Reviewer's report

Title: Phenotype, donor age and gender affect function of human bone marrow-derived Mesenchymal Stromal Cells

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Reviewer: Darwin J Prockop

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This paper presents a monumental effort to address an important problem: Variability in cultures of mesenchymal stem cells (MSCs) obtained from different donors of bone marrow. The strategy is comprehensive in comparing MSCs from 53 donors and the amount of data generated is overwhelming. At the same time, it is difficult to answer the question of how much the results advance the field and the very difficult biology of the cells.

Among the limitations of the data:

1. The conditions used to obtain the marrow, i.e. from patients undergoing orthopedic surgery, are not frequently used by other investigators in the field. Most use bone marrow aspirates from the iliac crest; this may introduce different variables.

2. A more serious concern is the conditions for tissue culture because of the vagueness on the details presented (page 23). “Subconfluency” is not defined. Not clear at what stage the P1 cells are harvested, etc.

3. The authors did not look at the effects of culture density or time in culture that can have major effects on MSCs.

It would be unreasonable to ask the authors to carry out the additional experiments to address these and several related issues.

However, one issue that can be addressed is that the authors draw major conclusions from small differences in their data. In particular the major conclusion that female donors are better for immunomodulatory therapies (page 3) is based on marginally significant changes (page 10). This is, in this reviewer’s opinion, an over-interpretation of the data.

Declaration of competing interests:

I am member of the scientific advisory board and have a very equity stake in an unfunded biotech (Temple Therapeutic LLC) with an interest in therapies with MSCs. I do not think this has prejudiced my review.