

## Answers to reviewers comments

We thank the Editor and the Reviewers for their thoughtful comments and constructive suggestions. Our response is as follows:

Reviewer #1. *"Apart from minor editing and language polishing, the letter is well written and an overall constructive feedback is adequately covered".*

Reply: We appreciate the reviewer #1 for his positive feedback. The paper has been thoroughly edited and a number of words/sentences have been substituted or re-phrased appropriately, according to the reviewer's suggestion.

Reviewer #2. a. *"The message provided by the authors is very interesting, but it is not sustained by any data or methodological details. We have to believe the assertion that "several other genes coding for transmembrane ABC transporters....., efflux proteins..... were...significantly upregulated..." and that "enhanced biofilm production was primarily attributed to downregulation of mketK and luxS genes.....". A table and/or a figure would aid in the evaluation of the scientific validity of this communication.*

b. *"...minor language polishing."*

Reply: We thank the reviewer #2 for his constructive comments. a. We have now included certain methodological details in brief (main text, lines 13-16) and a representative figure from our data analysis (GeneSpring software) together with a descriptive legend that provides additional information regarding the methods applied to our current research, according to the reviewer's suggestion.

b. The paper has been thoroughly edited and a number of words/sentences have been substituted or re-phrased appropriately, according to the reviewer's suggestion.

Reviewer #3. *"The Letter to the Editor comments on the recent findings by Attaran et al., reported in WIG (ref. 1), regarding the role of Hp-formed biofilm in a decreased susceptibility of the bacterium to antibiotics. The authors of the Letter suggest that sublethal concentrations of antimicrobial peptides, including defensins (h $\beta$ Ds) may actually promote the enhancement in Hp biofilm formation, and hence affect the resistance of Hp to antibiotic. However, neither the original publication, Ref.1, nor the Letter take under consideration the fact that gastric mucosa does not*

*present a stationary surface, but has a fast rate of epithelial renewal. Hence, the question is how this so-called Hp biofilm can form and persist under these dynamic conditions ?”*

Reply: We appreciate the reviewer #3 for his valuable comment. Despite the use of well-validated techniques, our *in vitro* studies, have certain limitations. Establishing successful *in vivo* models to study biofilm formation in the context of the dynamic interface of Hp-epithelial crosstalk remains a challenge that needs to be addressed in the future. Furthermore, future studies will have to consider that individual genomic variability affecting defensin expression may dictate Hp-related disease susceptibility. Therefore, we have added a final sentence in the revised version, in response to the reviewer’s comment.

Reviewer #4. *“The Letter has complementary data on the article by Attaran et al., However, some revisions should be made, such as references and grammar of the text”.*

Reply: We thank the reviewer #4 for his comments. The paper has been thoroughly edited and a number of words/sentences have been substituted or re-phrased appropriately. Additionally, we have carefully reviewed the references section and removed redundancies as shown in the revised manuscript, according to the reviewer’s suggestion.