Reviewer's report

Title: p21 is decreased in polycystic kidney disease and leads to increased epithelial cell cycle progression:
Roscovitine reverses this effect

Version: 1 Date: 7 June 2007

Reviewer: Rudolf P. Wüthrich

Reviewer's report:

General

The report describes the downregulation of p21 in human ADPKD and in male Han:SPRD rats with PKD, and examines p21 in MDCK cells and in particular the effect of the CDK inhibitor roscovitine on p21 in MDCK cells.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The study focusses exclusively on p21 dependent cell proliferation, however p21 influences also apoptosis. To gain a full understanding of the effect of roscovitine and the ODN anti-sense approach it would be desirable to examine also apoptosis for example with annexin V staining of MDCK cells.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Methods: details regarding HGF should be given, and how the cell culture was set up with HGF.

Results:
- the immunohistochemistry figures are of poor quality (might be due to the pdf conversion); there should be in addition higher magnifications to show the subcellular localization of p21, and the tubular staining
- it would be important to control for the toxic effect of the ODN by assaying for example the LDH release at 200 and 400 nM; a full dose-response curve would be desirable (why was 200 and 400 nM chosen?)
- page 13: typo (“showed an increase”)

Discussion:
should be shortened by at least one page

Table 1: indicate the age of animals (12 weeks?)

Fig. 1 need low resolution
Fig. 4: what is QM ? Why is there a double band for p21, and one a single band in vivo ? Explain
Fig. 5: why is SC 200 also decreasing p21 ? Abbreviations GJ and CM need to be explained (controls)
Fig. 6: SEM is very large in GJ, needs to be repeated.
Fig. 7a: dose-response only between 1 and 10 is shown. A fuller dose-response would be desirable (0.1 and 100 ug/ml)
Fig. 7b it is surprising that there is no p21 with 1 ug/ml roscovitin compared with ser and QM (explain these abbreviations in the legend; also it is ug/ml and not mg/ml)
Fig. 8: could be deleted since there are not data on apoptosis in this report

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Discretionary Revisions (which the author can choose to ignore)

none
What next?: Accept after minor essential revisions

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.