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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Bone marrow-derived endothelial progenitor cells have been shown to contribute to neovascularization in mice and human. Notably, EPC ablation or loss of EPC function is associated with impaired angiogenesis. Published studies have shown that the dominant negative transcription factor Id1 and integrin alpha 4 are required for EPC-mediated angiogenesis. However, the molecular mechanisms by which these factors regulate EPC mobilization and recruitment remains unknown.

In this study, Su et al investigate the effect of Id1 on circulating EPC mobilization and recruitment and the possible role of PI3kinase/AKT signal transduction pathway on Id1 and integrin a4 in EPCs from patients with ovarian cancer. Total mononuclear cells were isolated from peripheral blood of 25 ovarian cancer patients (various stages) and controls and cultured in vitro to expand EPCs. These EPCs exhibited upregulated Id1 levels. shRNA-mediated Id1 knockdown reduced proliferation, migration and adhesion of these cells as compared to cells transduced with control vector. Furthermore, Id1 suppression reduced integrin a4 levels. The authors show that pharmacological inhibition of PI3-k pathway impaired EPC functions via Id1 and integrin a4. These findings have provided valuable insights on the role of PI3K-Id1-Integrin pathway in EPC function in ovarian cancer. I would recommendation publication after some issues have been resolved

1. Fig. 1 EPCs were cultured form the mononuclear fraction derived from peripheral blood. EPCs were defined as-LDL+ lectin+ and expressed vWF ,VEGFR2, and CD31.

To call these progenitors the authors must use a progenitor marker such as c-kit. Are these cells negative for classical hematopoietic markers such as CD11b, CD45, macrophage markers.

What about their functional attributes. DO they from endothelium or incorporate into nascent vessels?

2. The authors claim that pharmacological inhibition of the PI3K pathway blocks EPC functions in a Id1 and integrin a4 dependent manner. Will overexpression of Id1 or integrin rescue the EPC defects following PI3K inhibition (migration, adhesion).