Reviewer’s report

Title: The PI3K/ Akt pathway upregulates Id1 and integrin alpha4 to enhance recruitment of human ovarian cancer endothelial progenitor cells

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Reviewer: Oliver Renner

Reviewer’s report:

Regarding the manuscript “The PI3K/AKT pathway upregulates Id1 and integrin #4 to enhance recruitment of human ovarian cancer endothelial progenitor cells”.

This manuscript by Su and colleagues investigates the role of Id1 in the recruitment of endothelial progenitor cells of ovarian cancer patients. The authors provide evidence that Id1 is upregulated in ovarian cancer patients leading to changes in biological features like proliferation, migration and upregulation of integrin #4. They show that inhibition of Id1 expression by a specific shRNA or inhibition by a inhibitor of PI3K reverses these changes.

This is a very interesting manuscript that contains important data which might improve therapeutic strategies against ovarian cancer. Overall, I would like to recommend this manuscript for publication. However, there are some issues that need to be addressed:

Minor essential revisions:

1. The actual values of figures 2C and 4B, including numbers for standard error and number of analyses conducted (n), should be stated in the results section or in the legend. To what do the relative protein levels relate to (what is set “1”)? Which statistical method was used to determine the p-values?

2. The quality of figure 3 B should be improved. Enhancing the resolution might help. A smaller image with a higher magnification could be inserted into each panel.

3. The panels of figure 3 B have to be labeled.

4. The authors should be more accurate with the phrasing.
   • By example in the second sentence of the abstract, the term “EPCs with ovarian cancer” should be replaced by “EPCs of patients with ovarian cancer”.
   • In the first sentence of the introduction, the authors state that angiogenesis is “chiefly mediated” by endothelial progenitor cells. While this can be discussed for the adult organism, this can certainly not be stated for angiogenesis in general.
   • In the last sentence of the introduction, the authors suggest that inhibiting Id1 might “disrupt” ovarian cancer cells. What exactly do they mean with this?

These are just examples of inaccuracies in phrasing and the usage of the language. I strongly recommend the manuscript to be checked again carefully for accurate phrasing.
5. Regarding the description of the material used for the Western blot:
   • There are various antibodies commercially available from Cell Signaling against P-Akt (phosphorylated AKT). Please indicate the exact reference. This is specifically important since some of these antibodies recognize different phosphorylation sites with different biological relevance.
   • What is “T-Akt”?

Discretionary revisions:
6. The quality of figure 4 A should be improved.
7. Figure 1: The panel in the lower right corner is labeled as “overlay”, but it is not clear what is overlaid here. Please indicate this in the legend, in the text, or in the figure.

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

**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.