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LETTER

Taking Precautions When Targeting Ferroptosis in Cancer Patients [Letter]

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Dear editor

We eagerly read the article by Yang et al.[1] This review sheds light on the involvement of ferroptosis as a potential therapeutic approach for cholangiocarcinoma (CCA), a challenging form of cancer. Ferroptosis has gained significant attention in the past decade as a distinct type of cell death, differing from well-known mechanisms like apoptosis. Its relevance has been implicated in various diseases, including cancer.[2]

While we find the review intriguing and appreciate the exploration of ferroptosis in CCA treatment, we believe there are certain contradictions in the discussion that warrant further consideration. Ferroptosis primarily relies on increased iron levels and lipid peroxidation at its core.[3] However, it is important to note that not every instance of increased iron and lipid peroxidation leads to ferroptosis. The article mentions two studies demonstrating increased iron accumulation in cancer patients, which is associated with a poor prognosis. These findings alone raise caution and suggest that ferroptosis might not be the promising strategy it initially appeared to be for cancer treatment. Moreover, it is crucial to recognize that harnessing ferroptosis as a therapeutic approach remains controversial due to its potential impact on normal healthy cells. The healthy cells also rely on similar oxidant defense systems to maintain their redox balance. Consequently, increasing lipid peroxidation or iron levels could have adverse effects on patients, potentially leading to harmful outcomes and contributing to a poor prognosis.[4]

In addition to the above concerns, the review highlights that certain ferroptosis-related markers, including glutathione (GSH), glutathione peroxidase (GPx), and ferrous iron, are found to be depleted in the bile fluids of CCA patients compared to patients with common bile duct stones. However, the lack of a proper control group consisting of healthy individuals poses a limitation to the interpretation of these results. It is therefore essential to conduct further investigations that encompass a broader range of cancer types to comprehensively compare the status of ferroptosis markers in CCA. Only through such studies will we be able to draw solid conclusions regarding the potential of ferroptosis as a viable treatment strategy for various cancers.

In conclusion, we appreciate the efforts put forth by Yang et al in their review of ferroptosis as a potential therapeutic avenue for CCA. However, it is crucial to consider the contradictions and complexities surrounding the utilization of ferroptosis in cancer treatment. The adverse effects on healthy cells and the inconclusive results of marker depletion in CCA patients emphasize the need for further investigation. Until we gain a deeper understanding of the specific mechanisms and develop targeted approaches to exploit ferroptosis in cancer cells while minimizing harm to healthy cells, drawing conclusive remarks on its therapeutic potential remains challenging.

Disclosure

The authors report no conflicts of interest in this communication.

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