Dear Journal of Visualized Experiments editorial office,

This letter accompanies submission of a revised version of the manuscript JoVE58600

entitled, “From Start to Finish: A Guide for the Development and Angiographic Use of the Rabbit VX2 Model for Liver Cancer.” We thank the reviewers for their careful appraisal and suggested revisions, which have resulted in a strengthened manuscript. Responses to specific requested revisions are listed below, addressed after each reviewer comment. Also, please note that both an annotated and clean revision of the paper has been resubmitted.

Editorial Comments:  
  
• Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammatical errors.

**RESPONSE: We have reviewed the manuscript as suggested.**   
  
• Please include an ethics statement before your numbered protocol steps indicating that the protocol follows the animal care guidelines of your institution.

**RESPONSE: An ethics statement has been added, as requested (line 68-69, Ethics Statement: “The following protocol follows all requirements and guidelines mandated by the University of Illinois - Chicago. It was reviewed and approved by IACUC prior to execution.”**  
  
• Protocol Detail: Please note that your protocol will be used to generate the script for the video, and must contain everything that you would like shown in the video (e.g. all surgical tools and actions need to be mentioned, oxygen flow rate, dosages etc.). Please ensure you answer the “how” question, i.e., how is the step performed? Alternatively, for steps that will not be filmed, add references to published material specifying how to perform the protocol action. There should be enough detail in each step to supplement the actions seen in the video so that viewers can easily replicate the protocol.

**RESPONSE: We have reviewed the manuscript as suggested.**  
  
• Protocol Highlight: Please highlight ~2.5 pages or less of text (which includes headings and spaces) in yellow, to identify which steps should be visualized to tell the most cohesive story of your protocol steps.

1) The highlighting must include all relevant details that are required to perform the step. For example, if step 2.5 is highlighted for filming and the details of how to perform the step are given in steps 2.5.1 and 2.5.2, then the sub-steps where the details are provided must be included in the highlighting.  
2) Some of your shorter protocol steps can be combined so that individual steps contain 2-3 actions and maximum of 4 sentences per step.  
3) The highlighted steps should form a cohesive narrative, that is, there must be a logical flow from one highlighted step to the next.  
4) Please highlight complete sentences (not parts of sentences). Include sub-headings and spaces when calculating the final highlighted length.  
5) Notes cannot be filmed and should be excluded from highlighting.  
6) Please bear in mind that anesthesia/euthanasia will not be filmed and should not be highlighted.

**RESPONSE: Tumor Implantation and fluoroscopy have been highlighted.**

• Discussion: JoVE articles are focused on the methods and the protocol, thus the discussion should be similarly focused. Please ensure that the discussion covers the following in detail: modifications and troubleshooting, limitations of the technique, significance with respect to existing methods, future applications and critical steps within the protocol.

**RESPONSE: We have reviewed the manuscript as suggested.**  
  
• Figures:

1) Please number your figures 1, 2, 3 etc and avoid the current hyphenated number scheme.  
2) Please ensure that figures are called outs at appropriate locations in text.  
3) Please add scale references to all figures where relevant.

**RESPONSE: All figures were renumbered. Scale was added were relevant.**

• Please define all abbreviations at first use.  
**RESPONSE: We have reviewed the manuscript as suggested.**

• Please use standard abbreviations and symbols for SI Units such as µL, mL, L, etc., and abbreviations for non-SI units such as h, min, s for time units. Please use a single space between the numerical value and unit.

**RESPONSE: We have reviewed the manuscript as suggested.**  
  
• If your figures and tables are original and not published previously or you have already obtained figure permissions, please ignore this comment. If you are re-using figures from a previous publication, you must obtain explicit permission to re-use the figure from the previous publisher (this can be in the form of a letter from an editor or a link to the editorial policies that allows you to re-publish the figure). Please upload the text of the re-print permission (may be copied and pasted from an email/website) as a Word document to the Editorial Manager site in the "Supplemental files (as requested by JoVE)" section. Please also cite the figure appropriately in the figure legend, i.e. "This figure has been modified from [citation]."

**RESPONSE: No figures or tables from previous publications were used.**

Comments from Peer-Reviewers:   
Reviewer #1:  
  
Manuscript Summary:  
The description of VX2 model in rabbit is in detail and would be useful for the experiment of other, so it was interesting.  
  
Minor Concerns:  
1. In line 84, cause the hair of rabbit was not easy to shave, so do you have better method to do this? If you have some trick, please add it into the manuscript.

**RESPONSE: The following has been added to the manuscript: “Note: Rabbit fur is difficult to shave. It is recommended that the researcher perform multiple passes, first focusing on clearing a bulk of the fur and then pressing the clippers against the skin and going against the grain.”**

2. In line 204, the volume or size of tumor piece should be clear in here.  
**RESPONSE: Placed a size estimate in the line in question. Now in line 213.**  
  
Reviewer #2:  
  
Manuscript Summary:  
The Manuscript is well-structured and describes the methods for the development of VX2 rabbit liver model and its use for the study on liver cancer.  
  
Major Concerns:  
None  
  
Minor Concerns:  
The bibliography needs to be improved.  
Please add:  
  
1) Induction of VX2 para-renal carcinoma in rabbits: generation of animal model for loco-regional treatments of solid tumors.  
Bimonte S, et al. Infect Agent Cancer. 2016.  
Authors  
Bimonte S,Leongito M, Piccirillo M, Tamma ML, Vallifuoco M, Bracco A, Mancini A, Di Napoli D, Castaldo S, Cozzolino S, Iacobellis F, Grassi R, Granata V, Lastoria S, Curley S, Izzo F  
  
1) Radio-frequency ablation-based studies on VX2 rabbit models for HCC treatment.  
Bimonte S, Leongito M, Piccirillo M, de Angelis C, Pivonello C,Granata V, Izzo F.

**RESPONSE: As requested, added citations to paper in lines 49 and 55.**