

We are submitting the manuscript (**resubmission of manuscript no. 25967**) entitled **“Polyphosphate and associated enzymes as global regulators of stress response and virulence in *Campylobacter jejuni*”**, which has been modified in response to the comments of 3 reviewers. The concerns raised by the reviewers were to: 1) summarize the chicken colonization data in a table, 2) rewrite the “poly P metabolism in *C. jejuni*” section to avoid repetition of the authors names, 3) provide subheadings under “PPKs: Role in virulence associated phenotypes” section and 4) cite original research papers in Table 1.

We thank the editor and the reviewers for their thoughtful comments; we agree with the comments made by the reviewers.

Our responses to reviewers’ comments are as follows:

Reviewer 1:

- 1) The section “PPKs: role in chicken colonization” would be aided with a table which summarizes the data. Currently it is difficult to keep track of just as numbers in the main body of the text.

Response: We thank the reviewer for this suggestion. The revised manuscript now includes a new table (**Table 3**) summarizing the chicken colonization data.

- 2) Table 2 is quite useful in providing a summary of mutants and their phenotypes in the context of poly P metabolism. It would be useful though to enhance figure 1 (or add a new figure) which links mutations in the various Poly P metabolic steps to observed phenotypes.

Response: We have summarized all the mutants and their associated phenotypes in Table 2. We believe extending figure 1 by adding the phenotypes associated with the mutants or including a new figure summarizing the phenotypes would be redundant with Table 2.

Specific corrections:

- 1) Page 3 line 83, delete “on” and define PPK.

Response: We have deleted “on” and expanded PPK in line 83.

- 2) Page 4, line 99 replace “of human and animal origin” with “which are human and animal pathogens”.

Response: We have incorporated the suggested changes in line 99.

3) Page 5, 138, correct to “does not”.

Response: We have made the suggested change in line 138.

4) Page 5, line 141, correct to “including a”.

Response: We have made the suggested change in line 141.

5) Page 6, line 154, correct to “the subatomic” and “the origin of the universe”.

Response: We have made the suggested change in line 154.

6) Page 6, line 156 should this be “ten to one hundred”?

Response: We have changed “ten to hundred” to “ “ten to hundreds of” for clarity in line 157.

7) Page 7, line 176, delete the greater than sign.

Response: We have deleted the greater than sign in line 176.

8) Page 7, line 199, would help to refer to Figure 1 at the end of the first sentence in this section.

Response: We have added the reference to figure 1 in line 198.

9) Page 9, line 248, RpoS should be defined.

Response: We have now defined RpoS in line 245.

10) Page 10, line 261, spoT should be defined.

Response: We have now defined SpoT in line 257.

11) Page 10, line 285, “speculate” would be a better word to use here than “wonder”.

Response: We have replaced “wonder” with “speculate” in line 281.

12) Page 11, line 291, the targets of these antimicrobials should be included.

Response: We have added this information in lines 289- 290.

13) Page 11, line 305, in this paragraph what is specifically meant by “naturally competent” and “natural transformation”?

Response: We have now defined natural competence in line 302.

14) Page 12, line 336, should read “The authors”.

Response: We have made the suggested change in line 333.

15) Page 12, line 338, further define AI-2.

Response: We have now defined AI-2 in line 336.

16) Page 12, line 341, with reference to “several genes”, which ones?.

Response: We have now added the gene names in lines 338-339.

17) Page 13, line 363 should read “in colonization” and replace “as to” with “in”.

Response: We have made the suggested changes in lines 359 and 360.

18) Page 13, line 366 “bursa of” should read “bursa”.

Response: We have made the suggested change in line 362.

19) Page 14, line 377 and 378 should read “in colonization” and replace “as to” with “in”.

Response: We have made the suggested changes in lines 373 and 374.

20) Page 14, line 397, should read “display no or reduced colonization”.

Response: We have incorporated the suggested change in line 393.

21) Page 15, line 433, what are the “several phenotypes”?.

Response: We have now added the phenotypes in lines 430-432.

22) Page 17, line 483, should read “overlap”.

Response: We have made the suggested change in line 481.

23) Page 17, line 488, should read “the enzymes”.

Response: The suggested change is incorporated in line 485.

24) Page 19, line 529, should read “vaccine candidates”.

Response: We made the suggested change in line 528.

25) Page 19, line 548, should read “proteomics”.

Response: We have made the suggested change in line 547.

26) Page 20, line 574, delete extra full stop and need to cite reference with respect to IL-8 work.

Response: We have deleted the extra full stop and cited the reference in IL-8 work in line 573.

27) Figure 1 legend, should read “the PhosP/PhosR” and “the high affinity”.

Response: We have made the suggested changes in the figure legend.

Reviewer 2:

- 1) The paper could benefit from some minor structural changes: - In the Poly P Metabolism in *C. jejuni* section, the author names of the articles under review are repeated quite often. It eventually becomes a bit distracting and would be a stronger section if it was re-written slightly to reduce the repetition.

Response: We have modified the “Poly p metabolism in *C. jejuni*” section to avoid repetition of authors’ names in lines 205, 208, 211-212, and 217-218.

- 2) In section PPKs: Role of virulence-associated phenotypes, the reader would benefit from short subheadings if they journal allows it (ABR, Motility, Biofilms, etc).

Response: We have now added subheadings under “PPKs: Role in virulence-associated phenotypes” section in lines 311 and 340.

- 3) Line 488 needs a space between the_enzymes - Line 574 has two periods

Response: We have made the suggested corrections in lines 485 and 573.

Reviewer 3:

- 1) My main comments are on Table 1. 1. Table 1 is a summary of *Campylobacter* infections in humans. For a table like this, the authors should cite original papers rather than simply take information from another review paper. Please cite original research papers for information included in Table 1. 2. Please ensure that precise information is included in the Tables. For example, in Table 1, it is written that Gut dysbiosis is a risk factor for *C. concisus*, *C. showae*, *C. hominis* et al. human infections? The authors need to provide evidence for this by citing original research papers.

Response: We have now cited the original research papers for the information included in Table 1.