Reviewer1:
This manuscript presents the data, obtained with human and animal gastric epithelial cells, that Hp. Infection leading to gastric carcinogenesis exhibit reduced expression of a gap-junction protein, Cx32. Further, the results show that inhibited transcription of PBX1 factor leads to Cx32 upregulation. Using dual-luciferase reporter assay, it is concluded that PBX1-Cx#2 targeting site could offer a new insight to the mechanism of Hp-induced gastric carcinogenesis. The topic is well presented and the interpretation of the results is based on a solid experimental evidence. My only suggestion is that you should check the text for grammar, spelling, and the word usage (i.e., disintegrity ? or syncronized?).

A: Thank you for your kindly suggestion, and we have tried our best to optimize the word usages and spelling/grammar by ourselves and with the help of language editing services.

Reviewer2:
In the introduction it is recommended to introduce also genetic risk for Gastric cancer, not only the H. pylori gastritis-cancer chain. Altough, this is more evident in Caucasian patients. Figure 4 could be implemeted by PBX1 and Cx32 immunohistochemistry.

A: We highly appreciate the first suggestion and we have put the genetic factors of GCs at the very beginning of introduction part.

As for the second suggestion, it is unfortunate to show the positive signals in Mongolian Gerbils tissue due to the issue of species. Though a series of IHC experiments were conducted, no PBX1 or Cx32 antibodies (anti-mouse and anti-Rat from made by different companies) work on Mongolian gerbils. We are hoping that this part be implemented in our further manuscripts.

Reviewer3:
This is very well designed, performed and written clinical and experimental study for analyzing of impact of Helicobacter pylori on downregulation of connexin32 (CX32) in gastric mucosa epithelial cells and its association with gastric carcinogenesis. This study is an extension of the previuos study of the authors concerning the expression of Cx32 in human adenocarcinomas. The authors used the clinical specimens of gastric mucosa obtained from patients who made gastroscopy as well they used animal tissues from Mongolian gerbils. The authors used a large panel of methods, like RT-PCR, Western blot, transcriptional factor/DNA array and plasmid construction and dual-luciferase assay The authors found that H. pylori retarded gap junction function by

significant reduction of Cx32 expression and trigger the important augmentation of transcription factor PBX1 which is associated with gastric carcinogenesis. This clinical investigation gives an additional knowledge to understand the role of H. pylori in gastric carcinogenesis and therefore have an important clinical outcome. The study is set up correctly. The paper is written well. Introduction gives a good overview of the study background and the authors raised clearly the aim of the study. The aim of the study is fulfilled. The material studied is large enough and allows to drawn the conclusions. The Figure of high quality give a good overview about the results. However, the following point needs to be considered: 1. In Material and method by description of the patients studied is necessary to mention the number of the persons studied, also the age, gender, as well as to present more precisely the diagnosis and the localization of gastritis or gastric carcinoma.

A: Thanks for this valuable suggestion to make our manuscript understandable in the field of clinical research. We thus mainly revise in the M&M part as follows: 1) add the sentence "Clinical specimens of gastric antrum mucosa were obtained from a total number of 4190 patients". 2) add Table 1 that shows the clinical characteristics of the study population such as the age, gender, disease duration. 3) For the endoscopic and pathological diagnosis, the detailed criteria are the combination of 8th edition of the Cecil Essentials of Medicine, Chinese consensus on chronic gastritis and Chinese guidelines for diagnosis and treatment of gastric cancer (2011 edition). Since these criteria could be found in our previous paper "Wang Y et.al. Connexin 32 and 43 promoter methylation in *Helicobacter pylori*-associated gastric tumorigenesis", we cited this reference in this revised manuscript to avoid hundreds of words redundancy.