Reviewer's report

Title: The fate of bone marrow-derived cells carrying a polycystic kidney disease mutation in the genetically normal kidney

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Reviewer: Hanna Rennert

Reviewer's report:

In this manuscript the authors examined the potential of transplanted BM cells harboring PKD-causing mutations to give rise to renal epithelial cells and form cysts in normal female mice, using the Y chromosome to track mutant BM-derived cells in conjunction with markers of renal epithelial phenotype. The paper is well written and the data overall are sound and carefully presented. The manuscript could be improved further for clarity without losing the important information and conclusions. In particular:

1. It is not clear from the results how successful the BMT was. Figure 1 demonstrates results of PCR analysis for the sry gene, but does not provide any quantitative information regarding the success rate. The authors should be more specific regarding the number of animals and the number of cells that successfully engrafted.

2. In Figure 3 the authors show that the percentage of Y chromosome-positive cells is declining in the kidney. Was that decline also observed in the animals' peripheral blood and how do the authors explain this decline?

3. This sentence in the Results section “These frequencies and total numbers of Y chromosome-positive cells observed are consistent with previous reports of BM-derived cells on the tubule [21]” should be moved to the Discussion. The authors should also clearly state the mean percentages of Y-chromosome positive cells in the peripheral blood and kidneys as well as the number of animals assessed.

4. The authors note in the Results that BM-derived cells were only found as scattered examples in the renal tubule. The low number of these cells in the kidney may reflect unsuccessful transplant which would be a limitation of this work, but this is not addressed in the Discussion and needs to be added.

5. The authors also indicate that the longer time point (twelve weeks) assessed is sufficient for the post-ischaemic recovery and the development of cystic pathology, however, this may not be sufficient time for complete engraftment, particularly since no information is provided regarding the success of the BM transplant. BM cells contribution to epithelial cells following HSCT is well documented, including in humans. However this may be depended on level of engraftment. This should be discuss in more details.
Minor

6. Introduction- ADPKD is caused by inherited mutations in one of two genes: PKD1 and PKD2, followed by secondary somatic mutations in the renal epithelial cells leading to cysts development. This is not indicated in the text and should be added.

7. Results, page 8- “Detection rates were not 100% because the Y chromosome is not necessarily be included in a cross-section of every nucleus examined”. “the Y chromosome is not necessarily included…”?

8. Results, page 9- “From 120 examples of Y chromosome positive cells examined from kidney 2, 4 or 12 wks after injury, only a 10 (2 at 2wk, 5 at 4 and 3 and 12wk) were sufficiently entwined with the tubule that an epithelial phenotype might be considered”. Check sentence. “…only 10 examples…”?

9. Discussion, page 12- “Many of the initial studies in this area appear to have overestimated the contribution of BM-derived cells to renal epithelia due to unreliable tracing and phenotype determination techniques.. Provide references.

10. Manuscript should be check carefully for typos and grammar. There are numerous typos throughout the text: Introduction-2nd paragraph change “donour” to “donor”. Figure legend 3: change “inury” to “injury”; Figure legend 6: change “modelling” to “modeling”, “epithithelial” to “epithelial”.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.