

**Reviewer #1:**

The Letter to the Editor entitled: "Candida accommodates non-culturable *Helicobacter pylori* in its vacuoles" touches on a very interesting topic, which has been under debate. However, the letter is formulated in a confusing manner. Hence its not clear which points are the actual hard core experimental facts provided by Siavoshi et al., Alipour et al., or those of the authors, to vote for or against one of the sides of the argument. I therefore recommend that the authors create a tables with 3 specific columns, listing each of the mentioned pieces of the experimental evidence provided by the 3 mentioned research labs and end with a very clear calculation of the scientific weight of each column, leading to a firm conclusion. Thus to bring this argument to a scientific closure.

**Response #1:**

To enhance the comprehension and ensure clarity, we designated the author of this review and the response letter as proponents while referring to the author of the December 2017 letter, who holds a divergent viewpoint, as an opponent. In the revised manuscript, we added a table with 3 specific columns, and present the views of the three parties, this table we named Table 1.

Table 1 Divergent perspectives about the intracellular occurrence of *H. pylori* inside *Candida*

Experimental facts and conclusions from Farideh Siavoshi and Parastoo Saniee (proponents) <sup>[2-8]</sup>	The opposing view from Nader Alipour and Nasrin Gaeini (opponents) <sup>[1]</sup>	Experimental facts and conclusions from our lab <sup>[9]</sup> .
The yeast cell can serve as a specialized niche and environmental reservoir for <i>H. pylori</i> . Koch's postulates aren't applicable.	Since Koch's postulates were not practiced in the study of <i>H. pylori</i> internalized <i>Candida</i> . The hypothesis that the yeast can act as the vehicle for transferring <i>Helicobacter</i> into humans is incorrect.	Although no live <i>H. pylori</i> have been cultured from <i>Candida</i> cells, <i>H. pylori</i> -specific genes, antigens, and urease activity are positive in these <i>Candida</i> strains. The potency of <i>H. pylori</i> internalized <i>Candida</i> in disease transmission and pathogenicity can

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The IgY- *H. pylori* antibody has been used as a marker for localizing *H. pylori* inside yeast vacuoles.

The presence of *H. pylori* in yeast cells demonstrated by IgY- *H. pylori* is inaccurate.

be determined by molecular Koch's postulates.

The presence of *H. pylori* in vaginal and fecal *Candida* has been determined through immunofluorescence microscopy with IgG- *H. pylori*.

The intracellular occurrence of *H. pylori* inside the vaginal yeast of expectant mothers provides potency for the transmission of *H. pylori* to newborns through vaginal yeast.

The intracellular occurrence of *H. pylori* inside yeast is not reliable. If yeast can host *H. pylori*, the prevalence of *H. pylori* infection should be higher in females than in males due to the higher yeast infection rate in the female population. However, the situation is the other way around.

The intracellular occurrence of *H. pylori* inside vaginal *Candida* of mothers and fecal *Candida* of newborns has been determined and suggests the transmission of *H. pylori* to newborns through vaginal yeast.

Our experimental results and perspectives are consistent with Farideh Siavoshi and Parastoo Saniee (proponents).

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**Editor:** When revising the manuscript, it is recommended that the author supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply PubMed, or a new tool, the Reference Citation Analysis (RCA), of which data source is PubMed. RCA is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>, or visit PubMed at: <https://pubmed.ncbi.nlm.nih.gov/>.

**Response:** We used the RCA system to analyze our research field and found a related article: Role of amoebae for survival and recovery of 'non-culturable' *Helicobacter pylori* cells in aquatic environments (FEMS Microbiol Ecol, 2021; 96: 5902844). Although this article also studies the 'non-culturable *Helicobacter pylori*', the content is related to amoebae, and has little to do with candida concerned in this article, so we do not cite and comment. Other relevant contents are mentioned and commented in the references.