Reviewer’s report

Title: Vasculature analysis of patient derived tumor xenografts using species-specific PCR assays: evidence of tumor endothelial cells and atypical VEGFA-VEGFR1/2 signalings

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Reviewer: Andras Nagy

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The authors developed mouse vs. human cell source discriminating (species-specific) Q-RT-PCR for several angiogenesis markers. They applied this assay on RNA samples obtained from a large number of PDX tumors, covering various types of human cancers. By quantitating the mouse vs. human sources of the angiogenesis markers, they observed large variations depending on cancer type. Although this study did not reveal any surprises, it is valuable by suggesting key attention points in using the PDX model to screen for efficient personalized anti-angiogeneic treatments.

This manuscript could however, could be further improved by addressing the following points:

Major Compulsory Revisions

1. Multiple reference genes should be selected for Q-PCR data normalization (see e.g. PLoS One. 2013;8(3):e59180), unless the author could explain why TBP alone is better than a set of house keeping genes.

2. To validate the estimate of mouse/human cell ratio in the xenografts, the authors should show the accuracy of the estimates by performing a standard curve obtained from a set of artificially created mouse human cell ratio (mouse/human: 0/100, 10/90, …, 90/10, 100/0).

3. The current analysis is overtly simple. There is much more the authors could do with the data. They should perform, for example, cluster analysis and principle component analysis on the 150 xenografts (having ten Q-RT-PCR values each) to show variance within and between tumour types and the order of genes regarding their discrimination value.

4. The authors should point out better that the human TEC could come from two sources: 1) Primary tumour resident “normal” endothelial cells and 2) Endothelial like cells converted from tumour cells. They should also emphasize that this study was not able to discriminate between these two sources.

5. The authors should provide immunohistochemistry analyses on tumor samples. For example, co-staining of TEC markers (CD31+/CD105+) with human mitochondria marker will show the human TEC component. The quantitation of immunohistochemistry sections should agree with their estimates based on Q-RT-PCR data.
6. The data described in the last paragraph of the result section is surprising. The author should discuss this in more depth. From this data, it looks that the mouse blood vessels respond to AVASTIN better than the human. According to the literature however, AVASTIN inhibits hVEGF better than mVEGF.

7. The authors should give a more detailed description of the PDX. For example, what passage(s) were used for their analysis, what was the stage/or grade of the primary cancer?

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**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