Reviewer’s report

Title: Abnormal phosphorylation of Tie2/Akt/eNOS signaling pathway and decreased number or function of circulating endothelial progenitor cells in prehypertensive premenopausal women with diabetes mellitus

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Reviewer: Ana Carolina Santos de Souza Galvão

Reviewer's report:

1. The first observation related to the presented work is the lack of control patients normotensive, premenopausal and diabetic. The authors demonstrated that the number and function of circulating EPCs is altered in prehypertensive, premenopausal and diabetic women. Since prehypertensive (non-diabetic) women had no alteration the question is: Is this alteration associated with the diabetes? Normotensive, premenopausal and diabetic women could be a control group able to answer this question.

2. In relation to the role of diabetes in number and function of circulating EPCs: the authors mentioned in the text that it is still known that the disease induces a reduction in these cells and their function. So it is clear that those alterations are direct causes of diabetes and are not related to prehypertensive status. Since authors showed that there are no alteration in function of circulating EPCs between hypertensive and normotensive women (no diabetic), why is the new knowledge covered by this work?

3. Why the proliferation assay was done with cells in absence of serum but measurement of NO, VEGF and GM-CSF was quantified in supernatant of cell growing in serum 20%? It is known that serum is able to modified growth rates of cells and the secretion of growth factors.

4. The item "Measurement of Plasma NO, VEGF and GM-CSF levels" starts describing the measurement of these molecules in cell culture supernatants. Is it right? The title of the item mentioned measurement in plasma. Additionally, the item "Measurement of NO, VEGF and
GM-CSF secretion by EPCs" seems describe the NO assay again but do not describe how the other molecules (VEGF and GM-CSF) were quantified (ELISA?)

5. The legend of figure 1 needs revision. In the first phrase there are repetition of words like "evaluated" and "by"

6. Maybe the molecular results about Tie2/Akt/eNOS are the great news of the work. However, the authors only show a cause-consequence of diabetes in NO production and circulating EPCs function. It would be interesting if the authors try something to prove this association at the molecular level maybe working with siRNA.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

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