Reviewer's report

Title: Bone marrow-derived cells can acquire renal stem cells properties and ameliorate ischemia-reperfusion induced acute renal injury

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Reviewer: Stephanie Cherqui

Reviewer's report:

The authors are studying the fate of bone marrow-derived cells within the kidney after acute ischemia-reperfusion and the effect of G-CSF treatment.

Major comments:

- Fundamental issue: Many studies have used surface markers of stem/progenitor cells in bone marrow to identify progenitor cells within tissues. However, it has been demonstrated now that many of these markers overlap or only mark differentiated cells in tissues. For instance, CD133, CD24 but also Sca-1 and c-Kit have all been shown to be heavily expressed in differentiated epithelia including renal epithelia. The authors based their entire study on Sca-1 and c-Kit to demonstrate the differentiation of bone marrow-derived cells into renal progenitors. Therefore, there is a fundamental conceptual problem of the study and misinterpretation of the results. The authors also used CD29, CD34 and Flk-1 as markers for renal progenitors. The authors should justify this surprising choice and discuss the results.

- The number of mice used for each study should be clearly stated in the results.

- Reconstitution of B-cell, T-cell and monocytes should be tested to show "hematopoietic reconstitution" as stated by the authors.

- Figure 1: Non-transplanted mice kidney should be shown as negative control for the green fluorescence

- Authors: Some tubular spaced cells were partially or completely derived from donor bone marrow cells based on GFP/CD45 expression (Figure 1C)

Reviewer: What does that mean exactly? CD45 stained for hematopoietic-derived cells not for proximal tubular cells. The authors should clarify.

- Figure 2B-C: how did the quantification of GFP+ cells have been done? The authors should describe their methodology of quantification.

- Figure 3: How were renal cells isolated for flow cytometry staining? A detailed description of the method should be provided.

- Define HPF.
- The investigators showed that G-CSF increased microvessel density in the ischemic kidneys. However, functional data should be provided to determine the impact of G-CSF on renal function in order to verify if this treatment really improves the recovery of kidney defects in mice treated with G-CSF compared to the non-treated.

- Authors: The role of BM derived stem cells in repair or rejuvenation of tissues and organs that undergo injuries or degeneration has been drawn increasing attention [18-20].

Reviewer: Yeagy et al., Kidney International, 2011 should be cited as this an example of kidney preservation by bone marrow stem cells in the context of CKD.

- Authors: We confirmed that BM cells can integrate with epithelial cells, glomerular cells, and interstitial cells.

Reviewer: what does that mean? Do the investigators mean trans-differentiated in these cell types because no evidence is provided in this manuscript for such a conclusion. The authors should clarify.

- Authors: Our results also revealed that ischemic/reperfusion injury to the kidney produces acute tubular necrosis and apoptosis followed by tubular regeneration and recovery of renal function with contribution of bone marrow cells.

Reviewer: The reviewer disagrees with this statement; the authors did not show any tubular necrosis and apoptosis after ischemia/reperfusion and they did not have any data to support the fact that tubular regeneration and recovery of renal function were obtained.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

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

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