Researchers discover iron-targeting approaches to halt proliferation of cancer cells

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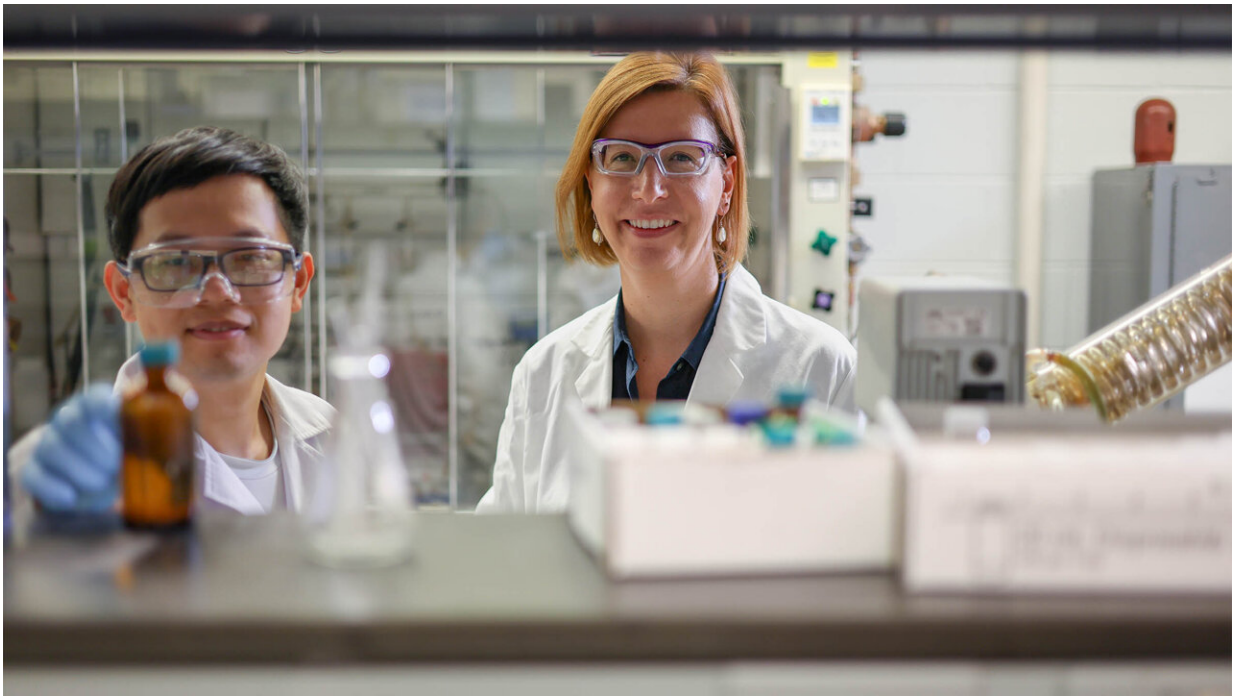


(From left) Yu-Shien Sung, doctoral student in the Tomat Lab, and University of Arizona Cancer Center member Elisa Tomat, PhD, are studying an iron-targeting molecule that may lead to the development of new anticancer drugs. Credit: University of Arizona Health Sciences

Researchers at the University of Arizona Cancer Center discovered a

new class of iron-targeting compounds that hamper the proliferation of cultured malignant cells in a laboratory setting. The results of the study were published in the Journal of the American Chemical Society.

