New cobalt complex triggers ferroptosis in cancer cells

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A team headed by Johannes Karges has developed a novel metal complex that triggers a form of cell death in cancer cells that has only recently been identified. Credit: RUB, Marquard

In programmed cell death, certain signaling molecules initiate a kind of

suicide program to cause cells to die in a controlled manner. This is an essential step to eliminate damaged cells or to control the number of cells in certain tissues, for example. Apoptosis has long been known as a mechanism for programmed cell death.

Ferroptosis is another mechanism that has recently been discovered which, in contrast to other cell death mechanisms, is characterized by the accumulation of lipid peroxides. This process is typically catalyzed by iron—ferrum in Latin—which is where the name ferroptosis derives from.

Research carried out by Dr. Johannes Karges' Medicinal Inorganic Chemistry group in collaboration with doctoral student Nicolás Montesdeoca and two Bachelor students, Lukas Johannknecht and Elizaveta Efanova, has been published in the journal *Angewandte Chemie International Edition*.

"Searching for an alternative to the mechanism of action of conventional chemotherapeutic agents, we specifically looked for a substance capable of triggering ferroptosis," explains Karges.

His group synthesized a cobalt-containing metal complex that accumulates in the mitochondria of cells and generates reactive oxygen species, more precisely hydroxide radicals.

These radicals attack polyunsaturated fatty acids, resulting in the formation of large quantities of lipid peroxides, which in turn trigger ferroptosis. The team was thus the first to produce a cobalt complex designed to specifically trigger ferroptosis.

Effectiveness demonstrated on artificial microtumors

The researchers from Bochum used a variety of cancer cell lines to show

that the cobalt complex induces ferroptosis in tumor cells. On top of that, the substance slowed down the growth of artificially produced microtumors.

"We are confident that the development of metal complexes that trigger ferroptosis is a promising new approach for cancer treatment," as Karges sums up the research, adding, "However, there's still a long way to go before our studies result in a drug."

The metal complex must first prove effective in animal studies and clinical trials. What's more, the substance doesn't currently selectively target tumor cells, but would also attack healthy cells. This means that researchers must first find a way to package the cobalt complex in such a way that it damages nothing but tumor cells.

More information: Nicolás Montesdeoca et al, Ferroptosis Inducing Co(III) Polypyridine Sulfasalazine Complex for Therapeutically Enhanced Anticancer Therapy, *Angewandte Chemie International Edition* (2024). DOI: 10.1002/anie.202412585

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