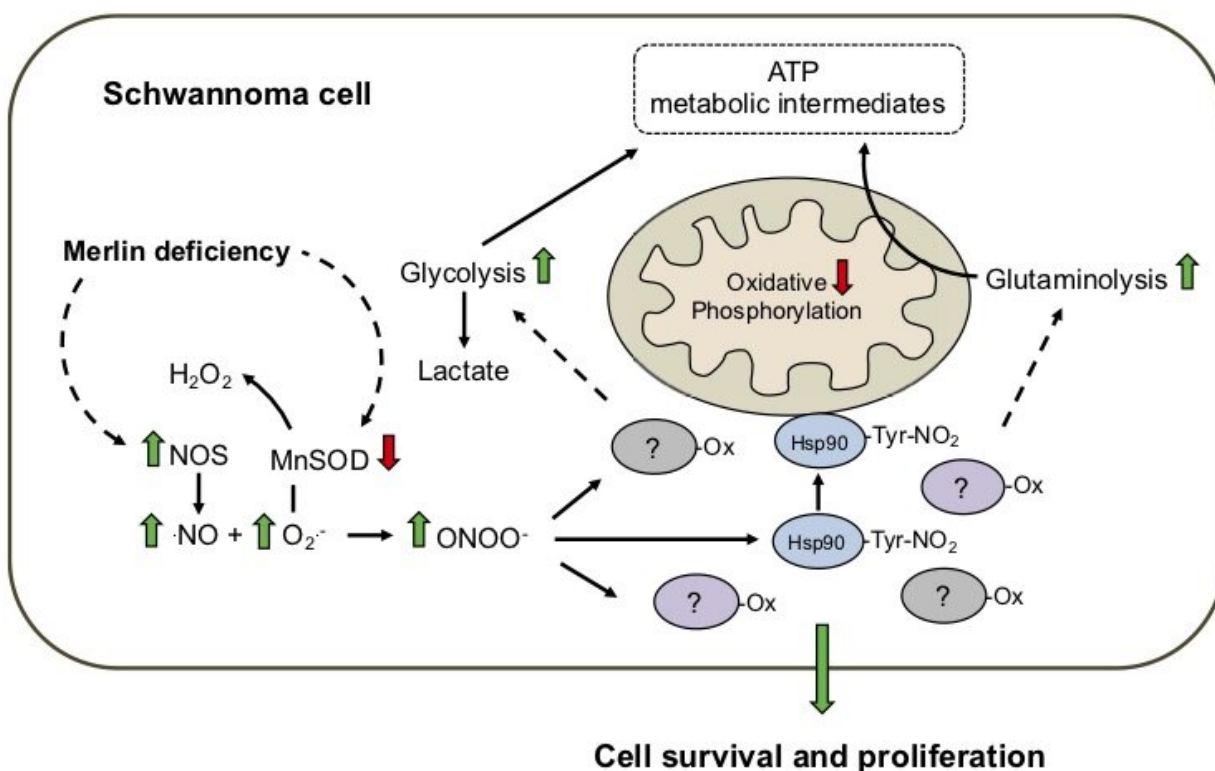


# Researchers take key step toward cancer treatments that leave healthy cells unharmed

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Researchers have opened up a possible avenue for new cancer therapies that don't have the side effects that oftentimes accompany many current cancer treatments by identifying a protein modification that specifically supports proliferation and survival of tumor cells. Credit: Maca Franco, OSU College of Science

Researchers have opened up a possible avenue for new cancer therapies that don't have the side effects that oftentimes accompany many current cancer treatments by identifying a protein modification that specifically supports proliferation and survival of tumor cells.

Depending on the kind of cancer and the type of treatment, a patient might suffer from many [side effects](#), including anemia, loss of appetite, bleeding, bruising, constipation, delirium, diarrhea, fatigue, hair loss, nausea, sexual issues or bladder problems.

Scientists at Oregon State University, the University of Central Florida and New York University made the [protein-modification](#) discovery while studying neurofibromatosis type 2. The condition, commonly known as NF2, is characterized by the development of tumors of the nervous system called schwannomas.

"The hallmark of tumor cell behavior is their uncontrolled growth," said Maca Franco, professor of biochemistry and biophysics in OSU's College of Science. "Tumors [cells](#) need to constantly produce energy and building blocks to replicate."

Researchers led by Franco and Oregon State undergraduate student Jeanine Pestoni found that schwannoma cells produce an oxidant and nitrating agent, peroxynitrite, which modifies an amino acid, tyrosine, in proteins.

When tyrosine becomes nitrated in specific proteins, an effect is the reprogramming of the tumor cells' metabolism, enabling them to proliferate.

"To sustain persistent growth, tumor cells change the way they produce energy and [building blocks](#) and present a signature metabolic phenotype that differs from that of [normal cells](#)," Franco said. "We discovered that

peroxynitrite, the most powerful oxidant produced by cells, controls the metabolic changes that occur in tumor cells of the nervous system and supports their growth. We believe that there are specific proteins that when they become nitrated acquire a new function they did not have before, and this new function may control [tumor](#) growth."

Peroxynitrite is produced at high levels in "pathological conditions," she said—such as those found in tumors—but not in normal tissues.

"This opens up the exciting possibility of targeting peroxynitrite production exclusively in [tumor cells](#) as a new therapeutic strategy for the treatment of tumors of the nervous system, with minimal to no side effects on normal tissues," Franco added. "We are uncovering a completely new category of targets for the treatment of solid tumors, and not only tumors of the nervous system—it may have broader implications for the treatment of several cancer types. We can go after proteins that usually aren't modified in normal cells; we can target those modified proteins with inhibitors that don't affect normal cells, hopefully developing a treatment with minimal side effects."

Findings were published in the *Journal of Biological Chemistry*.

**More information:** Jeanine C. Pestoni et al, Peroxynitrite supports a metabolic reprogramming in merlin-deficient Schwann cells and promotes cell survival, *Journal of Biological Chemistry* (2019). [DOI: 10.1074/jbc.RA118.007152](https://doi.org/10.1074/jbc.RA118.007152)

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