Compounds for modulating ferroptosis and treating excitotoxic disorders

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Technology description

Summary

This technology describes a class of chemical compounds that specifically modulate cellular ferroptosis to treat a range of excitotoxic disorders.

Unmet Need: Small molecules for cell death inhibition

Regulated cell death, known as apoptosis, is a critical process in normal tissue function. However, the deregulation of this process can result in progression of various excitotoxic disorders including neurodegenerative disorders, cancer, and diabetes. Many of these excitotoxic disorders are resistant to traditional modulators of apoptosis. As such, unlocking parallel modes of cell death may enable the treatment and prevention of associated diseases. Ferroptosis is an iron-dependent type of programmed cell death that is distinct from other well-characterized cell death pathways. As such, manipulation of ferroptosis may provide a therapeutic target for the treatment of a wide range of diseases.

The Technology: Ferroptosis inhibitors to treat excitotoxic disorders

This technology describes a class of small molecules that specifically inhibit cellular ferroptosis. The ferroptosis inhibitors were identified through screening assays and further analogs were synthesized to increase the effectiveness and pharmacological properties of the small molecules. By modulating ferroptosis, a separate mode of cell death, this technology has the potential to treat a wide range of excitotoxic disorders including cancer, neurodegenerative disease, and diabetes.

The identified ferroptosis inhibitors have been demonstrated to modulate ferroptosis in both tumorigenic cells and rat hippocampal slice cultures.

Publications

Skouta R, Dixon SJ, Wang J, Dunn DE, Orman M, Shimada K, Rosenberg PA, Lo DC, Weinberg JM, Linkermann A, Stockwell BR. "Ferrostatins inhibit oxidative lipid damage and cell death in diverse disease models" J Am Chem Soc. 2014 Mar 26;136(12):4551-6.

Application area

Prevention of cell death

Inhibition of non-standard cell death pathways

Specific targeting of tumorigenic cancer cells

Protection against neurodegenerative diseases

Treatment of a range of excitotoxic disorders

Advantages

Ferroptosis offers a distinct pathway for the treatment of disease

Small molecule inhibitors are easily tuned through medicinal chemistry and inexpensive to produce

Distinct cell death mode may provide insight into biological pathways and cell death regulation

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