexosaminidase release parallels degranulation. Authors need to elaborate on this aspect as it is misleading the way it is described.

2. Since the results mainly depend upon the use of ketotifen, did authors image the intestine to visualize mast cell degranulation and its stabilization with ketotifen treatment?

3. Discussion should include some aspects of as to how mast cell activation may have mediated these alterations in villus and crypt cell Na-glutamine transporter kinetic parameters. Also, there are alterations seen in Na/K ATPase as well, along with changes in BBM enzyme kinetic parameters, it should be discussed as to which aspect is more critical for the final outcome.

4. The results in Figure 6 are mainly negative results and can hence be described in the text and figure deleted. Instead, it would be better to include the tables in the normal format of the article rather than in supplemental info.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I am applying for a faculty position at this institution