Reviewer's report

Title: Evaluation of protease and nucleoside reverse transcriptase inhibitors on intestinal cell proliferation, necrosis, apoptosis, electrolyte and water transport and epithelial barrier function.

Version: 2 Date: 26 March 2010

Reviewer: Michael George

Reviewer's report:

The authors present an interesting study of the effects of RT and PI, utilized in HAART of HIV-AIDS patients, on intestinal barrier function. This is an important unresolved question in the HIV field and one that is extremely difficult to address in human studies. The relevance of the study is somewhat hindered by its design, namely testing the effects of the drugs individually, instead of in combination, and the use of mice and cell lines, all of which limit the ability to extrapolate interpretation of the data with regard to antiretroviral therapy regimes in HIV infected humans.

The questions are relevant however, and while some limited answers are provided within the context of the experimental design, the study would be significantly strengthened by additional data that should be fairly straightforward to supply.

Major Compulsory Revisions:

1) The morphological measurements in Figure 1 would be strengthened by presentation of tissue sections (H & E stained) that highlight the differences in villus height and crypt depth visually.

2) Flow cytometry data showing increased apoptosis and necrosis in the IEC-6 cell line can be supported by parallel in vivo experimental data that should be readily available. How do apoptosis and necrosis compare in the mouse small intestine? Mice were treated with the same RT and PI to generate villus and crypt morphological data and these tissues should presumably be available for analysis of apoptosis and necrosis as well.

Minor Essential Revisions:

1) The different magnitudes in effects of the different PI and RT used in the study were not addressed adequately in the Discussion. There is an apparently greater effect from Nelfinavir than other compounds on cell proliferation and secretion, and a consistently reduced effect from Didanosine. These findings should be noted and potential explanations provided.

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