

In this review, the authors summarized recent research progress on the mechanism of ferroptosis and its role in gastrointestinal tumors. Ferroptosis is characterized by iron accumulation, excessive ROS production, and overwhelming lipid peroxidation, and is well known for a specific mechanism of sorafenib, but it is a mechanism that has recently attracted attention in the area of gastrointestinal disease, especially cancer. The topic is very appropriate, but there are some issues to raise.

1. The main content was not focused on gastrointestinal cancer. In the "Introduction" section, it is necessary to supplement the non-clinical and clinical background why ferroptosis is attention in gastrointestinal cancer in detail.

**Answer:** Thanks for your comments. We have revised the 2<sup>nd</sup> paragraph of the "Introduction" section to supply some non-clinical and clinical background why ferroptosis is attention in gastrointestinal cancer.

2. Most of the content that follows the Introduction section is the general theory of Ferroptosis. Therefore, an association with gastrointestinal cancer must be included in each paragraph.

**Answer:** Thanks for your comments. The association between the general theory of ferroptosis and gastrointestinal cancer has been illustrated in different sections of gastrointestinal cancer, such as "Ferroptosis and pancreatic cancer", "Ferroptosis and liver cancer", and "Ferroptosis and other GI tumors" part. Therefore, we don't think it is necessary to talk about the issue in "MECHANISM AND REGULATION OF FERROPTOSIS" section.

3. The full contents must be filled out from the table indicated by the author. The origin and mode of action of each inducer and inhibitor, as well as many applications including gastrointestinal cancer, must be described. Please refer to the section "FERROPTOSIS INDUCERS AND INHIBITORS".

**Answer:** Thanks for your comments. We have filled out the table in the section "FERROPTOSIS INDUCERS AND INHIBITORS", especially the target and function of each inducers and inhibitors. However, our aim of summarizing this part is to list the common inducers and inhibitors in the current research, and their sites of action, so as to provide hints for their subsequent research in gastrointestinal tumors. Additionally, The purpose of this article is not to summarize the sources, findings, structures, specific mechanisms, etc. of inducers and inhibitors in detail. As for the applications of some inducers and inhibitors in gastrointestinal cancer, we have summarized in separated parts that follows the section "FERROPTOSIS INDUCERS AND INHIBITORS".

4. It is recommended to separate the CRC from the gastric cancer section. Please refer to the section “Ferroptosis and other GI tumors”.

**Answer:** Thanks for your comments. We have separated the CRC and gastric cancer section from the section “Ferroptosis and other GI tumors”.

5. The clinical cases that utilize the mechanism of ferroptosis must be summarized separately (eg Sorafenib, Cisplatin). Please cite the following reference: Yanwei Su, et. Al., Volume 483, 28 July 2020, Pages 127-136, Cancer Letters.

**Answer:** We have summarized the clinical cases that utilize the mechanism of ferroptosis in gastrointestinal cancer in separated parts that follows the section “FERROPTOSIS INDUCERS AND INHIBITORS”. And the references you provided helped us a lot, and we decided to cite it.