

Dear editor,

Thank you for your helpful comments. We have revised our paper accordingly and feel

that your comments helped clarify and improve our paper. Please find our response (in

red) to reviewer's specific comments (in black) below.

#### Response to reviewer 1

Comment 1: The role of E2F1 and Mi-RNA-34 family in gastric cancer and drug resistance of gastric cancer are well recognized (see references below), therefore the authors should clearly spell out what is new in their paper comparing with the literature.

Reply: Wang AM et al. showed that miR-34 family inhibited gastric cancer tumor formation by down-regulating the Yin Yang 1 gene, while Riquelme et al. revealed that miR-34a/b inhibited cell survival and drug resistance by down-regulating Bcl2 and NOTCH proteins. Both studies discuss the effects of miR-34 family on gastric cancer cells by the downstream mechanism of miR-34 family. While the innovation of this paper is that from the perspective of the upstream regulatory factors of miR-34c, the specific mechanism that E2F2 and miR-34c jointly regulate the drug resistance of gastric cancer cells is elaborated -- silencing E2F2 inhibits resistance of gastric cancer cells to paclitaxel combined with cisplatin through targeted up-regulation of miR-34c.

Comment 2: Numerous studies demonstrated that in significant proportion of gastric cancer H. Pylori genome is incorporated into cancer cells. The authors should at least elaborate on that and how this would change potential role of E2F1 and Mi-RNA-34

Reply: Thank you for your advice. Indeed, Yousefi et al. [1] studied that H. Pylori could regulate cell process-related pathways by regulating miRNA, so the apparent regulation of h. Pylori cannot be overlooked in the molecular mechanism of gastric cancer. How H. Pylori genome affects the E2F2/ mirR34c axis will be further discussed in our follow-up experiments.

Comment 3: The paper would significantly benefit from including a diagram representing graphically representing the role of E2F1 and Mi-RNA-34 in gastric cancer and its resistance.

Reply: Thank you for your suggestion, the related mechanism diagram has been added as Figure 7.

Comment 4: The paper requires extensive linguistic revisions.

Reply: The language has been modified and refined. We appreciate your comment and suggestion that this reference provided.

Response to reviewer 2

Reply: Thank you for the referee's kind attention.

Best regards,

Hong Zheng