Author’s response to reviews

Title: Cytotoxicity of VEGF121/rGel on Vascular Endothelial Cells Resulting in Inhibition of Angiogenesis is Mediated via VEGFR-2

Authors:

Khalid A Mohamedali (kmohamed@mdanderson.org)
Sophia Ran (sran@siumed.edu)
Candelaria Gomez-Manzano (cmanzano@mdanderson.org)
Latha Ramdas (LRamdas@mdanderson.org)
Jing Xu (Jing.Xu@UTSouthwestern.edu)
Sehoon Kim (SehoonKim@sbcglobal.net)
Lawrence H Cheung (LCheung@mdanderson.org)
Walter N Hittelman (Whittelman@mdanderson.org)
Wei Zhang (WZhang@mdanderson.org)
Johannes Waltenberger (waltenberger@ukmuenster.de)
Philip E Thorpe (Philip.Thorpe@UTSouthwestern.edu)
Michael G Rosenblum (mrosenbl@mdanderson.org)

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Author’s response to reviews: see over
July 15, 2011

The Editors  
BMC Cancer  
BioMed Central Ltd,  
Floor 6, 236 Gray’s Inn Road  
London, WC1X 8HB  
United Kingdom

Re: MS 1605395934542378  
Cytotoxicity of VEGF121/rGel on Vascular Endothelial Cells Resulting in Inhibition of Angiogenesis is Mediated via VEGFR-2 by Khalid A. Mohamedali et al.

Dear Editors,

On behalf of my colleagues, I respectfully enclose our revised manuscript for consideration for publication in BMC Cancer. We have modified the manuscript according to the suggestions of the reviewer. As described below, we provide a point by point explanation of how the manuscript has been modified according to the reviewer’s comments. In addition, as requested by the Journal Editorial office, we have formatted the manuscript according to the BMC Cancer template on http://www.biomedcentral.com/info/ifora/medicine_journals, including:

- List email addresses for each co-author (page 1)
- Add a Methods section to the abstract (page 3)
- Add “Authors’ Contributions” and “Acknowledgements” sections (page 21).
- Reformat Table 1 in portrait format and include it at the end of the main manuscript file (page 29).

We have also updated the address of Dr. Jing Xu and Dr. Johannes Waltenberger.

We hope you agree that this manuscript is now acceptable for publication.

Thank you for consideration of our manuscript. My colleagues and I look forward to your favorable response. Please feel free to contact me if there are any questions.

Sincerely,

Khalid A. Mohamedali, Ph. D.  
Department of Experimental Therapeutics  
University of Texas M.D. Anderson Cancer Center  
1515 Holcombe Blvd, Unit 1950  
Houston, TX 77030  
Tel: 713-792-5954  
kmohamed@mdanderson.org
Response to BMC Cancer Reviewer Comments, resubmission due July 22, 2011
“Cytotoxicity of VEGF₁₂₁/rGel on Vascular Endothelial Cells Resulting in Inhibition of Angiogenesis is Mediated via VEGFR-2” by Khalid A. Mohamedali, et al.

Reviewer Comment 1: In Methods under Cytotoxicity and Internalisation of VEGF₁₂₁/rGel and rGel the authors refer to a cytotoxicity assay “as described” with a reference to Veenendaal et al 2002. The reference quoted described three different cytotoxicity assays and the authors should name which is the one to which they refer.
Response 1: We appreciate the Reviewer pointing this out. In the Methods section (page 8, line 7), the following statement has been modified (added portion is italicized here for clarity):

Cytotoxicity of VEGF₁₂₁/rGel and rGel against log phase PAE/VEGFR-2 cells was performed over 72 hours as described for PAE/KDR and PAE/FLT-1 cells.

Reviewer Comment 2: In Methods under Angiogenesis Assessment…. The authors refer to the number of branch point were quantified by two researchers (C.G-M and J.X). Was this done blindly? This should be stated.
Response 2: The assessment was, in fact, done blindly by the two researchers. The statement in question (page 9, line 22) has been modified (added portion is italicized here for clarity), and the Reviewer’s comment is appreciated:

The numbers of blood vessel branch points were independently and blindly quantified by two researchers (C.G-M. and J.X.) and compared with the numbers in the treatment controls

Reviewer Comment 3: Under Results Cytotoxic effects of VEGF₁₂₁/rGel on endothelial cells, the first two sentences beginning “Depending on the number of rGel molecules……” are not appropriate for the Results section and should be moved to the Discussion section.
Response 3: The two sentences in the Results section (page 13) have been deleted. In the Discussion, the second full paragraph on page 18 makes reference to these points, i.e., that the mechanism of rGel-based cytotoxicity may or may not involve apoptosis, and cites the same two references. Therefore, no change was made to the Discussion.

Reviewer Comment 4: Figure 2A uses the abbreviations KDR and p-KDR and yet calls these VEGFR-2 and p-VEGFR-2, respectively in the figure legend. The authors must adhere to the same nomenclature throughout to avoid confusion and use one or the other throughout. I would suggest using the former as this is more readily understood.
Response 4: The authors agree with the Reviewer and appreciate his pointing out the error and his suggested nomenclature. Because the entire manuscript text uses VEGFR-2 rather than KDR, we have opted to use the former nomenclature. We note that the alternative nomenclatures for VEGFR-1 and VEGFR-2 are cited in the second paragraph of the Background (page 5). In addition, the commonly used nomenclature p-KDR is now added in parentheses in the Western Blot Analysis section (page 7) in the Methods. We hope that this is acceptable to the Reviewer.