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Ferroptosis is an iron-dependent programmed cell death distinct from **apoptosis**, **necroptosis**, and **autophagy**[1]. This concept was proposed ten years ago and its popularity has remained strong. Ferroptosis occurs through phospholipid peroxidation, a process relying on the transition metal iron, **reactive oxygen species (ROS)**, and phospholipids containing polyunsaturated fatty acid chains (PUFA-PLs)[2]. There are three major iron death control systems within cells: Cystine/GSH/GPX4 system, CoQ10/FSP1 system, and GCH1/BH4/DHFR system[2].

Regulation of Ferroptosis on Tumor Immune Cells

Ferroptosis modulates antitumor immunity by affecting the activity of immune cells, including T cells, macrophages, and B cells[3]. **IFNγ** released from $CD8^+$ T cells downregulates the expression of SLC3A2 and SLC7A11, two subunits of the glutamate-cystine antiporter system Xc^-, impairs the uptake of cystine by tumor cells, thus promoting tumor cell lipid peroxidation and ferroptosis[4]. As an eat-me signal, SAPE-OOH distributes on ferroptotic cancer cells, which is recognized by **TLR2** on macrophage leading to increased phagocytosis[5]. Loss of **GPX4** expression in B1 cells and MZ B cells induces lipid peroxidation and ferroptosis[6].

Cancer Immunotherapy Strategies Based on Ferroptosis

Ferroptosis has a certain degree of crosstalk with the immune system. Given cancer cell metabolism and differentiation characteristics, the following six immunotherapy strategies

based on ferroptosis may provide promising therapeutic potentials for cancer treatment[7].

(1) Combination of ferroptosis and **tumor immune checkpoint inhibitor** therapy.

(2) Activation of tumor immune cells through ferroptosis and reverse resistance to radiotherapy.

(3) Targeting tumor metabolic features and specifically inducing ferroptosis.

(4) Inducing innate transformation of anti-cancer macrophages through ferroptosis.

(5) Inducing damage-related molecular pattern (DAMP) generation.

(6) Targeting plasticity in cancer cell differentiation.

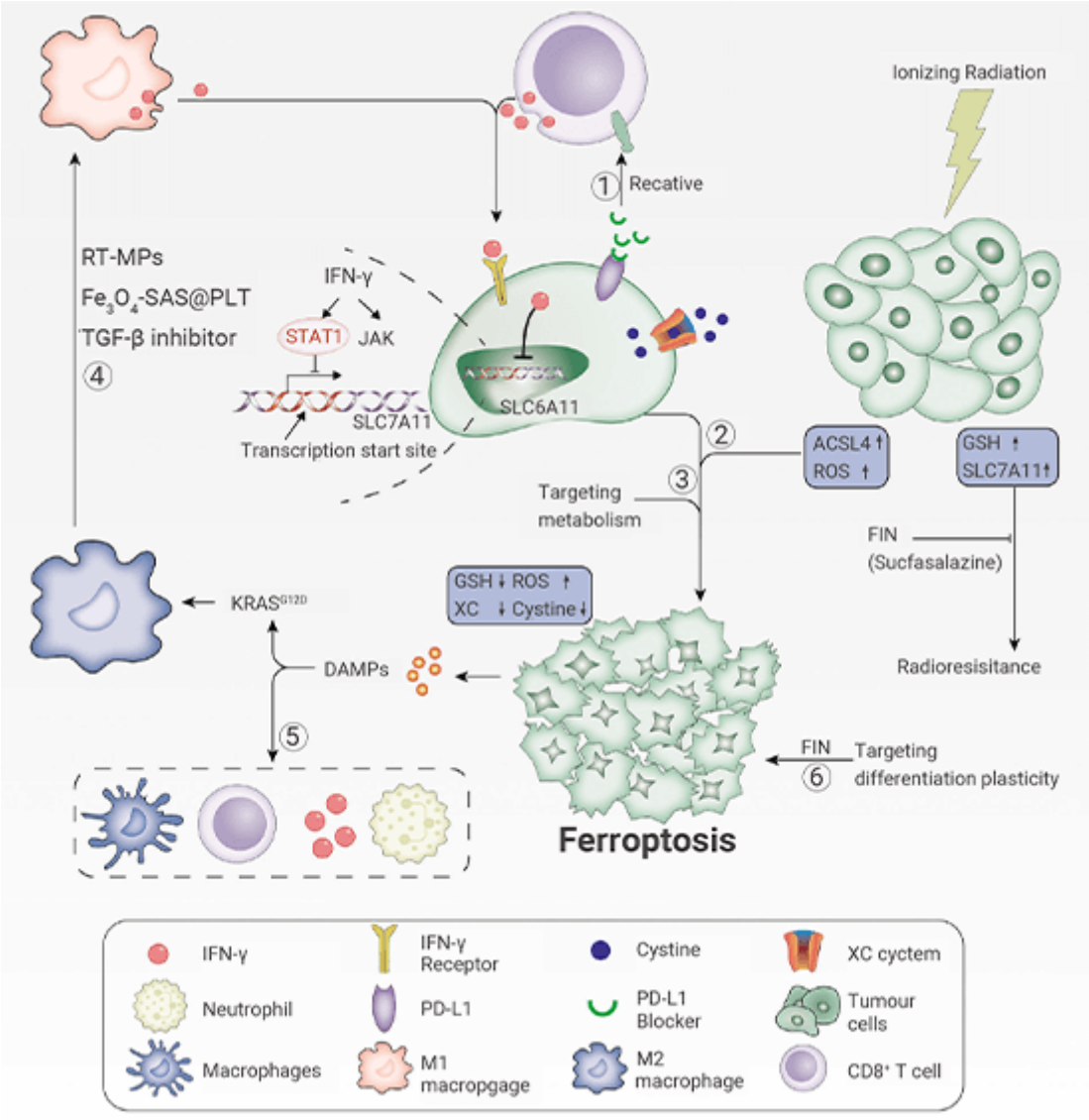

Fig.1 Ferroptosis and tumor immunotherapy[7]

MedChemExpress

- MCE provides 200+ small molecules targeting ferroptosis and ferroptosis pathway related compound libraries.

- MCE also provides 20,000+ other cancer-related products.

Product Name	Description
Ferrostatin-1	A potent and selective ferroptosis inhibitor.
Erastin	A ferroptosis inducer targets cells expressing oncogenic mutants of RAS.
Cisplatin	Cisplatin activates ferroptosis and induces autophagy.
RSL3	An inhibitor of glutathione peroxidase 4 (GPX4) (ferroptosis activator).
MMRi62	A ferroptosis inducer targets MDM2-MDM4 (negative regulators of tumor suppressor p53).
YL-939	A potent ferroptosis inhibitor targets the PHB2/ferritin/iron axis.
Ferroptosis Compound Library	A unique collection of 766 bioactive ferroptosis signal pathway related compounds.

References:

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