Reviewer’s report

Title: Therapeutic potential of placental mesenchymal stem cells after transplantation through portal vein into Chinese miniature pigs with acute liver failure

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Reviewer: Maurizio Parola

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The experimental study by Cao et al (BMC-Medicine) has been designed in order to address two aims, the feasibility of a procedure to generate mesenchymal stem cells from human placenta (hPMSCs) and the efficacy of their transplantation in vivo to counteract acute liver failure induced by D-Galactosamine in the model of Chinese miniature pigs. Authors provide evidence indicating that well characterized hPMSCs can be easily obtained from human placenta; these cells maintain their plasticity and can be forced to differentiate into adipocyte-, osteogenic- and hepatocyte-like cells. Moreover, when transplanted via portal vein guided by B ultrasonography (but not via giugular vein) in the animal model of ALF these cells can engraft the injured liver and can afford a significant degree of protection versus standard parameters of ALF. On the basis of their results Authors conclude that hPMSCs are an attractive stem cell candidate for therapy of ALF and possibly other liver diseases because, in addition to be strongly immunosuppressive as described for MSCs of other sources, these placental-derived cells can be easily available (also in terms of number), do not require invasive procedures and are free of ethical concerns.

Although reports concerning the ability of transplanted MSC of different origin to provide protection against either acute or chronic liver injury are already available in the literature, this is possibly the first study investigating the therapeutic potential of hPMSCs in a large animal model of ALF. Protocol design, MSC characterization and methodology employed seem appropriate and most results are somewhat straightforward. I can offer the following comments.

1. In order to improve and complete their characterization, Authors should further analyze the hepatocyte-like phenotype of hPMSCs by investigating critical functional parameters like urea synthesis, LDL uptake and glycogen storage; Authors should also offer data on whether these cells may operate drug metabolism by investigating mRNA or protein levels or enzymatic activity of selected CYP-450 isoforms.

2. It would be of interest to have more direct and time-depedent morphological informations concerning engraftment/localization of transplanted cells into injured liver; this could be accomplished (just by looking at the two relevant groups, that are Gal only and Gal plus hPMSCs via portal vein) by means of either immune-histochemistry or, even better, multiple indirect immune-fluorescence
analysis by employing antibodies versus human antigens.

**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