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.

Yan Q. elucidates the impact of Inflammatory Bowel Disease (IBD), comprising Crohn's disease and ulcerative colitis, is a rising global prevalence. Additionally, ferroptosis, a type of cell death triggered by iron-dependent lipid peroxidation, is pivotal in IBD pathology. The author dissects the ferroptosis's mechanisms, including GPx4 and Nrf2-HO-1 pathways, alongside iron metabolism's dual role in intestinal health and disease and explores how ferroptosis influences intestinal epithelial cell death, barrier function, and immune response, and its novel therapeutic use. According to the authors, the novelty of this study is that the exploration of ferroptosis in the context of Inflammatory Bowel Disease (IBD) offers a significant avenue for both understanding and treating this complex condition, delving into the intricate interplay between iron metabolism, intestinal epithelial cell integrity, and immune responses, ferroptosis emerges not only as a cellular event but also as a potential therapeutic target.

Moreover, the dual role of iron, an essential nutrient yet a facilitator of oxidative stress, underscores the delicate balance required in managing IBD. The objectives of this study carry significant importance; however, I have a hard time justifying the fact that there are crucial reviews that came out in the last few years on “the role of ferroptosis in IBD”- like https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10198063/ and/or https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9880170/, it is very hard to understand or differentiate the novel findings in this review compared to recently published studies.

The designs for this review are justified. The introduction and the discussion were written shortly without proper information and references. Several of the discussion points missing crucial information as well as references. Nonetheless, the article seemed to possess good value toward ferroptosis emerging as a potential therapeutic target for IBD. Overall, the clarity of the text needs very readjustments. The manuscript has minor typographical and grammatical errors. In general, the manuscript can accomplish the caliber of quality for consideration for publication in Qeios. The authors are advised to consider the comments below:

Comments:

1. **There are several discussion points without proper references.**

A. Autophagy and Ferroptosis

https://www.nature.com/articles/s41419-023-05978-8

https://www.nature.com/articles/cr201695

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6936238/

A. Immune cells and Ferroptosis
B. The GPX4-GSH Pathway and Ferroptosis
C. The FSP1-CoQ10 Pathway and Ferroptosis
D. GCH1-BH4-Phospholipid Pathway and Ferroptosis
E. The Mechanism of Nrf2-HO-1 Pathway Regulated Ferroptosis in IECs in IBD
F. Endoplasmic Reticulum Stress Regulated Ferroptosis in IECs in IBD
G. The Role of Iron in IBD

1. **Please provide a cumulative figure illustrating all the mechanistic pathways of ferroptosis and how it could be manipulated to treat IBD.**