To Reviewer 1:

Thank you for your detailed review and valuable suggestions for revision. We have revised the manuscript according to your suggestions as follows:

Question 1:

My major concern is that authors have four figures and two tables from previous studies. However, authors failed to label these figures and tables in a right way to show if these figures or tables are directly from previous studies (if this is the case, authors should delete these figures and tables) or adopted from previous studies (if this is the case, authors should clearly show they were adopted or summarized from previous studies).

Answer 1:

In response to the reviewers' suggestions, we have removed the original Figure 2 (Line 109) and the original Table 1 (line 171) and Table 2 (line 176) from the manuscript that summarized previous work in the Introduction. We have revised Figure 1 (line 63) to show all the amino acids of cytochrome c that we mutated to determine the effect of evolution from horse to human Cc, a major goal of this paper. This figure is based on a crystal structure of horse Cc in the protein data bank, which we reference in the caption, and has not been published previously showing these amino acids. The original Figure 3 (Now Figure 2) (line 163) has been revised to show all the amino acids that we have mutated to study both the evolution of Cc and the effect of phosphorylation of Cc amino acids (line 163). The crystal structures it is based on are given in the caption. It has not been previously published showing these amino acids. The original Figure 4 (Now Figure 3) (line 234) is the same as in the original manuscript. It has not been previously published showing these amino acids.

Question 2:

Minors:

Abstract: Cc first shows in the manuscript should be listed the full name followed by the abbreviation. Please change the first "Cytochrome" to "Cytochrome c (Cc)".
Line 44, please change "Rb. Sphaeroides" to "Rhodobacter sphaeroides". Etc.

Answer 2:

We have addressed all of the minor points raised by the reviewer. The abbreviations and italics have been revised throughout the manuscript to be consistent. The * in lines 407 and 408 of the original manuscript has been removed. It referred to the excited state of lumiflavin.

All the other minor points were about the Figures and Tables that have been removed or revised, as discussed in Question 1 above.