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: 11 March 2010

Reviewer: Reiner Ullrich

Reviewer's report:

This is an interesting study of effects of some anti-retroviral drugs on the intestinal epithelium using an in vivo mouse model and culture of rat jejunal crypt cells. Overall, the work appears sound, but there are serious inconsistencies and errors in the data and presentation which need to be addressed:

- Major Compulsory Revisions

1) The reporting of results in the abstract is incomplete and sometimes misleading; e.g crypt data are missing, DDI did not affect Cl- or water transport, lack of effects on M/L absorption or cell proliferation is not stated. Background and conclusions are rather vague at present and should be much more specific

2) Reference numbering needs attention, e.g. numbers jump from Ref 15 (p.4) immediately to Ref 24 (p7) which probably refers to Ref 22 in the reference list.

3) p.12 The „remarkable blunting effect“ of IND in the ileum is absent in figure 1A; the crypt length is not increased in the jejunum by IND.

4) In the methods section at least six mice per group are mentioned; in the legend to Fig. 2 there are only 4 mice per group (line 2) and later six rats per group (line 6). Six rats are also mentioned in the Fig.1 legend.

5) p.13f The extremely variable cell proliferation seen in the controls is surprising; the comparatively small effects of INV or NELF should be viewed with caution.

6) An explanation why the authors used different statistical tests (ANOVA, Student’s t) would be helpful.

7) It would be interesting if the authors could correlate and integrate their various findings in the discussion. The conclusion should be more focussed on the actual data.

- Minor Essential Revisions

1) The choice of references (e.g. 1-4) seems a little odd at times and out of date (most recent reference from 2007). Maybe the authors can include some authoritative recent citations.

2) p.1 Title should include a reference to HIV or antiretroviral therapy and identify the animal model/cell culture used.

3) p.2/3 The abbreviations AIDS and HIV should be correctly defined.
4) p.3 Ca+2 should read Ca2+

5) p.6 Please specify whether morphologic analyses were done by one or more investigators and include assessments of inter- or intraindividual variability.

6) I did not understand some sentences (last sentence of p.9; p.12, para 1, last sentence; p.16, line 9 and para 2, first sentence)

7) p.10 „ApoAlert“ kit and „Binding Buffer“ should be specified.

8) Data on body weight would be of relevance. Can the authors exclude differences in nutritional intake between the groups?

9) p.12ff In general, the repetition in the text of values shown in the Figures may not be necessary

10) Conflicting statements (e.g. abstract vs. discussion) regarding the importance of GI side effects of antiretrovirals should be reconciled.

- Discretionary Revisions

1) At n<10 I would prefer to see the individual data points in diagrams.

2) It may be more helpful to explain the physiological background of the lactulose/mannitol tests earlier in the paper.

3) The methods section of the abstract could profit from some shortening and a clear distinction between in vivo and in vitro experiments.

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

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests.