Author's response to reviews

Title: Drug discovery in ophthalmology: past success, present challenges, and future opportunities

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Dear Editor

Re: Drug discovery in ophthalmology: past success, present challenges, and future opportunities

Thank you for your email dated 18th September 2015. We are very grateful to the reviewers for their comments and welcome the opportunity to submit a revised manuscript. We were pleased that the reviewers considered this to be an article of importance in the field. The reviewers raise a number of interesting points and we have addressed their recommendations below:

Reviewer 1

Reviewer comment (1): “the aim of the review is very poorly reported in the background section, where a generic sentence was reported, “In this review we consider this changing landscape in general and specifically in the context of ophthalmology”. A better specification of the objective would help the reader. Later in the results section, more informations on the objective of the paper are reported, lines 172-176. These informations, should be reported and detailed in the background section, and their reporting here make the line of the story very complicated and difficult to understand.”

Author Response (1): We have amended the background section to provide a clearer description of the objective of the review.

Reviewer comment (2): “As consequence, in example, it is difficult to evaluate what is included in the "past success" paragraph: why the authors included only informations on anti VEGF drug, and
no more informations on other ocular drug discovery. An explanation about this "single" reporting, is needed.

**Author Response (2):** Thank you. We believe that the alteration of the Background now highlights that the ‘anti-VEGF’ story is being utilised as an instructive case-study of success but that this contrasts with the increasing failure rates of other pipelines. In order to have more major breakthroughs such as the anti-VEGFs we need to look at the principles of drug discovery across the sector and see how these can apply to ophthalmology (as discussed in the later sections of the article). As highlighted by the reviewer we are not trying to provide an exhaustive list of drug discovery successes in ophthalmology.

**Reviewer comment (3+4):** The authors reported that they will consider “...what these challenges are and discuss how they are being addressed in the industry as a whole and how this compares to the ocular drug discovery sector.” Mixing the problems of the ocular drugs discovery with that of the general industry, could make the reader quite confused on the content of the paper. Moreover, we found that the drug discovery problem in general is poorly addressed, and above all, poorly answered. - To increase the linearity of the story, we suggest to make the review more focused on the ocular drug discovery problems, and to try a more detailed definitions of the scope, as well as a better definitions of the paragraph's content.

**Author Response (3+4):** We appreciate the reviewer’s consideration on this, but in this instance we respectfully disagree. We feel that it is a key strength of this paper that we encourage people to consider these issues side by side - a view shared by the other reviewer. We trust that our clarification of the aims and purposes within the introduction section (and within the abstract) will ensure that readers are clear about the intention, and can be both informed but also encouraged to think ‘outside the box’ on this. We agree with the reviewer that the key issue is to provide better clarification of the aim and scope of the article."

**Reviewer 2**

**Reviewer comment (1):** I plaude the authors for their very interesting review paper. I suggest the authors to introduce some summary table of drugs and phase of development (I to IV) results of trials etc.. in order to help the readers in having a more precise scenario.

**Author Response (1):** We thank the reviewer for their kind comments. We have added a summary table of glaucoma drugs in phase II and III. Whilst this list is not exhaustive it should give the reader a clearer idea of the range of new drugs that are in the later stages of development.
Thanks for your positive comments regarding our article. We hope that we have addressed the reviewers’ comments adequately but would be happy to provide further clarification or additional information as necessary. We eagerly await your final decision regarding our manuscript.

Yours sincerely,

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