Author's response to reviews

Title: A reproducible brain tumour model established from human glioblastoma biopsies.

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Author's response to reviews: see over
Dear sirs,

We are most delighted to hear that our manuscript is now accepted. As suggested by the editor, we have tried to further improve the manuscript in response to the reviewers comments to our revised submission. According the reviewer 2, we have corrected some typographical errors and discussed some of the mechanistic data in relation to the phenotypic switch observed in the xenograft tumors. However, from the attached comments by reviewer 3, no further changes were suggested, as she found that the revisions already made addressed her concerns. Thus, we hope the editor will find our revisions satisfactory.

Yours sincerely,

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Response to referees:

Re 2: The author have provided an adequate update on their manuscript, however, the most exciting issue in the paper namely a switch from diffusely infiltrative phenotype to a more mass forming tumor in the early and late passage tumor sphere need further development. I would like to know what will happen if the author keeps and passage the tumor spheres in vitro for a longer period and then implant the spheres from the higher passage number. Will these spheres then form a mass lesion?

Au: The experiments also included spheroids that underwent prolonged culture in vitro, of 60 days (table 1). These spheroids were also tumourigenic at high take rates, maintained their invasive features, and did not differ from spheroids implanted after 3-4 days of culture in vitro. However, these findings have now been mentioned more specifically in the result section: “Culture time in vitro of the biopsy spheroids did not impact on tumour histology in these experiments as spheroids cultured for both 3 days and 60 days grew highly invasive.”

Re2: There is a couple of typos in the discussion section, the authors may want to recheck such as "microhemorrage” to microhemorrhage.

Au: These typos have now been corrected.

Re2: I still think it would be a land mark paper if the authors can incorporate some of the mechanistic data on the "transition switch" if ever possible as in their previous publication.

Au: The mechanistic data has been published in one of our previous paper cited in this submission. Furthermore, we have now included a brief discussion of these data in relation to our main findings in this current submission: “Moreover, gene expression profiling and protein arrays demonstrated that this phenotypic shift coincided with alterations in signaling pathways [1]. Whereas components of the Wnt, PI3K, and NF-kβ signaling pathways were overexpressed in the invasive first-generation tumors compared with the high-generation tumours, the Ras signaling pathway was up-regulated in the high generation tumors.”

Re3: This revised version constitutes a much improved manuscript which should be of interest to the readership of BMC Cancer. The authors have addressed all the comments raised by this reviewer.

Au: No additional changes have been made in response to reviewer 3.

References: