Author’s response to reviews

Title: The use of biofluorescence and high-frequency ultrasound imaging for in vivo evaluation of gene therapy vectors

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Author’s response to reviews: see over
Dear Editors,

Thank you for sending the reviewers’ comments on our revised manuscript MS: 4742994769083315.

In our second revision of this manuscript, we have addressed the typographical error spotted by reviewer 3 (page 12, line 10) and note that both reviewer 3 and reviewer 4 are now entirely happy with the manuscript and deem it to be interesting and worthy of publication in BMC Medical Imaging.

There is obviously some misunderstanding of this manuscript by reviewer 1 and we are somewhat surprised that this reviewer has now stated that the manuscript is not of sufficient interest to warrant publication in BMC medical imaging. However, we have specifically addressed the 2 comments made by this reviewer, as detailed below in the amended manuscript, to improve clarity and to avoid misunderstanding.

Given the length of time that this paper has now been under review and the fact that we have fully addressed all reviewers’ comments, we hope that this manuscript is now acceptable for publication in your journal and would appreciate a rapid editorial decision on this.

Many thanks and best wishes,

Dr Nicola Ingram

Reviewer 1 comments

Comment 1. The authors hypothesized that GFP gene acts on tumour growth. What is the mechanism or biological basic? Is there any support from previous research? The authors thought it an unexpected result. Since the hypothesis is unstable, the results, such as lobe formation and increased growth, are not reliable enough.

The authors DO NOT directly hypothesise that GFP is affecting tumour growth in this system. Indeed we are suggesting that it was either something within the vector backbone or indeed high levels of GFP that causes lobe formation as this was not observed in uninfected cells. The exact mechanism of lobe formation is far beyond the scope of this paper and is secondary to the fact that we are able to detect and image effects of viral vectors in vivo.

Comment 2. “The lighter areas corresponded to denser tumour tissue” is not the rule in ultrasonics. The authors could ask for advices from specialists in ultrasonics.

The confusion here seems to arise from the fact that we are referring solely to relative greyscale intensities and tissue appearance within the xenograft tumour and confirm the interpretation with tissue histology. We routinely work with sonographers and experts in ultrasound which is irrelevant given the data presented.
However, we have reworded the text (page 10, line 23) to make it clearer that we are describing areas within the xenograft only and that tissue histology shows that the lighter greyscale areas were not due to adipose tissue (as previously suggested by reviewer 1) and that darker areas within the xenografts corresponded to areas of necrosis which often contained a liquefied core as we have previously responded to this reviewer.