Reviewer's report

Title: Early stage transplantation of bone marrow cells markedly ameliorates copper metabolism and liver function in Wilson's disease mice

Version: 1 Date: 6 October 2010

Reviewer: Valentina Medici

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Chen X et al. conducted a study on bone marrow transplantation in an animal model of Wilson disease characterized by spontaneous hepatic copper accumulation (the tx mouse). The authors transplanted bone marrow cells after sublethal radiation. Mice were transplanted at early (2 months) or late stage (5 months). Donor cell population, parameters of copper metabolism (hepatic copper concentration and serum ceruloplasmin), and AST levels were measured at 1, 4, 8, and 12 weeks after transplant. The bone marrow cells population was higher in the early transplanted group compared to the late transplanted group. However, the expression of Syr gene peaked at 4 weeks and decreased rapidly up to week 12. Hepatic copper concentration was lower and serum ceruloplasmin higher in the early transplanted group. AST levels remained stable in the early transplanted group while they actually decreased in the late transplanted group.

Previous studies demonstrated poor results after bone marrow stem cell transplantation in the same animal model. In the current study, the main problem is the short duration of copper metabolism correction and the short term liver population. The same problem was encountered in previous studies.

Major critiques:
1) the hepatic copper concentration in the early group is lower than control group at all time points. However, the control group presents a trend in reduction in hepatic copper as well. Any explanation for this?
2) Why is hepatic copper level decreasing in the late group, both bone marrow transplanted and control?
3) Similarly, why ceruloplasmin tends to increase in the late control group?
4) Why AST levels decrease in the late control group?

Other critiques:
the manuscript requires a major revision of the English language. For example:
- I recommend the use of “Wilson disease” instead of “Wilson's disease”
- Background, line 3: variable or various organs?
- Methods: “...were allocated to one of four groups as followed” or as follows
- Methods: please specify DNA method extraction
- Results, page 11, line 1: 2nd week or 4th week?
- Discussion: “we found that BM cells transplantation starting at 2 months of age corrected liver injury”. I do not think the authors can make this conclusion. Their study is not really looking at parameters of liver injury but essentially only at metabolic parameters.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**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