Reviewer's report

**Title:** Mutant polycystin-2 induces proliferation in primary rat tubular epithelial cells in a STAT-1/p21-independent fashion accompanied instead by alterations in expression of p57KIP2 and Cdk2

**Version:** 2  **Date:** 19 June 2008

**Reviewer:** Feng Qian

**Reviewer's report:**

The authors have addressed all of my concerns.

My major concern has been that the affected TECs, ie of proximal nephron origin, derived from PKD2(1-703) kidney may not adequately match to those from the WT control kidney, thus confounding the interpretation of the results. Because the cystic dilation in the mutant kidneys is restricted predominantly to the proximal tubules, there must be considerably more TECs of proximal tubule origin in the mutant kidney than in the WT control kidney, relative to the TECs from other unaffected nephron segments. As a result, one would expect different ratios of TECs from various nephron segments between the WT and mutant samples, given the methods used enrich all epithelial cells rather non-discriminately. Because the differences of p57 and Cdk2 levels found between WT and mutant samples are fairly modest, perhaps rightly so, they could easily reflect nephron-segment specific basal levels, rather than being due to expression of PKD2(1-703) in the proximal tubules of the mutant kidney. Given the structural and functional diversity of the nephron segments, the former possibility seems fair, especially that the results found in the primary TECs are not recapitulated in HEK293 and NRK-52E.

The megalin blots are helpful, but do not directly address whether other nephron segments that may be present with different proportions between the WT and mutant samples may contribute to the difference of p57 and Cdk2 levels. I realize that there are no easy ways to resolve the issue within the scope of the paper. I would therefore suggest that the authors more specifically state these caveats in the paper.

**Minor Essential Revision:**

Point 2 is not adequately addressed. A difference of 40 aa between 742 and 702 PC2 should be detectable on PAGE for a protein in the range of 80 kDa, perhaps by PNGase F treatment and/or longer run. Lack of it would raise concern about the identity of the band being the expected 702 protein. This seems to be relevant, considering that the antigen of anti-PC2 overlap with 702 protein only by 20 aa.

**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.