Reviewer's report

Title: Membrane Transport of Camptothecin is Facilitated by Human P-glycoprotein (ABCB1) and Multidrug Resistance Protein 2 (ABCC2)

Version: 1 Date: 3 January 2004

Reviewer: Ikumi Tamai

Reviewer's report:

General
Luo et al. examined the involvement of ABC-efflux transporters in the transport of CPT for the purpose to clarify the mechanism of the inter-patient variation of PK characteristics of the drug. Especially, the study was focused on the intestinal transport process using Caco-2 cells and transporter-transfected cell lines. The obtained results are important to understand basic mechanism of CPT absorption and disposition and the experiments were well designed and performed. There are several concerns to be addressed.

Discretionary Revisions (which the author can choose to ignore)
1: p. 12, lines 10-13. The results at the higher concentrations of GF120918 on transport of CPT should be shown in Figure 5B.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1: The expressions of CPT and camptothecin are mixed in the manuscript.
2: Legend for figure 4, P.23, line 18. The unit of concentration of etoposide may be mM but not microM.
3: p. 6, line 13. What dose the (L) in the line mean?
4: p. 10, line 9. Add the description of sources of each antibody.
5: Figures 4B and 5B. Describe the unit of Y-axis.
6: Figure 5A. The numbers of Y-axis are strange. Check the numbers carefully.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1: All the part of Discussion is too general and major part of the Discussion should include the interpretation and speculation based on the obtained results and previous information.
2: In page 12, line 9, it was written that strong inhibition was observed. However, the inhibitory effect is not strong enough and the transport in some pints is likely increased in the presence of inhibitor, as long as the legend of figure is correct. Authors need to check the legend and figures or should discuss more carefully.
3: Figure 4A may not be clear enough to discuss the competitive inhibition kinetics on CPT transport by etoposide. The result will be clearer when the kinetics is analyzed by V vs. V/C plot (Eadie-Hofstee plot).
4. Figure 1A. Absorptive transport is significantly higher than the efflux transport in Caco-2 cells. This may mean that the inter-patient variability of PK of CPT is due to the variability in absorptive
transport rather than the efflux transport, which is examined in the present study. The importance of an influx transport should be discussed more in the manuscript.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

NONE