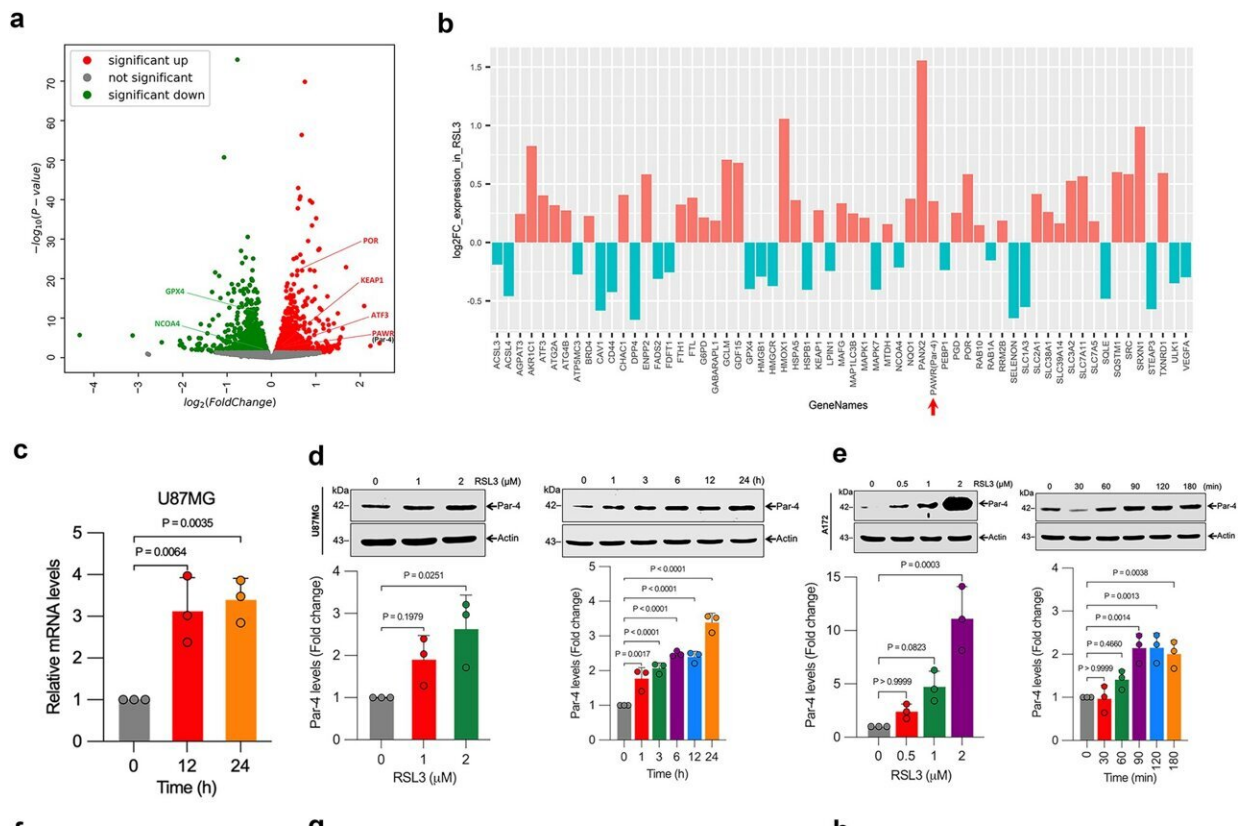


Tumor suppressor protein Par-4 found to trigger unique cell death pathway in cancer cells

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Identification of PAWR/Par-4 as a critical contributor of ferroptosis. Credit: *Communications Biology* (2024). DOI: 10.1038/s42003-024-06430-z

A team of researchers at NYU Abu Dhabi, led by Professor Sehamuddin

Galadari, has discovered that the tumor suppressor protein Prostate apoptosis response-4 (Par-4) can cause a unique type of cell death called ferroptosis in human glioblastoma—the most common and aggressive type of brain tumor—while sparing healthy cells. This new understanding has the potential to inform the development of novel treatments for various hard-to-treat cancers and neurodegenerative diseases.

Ferroptosis is triggered by the iron-mediated production of reactive oxygen species (ROS) and subsequent lipid peroxidation, which plays a crucial role in shrinking [cancerous tumors](#). This is the first time that Par-4, already known for killing cancer cells through apoptosis—a form of programmed cell death—has been shown to promote ferroptosis in glioblastoma cells.

The tumor suppressor protein Par-4 is widely expressed across species, but is often reduced, mutated, or inactivated in the presence of various cancers. In the study "[Tumor suppressor Par-4 activates autophagy-dependent ferroptosis](#)," published in the journal *Communications Biology*, the researchers identified that Par-4 plays an unanticipated role in promoting ferroptosis-mediated cancer regression.

They demonstrated that Par-4 triggers the activation of ferritinophagy (autophagic degradation of ferritin) through the nuclear receptor co-activator 4 (NCOA4). This activation is necessary for the accumulation of the labile iron pool, the production of ROS, and the subsequent lipid peroxidation, all of which lead to ferroptosis.

Ferroptosis plays a key role in various health issues, such as cancer, heart disease, [brain damage](#), kidney failure, lung injury, and diseases like Parkinson's, Huntington's, and Alzheimer's. The identification of Par-4 as a key player in ferroptosis is essential, as it is involved in the main processes and signals that make this alternative cell death pathway,

ferroptosis, occur. Many types of [cancer cells](#) don't respond to today's treatments or have developed resistance to existing drug therapies.

This research was a collaborative effort between Associate Professor Mazin Magzoub's lab at NYU Abu Dhabi and Professor Vivek M. Rangnekar from the University of Kentucky, who discovered Par-4 in 1993.

"Our team's discovery that Par-4 triggers ferroptosis is a breakthrough in the field of cancer treatment development," said Galadari, who is the Senior Vice Provost for Research and Managing Director of the Research Institute at NYU Abu Dhabi. "Developing methods to activate alternative [cell death](#) pathways presents new opportunities for the creation of more potent and effective therapies for glioblastoma and other deadly and debilitating diseases."

"Investing in research at institutions such as NYUAD is instrumental in transforming the UAE into a knowledge-based economy that attracts local, regional, and global talent—a symbiotic relationship that creates opportunities, knowledge, and wealth," Galadari added.

More information: Karthikeyan Subburayan et al, Tumor suppressor Par-4 activates autophagy-dependent ferroptosis, *Communications Biology* (2024). [DOI: 10.1038/s42003-024-06430-z](https://doi.org/10.1038/s42003-024-06430-z)

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