Reviewer's report

Title: Fast growth associated with aberrant vasculature and hypoxia in fibroblast growth factor 8b (FGF8b) expressing PC-3 prostate tumour xenografts

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Reviewer: Jehonathan Pinthus

Reviewer's report:

I have reviewed the manuscript by Tuomela et al entitled "Fast growth associated with aberrant vasculature and hypoxia in fibroblast growth factor 8b (FGF8b) expressing PC-3 prostate tumour xenografts"

This paper aims to investigate the angiogenic effects of FGF8b on the growth of PC3 xenografts. The authors compare it to the angiogenic effects of VEGF. They clearly show that while both FGF8b and VEGF induce neo vasculature in the xenografted tumors and while both promote tumor growth, the neo-vasculature induced by FGF8b does not contribute to the perfusion and oxygenation of the tumor, and the growth advantage is potentially mediated by pro-proliferative effects despite the hypoxic conditions.

The authors should be acknowledged for their labor intense study. However my main problem is with their experimental model: The study is based on over-expression of these angiogenic factors. I could not find any mentioning of the native FGF8b and VEGF expression of these factors in the parental PC3 cells. Moreover it is important to report the expression of VEGF in the FGF8b transfected tumors and that of FGF8b in the VEGF transfected tumors as in "real life" the balance between these factors dictates the tumor's behavior. Obviously over-expression of one or the other factors does not reflect the native status of the tumor and can counteract the effect of the natively expressed factors. In that respect adding loss of function experiments (i.e silencing/ knock down of FGF8b) is expected to provide important information and consolidate their findings.

I am aware however that this means a significant amount of experiments and would thus suggest the following so that the readers can get a more balanced view:

1. Change the title from "...(FGF8b) expressing PC-3 prostate tumor xenografts to "...(FGF8b) over-expressing PC-3 prostate tumor xenografts

2. Add into the discussion a paragraph discussing the limitations of the experimental system

Two other issues:

In the methods section of the abstract the authors state that they studied apoptosis. I could not see an evidence for that in the text. Please clarify 2. The
last sentence in the conclusion section of the abstract is too decisive for the level of data presented in the paper. The rest of the conclusions are good enough without it.