

ANSWERING REVIEWERS



November 14th 2013

Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 6093-Edited-Review.doc).

Title: CFTR chloride channel blockers: pharmacological, biophysical, and physiological relevance

Author: Paul Linsdell

Name of Journal: *World Journal of Biological Chemistry*

ESPS Manuscript No.: 6093

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated.
2. Revisions have been made according to the suggestions of the reviewers:
 - (1) (reviewer no. 00225325) – no comments
 - (2) (reviewer no.00227526) – no comments
 - (3) (reviewer no.02446659) – Figure 1 has been expanded to show the location of several key blocker-interacting residues from four different TMs, both in 3-dimensional (new Figure 1D) and 2-dimensional (new Figure 1E) representations of the TMs. I hope this

will make the location of important residues more apparent to the reader. I have retained Figure 3 in its original format as this figure is meant to illustrate a very different point, namely the relative location within the pore (and depth along the axis of the pore) of different sites to which the crucial blocker-interacting positive charge can be moved by mutagenesis. In other words, Figure 3 is a representation of the results of mutagenesis experiments whereas Figure 1 shows different representations of overall pore architecture.

I hope that these additions and clarifications will be sufficient to address the reviewers' concerns. Thank you again for publishing my manuscript in *World Journal of Biological Chemistry*.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Paul Linsdell". The signature is fluid and cursive, with the first name "Paul" written in a larger, more prominent script than the last name "Linsdell".

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