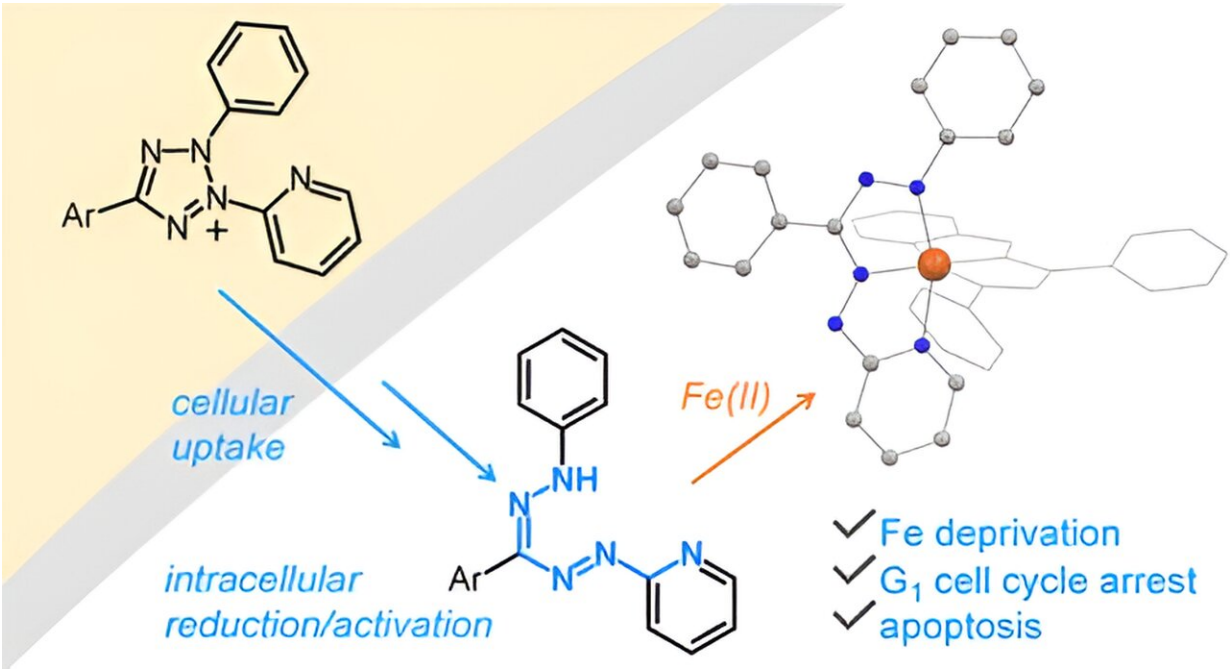
"Cancer cells are what we call 'addicted' to iron, and so we are making compounds that are able to interfere with the availability of iron in cancer cells," said Elisa Tomat, Ph.D., professor in the Department of Chemistry and Biochemistry at the UArizona College of Science and member of the UArizona Cancer Center.

The discovery could lead to the development of broad-spectrum, anticancer drugs that target iron metabolism.

The team has been working with Tech Launch Arizona, the university's commercialization arm, with the goal of licensing the technology to a company that will move it into the marketplace. A patent application is pending.

Iron is the most abundant transition metal in the human body and, according to Tomat, plays a crucial role in tumor progression and metastasis. Cancer cells rely on several iron-dependent processes to sustain their rapid proliferation rates and therefore have a higher demand for this element compared with normal cells.

Tomat said the research team's challenge was capturing iron within malignant cells yet keeping it available to the rest of the body. To do so, they targeted intracellular iron with compounds that are activated only after cellular uptake.



Graphical abstract. Credit: *Journal of the American Chemical Society* (2023). DOI: 10.1021/jacs.3c02033

"As chemists, we can design and synthesize molecules that are able to bind iron only under certain conditions and not throughout the body," Tomat said. "We've been working on various approaches toward this type of chemistry; we call these prochelator approaches because the chelator is the compound that binds the metal ion. The prochelator is the compound we designed to become activated only upon undergoing a certain reaction that occurs in cells."

The research was inspired by a "common reagent," a compound that is employed in laboratories worldwide to assess the ability of drug candidates to inhibit the proliferation of cultured mammalian cells.

"Because iron is such a fundamental player that is important in many

cancer types, and this high demand for iron is a general characteristic of malignancy, I've been interested in this strategy for a number of years," said Tomat, who has been exploring iron chelators and their role in tumor progression for more than 10 years.

"We're excited about this new strategy because we think this class of molecules can be further modified to optimize the properties and improve the antiproliferative activity and really become a way for us to impact the iron availability in malignant cells and halt cancer growth."

Tomat's co-authors include former postdoctoral associate Zoufeng Xu, Ph.D., and doctoral student Yu-Shien Sung.

More information: Zoufeng Xu et al, Design of Tetrazolium Cations for the Release of Antiproliferative Formazan Chelators in Mammalian Cells, *Journal of the American Chemical Society* (2023). DOI: 10.1021/jacs.3c02033

Provided by University of Arizona