Reviewer n<sup>o</sup> 1:

Dear reviewer,

Thank you for your great review and valuable comments on our manuscript. The suggestions you provided were crucial in improving the quality of our article. In order to respond to your suggestions, below are the point-by-point changes that were made:

- We made changes to figure 1 to better illustrate what was covered in the manuscript, and also added other figures in order to improve the quality of the article, and we mentioned all graphical representations in the text. (Highlighted in yellow in the manuscript file)
- We wrote the abbreviations in full the first time they appear in the text. (Highlighted in pink in the manuscript file)
- 3. We detail the mechanism that explains how increasing nickel concentration leads to a decrease in NikS expression, which in turn downregulates CagA levels, while high nickel concentration leads to an increase in CagA levels. In addition, we have included new figures for the main topics of the text to improve the quality of the article. (Highlighted in red in the text)
- 4. We added summaries to the SMALL REGULATORY RNAS and POST-TRANSCRIPTIONAL REGULATION OF *H. Pylori* VIRULENCE FACTORS BY NikS topics as requested. (Highlighted in blue in the text)
- 5. We corrected language errors throughout the text and the manuscript underwent a complete language review by a native English speaker. In addition, we made language changes, as well as reformulated some sentences to make the text clearer and more structured and, thus, improve the reader's understanding of the subject.

Reviewer nº 2:

Dear reviewer,

The comments you made on our manuscript were very important in improving its quality and we appreciate your crucial help. Here are the peer-to-peer changes as per your suggestions:

- 1. We have corrected language errors throughout the text and the manuscript has undergone a complete language review by a native English speaker. In addition, we made language changes, as well as reformulated some sentences to make the text clearer and more structured and, thus, improve the quality of the study.
- Replaced the word "Aspects" and corrected errors in the word "CagA" throughout the text as requested. (Highlighted in orange in the manuscript file)
- 3. We chose to change the title of the article as suggested, since the objective of the article is to address the most important and current information about NikS in the control of *H. pylori* virulence factors and the potential clinical repercussions of this modulation, therefore, we are unfortunate in the old title of the study which implies that other RNAs would be addressed. (Highlighted in green in the manuscript file)
- 4. We have included essential information about the NikR (Nickel Responsive Transcriptional Regulator) protein for the convenience of readers. (Highlighted in gray in the manuscript file)
- We address the role of Nicks in other virulence factors of *H-pylori* such as VacA and OMPs respecting the limited evidence available on the subject. (Highlighted in pink in the manuscript file)
- We created new figures for the main topics of the text to improve the quality of the article and make it more understandable for the reader. (Highlighted in red in the manuscript file)
- We have added a topic in the text that addresses the future of research, the main gaps in NikS regulation of *H-pylori* virulence, as well as the perspectives of our study as requested. (Highlighted in purple in the manuscript file)