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Original Article

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Ferroptosis: A Novel Anti-tumor Action for Cisplatin

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Purpose

Ferroptosis is a new mode of regulated cell death, which is completely distinct from other cell death modes based on morphological, biochemical, and genetic criteria. This study evaluated the therapeutic role of ferroptosis in classic chemotherapy drugs, including the underlying mechanism.

Materials and Methods

Cell viability was detected by using the methylthiazoltetrazlium dye uptake method. RNAi was used to knockout iron-responsive element binding protein 2, and polymerase chain reaction, western blot was used to evaluate the efficiency. Intracellular reduced glutathione level and glutathione peroxidases activity were determined by related assay kit. Intracellular reactive oxygen species levels were determined by flow cytometry. Electron microscopy was used to observe ultrastructure changes in cell.

Results

Among five chemotherapeutic drugs screened in this study, cisplatin was found to be an inducer for both ferroptosis and apoptosis in A549 and HCT116 cells. The depletion of reduced glutathione caused by cisplatin and the inactivation of glutathione peroxidase played the vital role in the underlying mechanism. Besides, combination therapy of cisplatin and erastin showed significant synergistic effect on their anti-tumor activity.

Conclusion

Ferroptosis had great potential to become a new approach in anti-tumor therapies and make up for some classic drugs, which open up a new way for their utility in clinic.

Key words
Ferroptosis, Cisplatin, Erastin, Glutathione, Glutathione peroxidase

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