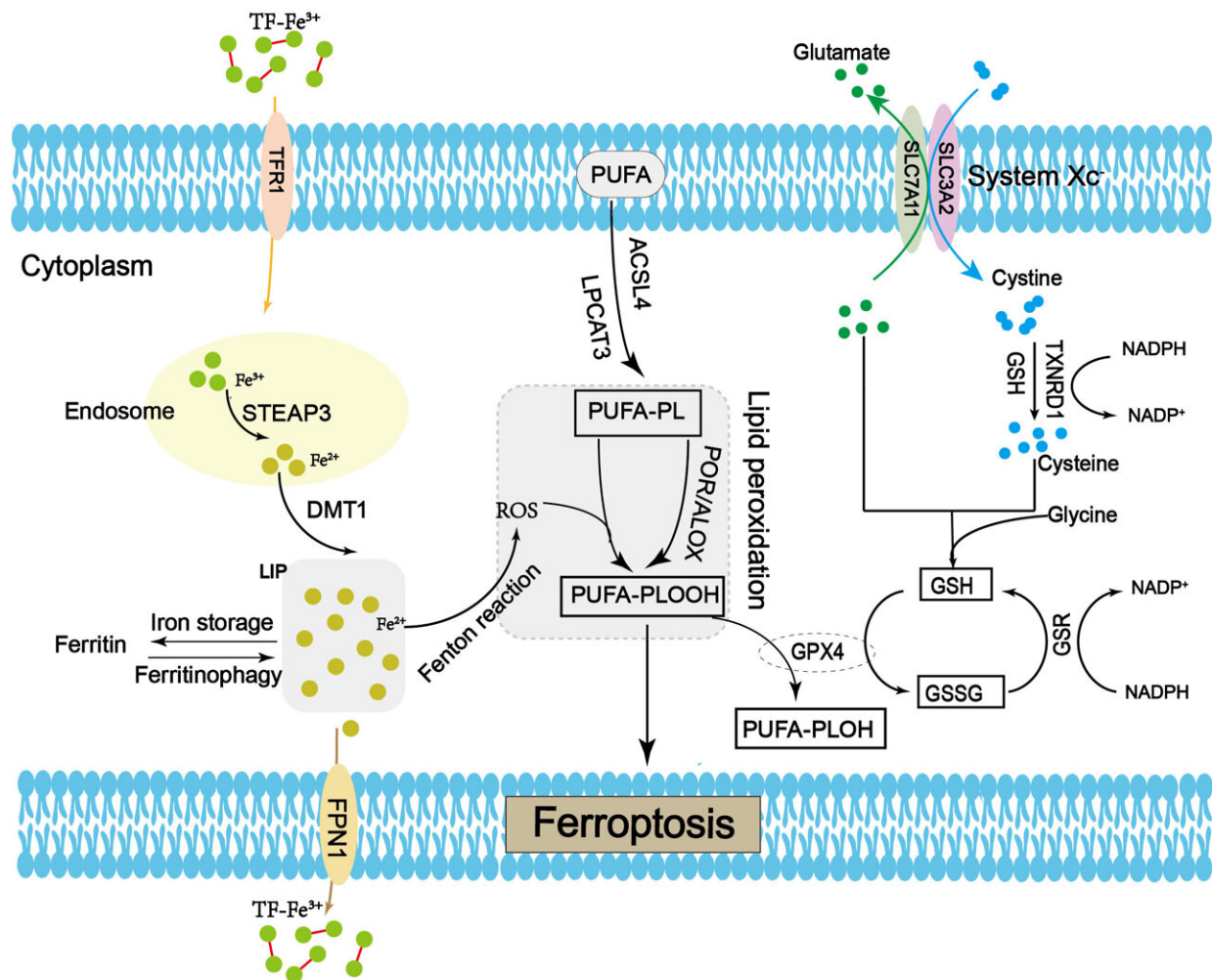


Exploring ferroptosis and its implications in lung cancer

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Even with advances in diagnosis and treatments, the survival rate of patients with lung cancer, remains to be low. Ferroptosis is a type of iron-dependent programmed cell death implicated in cancer, and targeting the ferroptosis pathway could be a therapeutic strategy to improve clinical outcomes.

Researchers in China summarized the mechanisms of ferroptosis and its application in cancer treatment. Credit: Chinese Medical Journal

An estimated 2.2 million people suffer from lung cancer worldwide, making it the second most common type of cancer. Though improvements in treatment have been made, the overall survival rate of lung cancer patients is low, and it remains a leading cause of death, accounting for 18% of total cancer-related deaths in 2022.

A major hurdle to improving clinical outcomes is treatment resistance that leads to lung cancer recurrence, and this has spurred efforts to develop new therapies to reduce mortality.

Ferroptosis—a type of iron-dependent programmed [cell death](#) induced by uncontrolled lipid peroxidation has been implicated in various diseases, including cancer. However, its precise role in cancer remains elusive.

Recently, researchers from the Renmin Hospital of Wuhan University, Georgetown University Medical Center, and the Beijing Institute of Lifeomics, China, aimed to outline the mechanism of ferroptosis in lung cancer and highlight ferroptosis targeting cancer treatments to provide a novel understanding of lung cancer interventions.

The article was published in the [Chinese Medical Journal](#).

"We particularly described the characteristics, mechanisms, and potential applications of ferroptosis in lung cancer, aiming to provide new insights for lung cancer treatment," says the lead author, Professor Qian Li.

For this, the researchers explored various metabolic pathways.

"Ferroptosis is a complex process involving multiple [metabolic pathways](#), including iron metabolism, amino acid metabolism, lipid metabolism, and antioxidant defense systems. The dysfunction of these pathways may cause lipid peroxidation. Identifying the diverse metabolic modulators might shed light on the physiological and pathological mechanisms and contexts in which ferroptosis is activated," explains Prof. Li.

The researchers studied the various regulatory molecules involved in ferroptosis that show aberrant expression during lung cancer. They believed that a deeper understanding of these molecules and the process by which they trigger ferroptosis could help define potential therapeutic strategies.

They observed that regulatory molecules, such as SLC7A11 (Solute carrier family 7 member 11), GPX4 (Glutathione peroxidase 4 pathway), FSP1 (Ferroptosis suppressor protein 1), and NRF2 (NF-E2 related factor 2), were involved in this process and could be used as potential targets for the prognosis and treatment of lung cancer.

The team also investigated the various therapies and their limitations in treating lung cancer. For example- radiotherapy, one of the most effective lung cancer treatments, suffers from the limitation of radioresistance. "The latest evidence has shown that [radiation therapy](#) can induce ferroptosis, and many ferroptosis regulators can influence lung cancer radiosensitivity," says Prof. Li.

Similarly, drug resistance during chemotherapy and targeted therapy limits their broad applications. However, researchers have found that all these therapies, including radiotherapy, [platinum-based chemotherapy](#), targeted therapy, and immunotherapy, can induce ferroptosis in lung cancer. The team outlined the attempts to use ferroptosis inducers along with these therapies to enhance their efficacies and overcome the hurdles of drug resistance.

Additionally, creating models that can predict lung cancer and [drug resistance](#) based on ferroptosis-related gene molecular typing could help in developing personalized treatment strategies.

Overall, the study suggests that ferroptosis could be a novel and effective target in lung cancer treatment and provides hope for decreasing the burden of [lung cancer](#).

More information: Qian Li et al, Emerging mechanisms of ferroptosis and its implications in lung cancer, *Chinese Medical Journal* (2024).
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