

Review of: "The Role of Ferroptosis in Inflammatory Bowel Disease: Mechanisms and Therapeutic Implications"

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Potential competing interests: No potential competing interests to declare.

This review article introduces the pro-ferroptosis mechanisms, the role of multiple pathways (e.g., GPx4-GSH, FSP1-CoQ10, GCH1-BH4-Phospholipid, Keap1-Nrf2, and NF-kB pathways) in inhibiting ferroptosis, the mechanism of ferroptosis in Inflammatory Bowel Disease (IBD) on intestinal epithelial cells (IECs), and the role of iron in IBD. The manuscript seems still preliminary. My detailed comments are as follows.

First, Fig. 1 is mentioned in the subheading for section 2.2 (i.e., "2.2. Mechanism of Ferroptosis (Fig. 1)") on page 3. However, the figure is missing in the main text. It would be better to use more figures or tables to summarize different sections of this article.

Second, previously reported ferroptosis inhibitors of various types should be summarized in a table containing some important information, including the mechanism of action, and particularly the ferroptosis inhibitors used in IBD.

Third, the references are insufficient, and many descriptions in the main text should be supported by previous reports/references that are missing in the current form of the manuscript.

Fourth, it seems unnecessary to have an independent section for the role of iron (i.e., "4. The role of Iron in IBD"); alternatively, this content can be merged into section 3.

Fifth, in the "System Xc- and Ferroptosis" part on Page 6, the full name for system Xc- should also be mentioned (i.e., cystine/glutamate antiporter), although it has been mentioned in the "Introduction" section. Moreover, should the phrase "the conversion of cystine (Cys-Cys) to cysteine (Cys)" be changed to "the conversion of cystine to cysteine (Cys-Cys)"? Similarly, for the convenience of readers, the full names for IBD and IECs should also be mentioned in the subheading of section 3 (i.e., "The mechanism of Ferroptosis in IBD on IECs") although they have been mentioned in the "Introduction" section.

Finally, reference 2 lacks a page/article number.