

NIH Scientists Pioneer Promising Treatment For Intractable Cancer Pain

Resiniferatoxin is a non-addictive pain therapy derived from a cactus-like plant.

May 30, 2025 By National Institutes of Health

National Institute of Health (NIH) scientists report that a first-in-human clinical trial of a new therapy based on the plant-derived molecule resiniferatoxin (RTX) shows that it is a safe and effective agent for pain control in patients with intractable cancer pain. [The study was published in [NEJM Evidence](#) on May 27, 2025.]

Researchers tested a single injection of small quantities of RTX into the lumbar cerebral spinal fluid (by lumbar puncture) of advanced-stage cancer patients and found that it reduced their reported worst pain intensity by 38% and their use of pain-relieving opioids by 57%.

“The effects are immediate,” said Andrew Mannes, MD, lead study author and chief of the NIH Clinical Center Department of Perioperative Medicine. “This is a potential new therapy from a new family of drugs that gives people with severe cancer pain an opportunity to return some normality to their lives.”

The trial enrolled research participants with terminal end-stage cancer who were among the 15% of cancer patients unable to find pain relief from standard of care pain interventions, including vast quantity of opiates without relief.

A single injection of RTX provided patients durable relief. Patients’ need for pain-relieving opioids declined sharply, and their quality of life improved. They no longer needed to spend significant periods being sedated with opioids and after treatment were able to reengage with their family, friends and communities.

The NIH scientists believe RTX has potential to treat many other pain conditions, including other types of cancer pain, chronic pain from nerve injuries called neuromas, post-surgical pain, a facial pain condition called trigeminal neuralgia, and chronic oral inflammatory problems following head and neck radiation therapy.

“Targeting specific nerves brings many pain disorders into range of RTX and allows physicians to tailor the treatment to the patient’s pain problem. This interventional approach is a simple path to personalized pain medicine,” said senior study author Michael Iadarola, PhD, a senior research

scientist in the NIH Clinical Center Department of Perioperative Medicine.

RTX is not addictive and doesn't cause a high. Instead, it prevents pain signals from reaching the brain by inactivating a specific sub-group of nerve fibers which transmit heat and pain signals from damaged tissue. RTX is an activator of the transient receptor potential vanilloid 1, or TRPV1 ion channel and a super-potent equivalent of capsaicin, the active molecule in hot peppers. The ability of RTX to open the channel pore in TRPV1 allows an overload of calcium to flood into the nerve fiber and block its ability to transmit pain signals.

"Basically, RTX cuts the pain-specific wires connecting the body to the spinal cord, but leaves many other sensations intact," Iadarola said. "These TRPV1 neurons are really the most important population of neurons that you want to target for effective pain relief."

Iadarola's contributions have led decades of basic science research into the neurobiology of pain and pain control. That body of research has informed them that to effectively block pain, you must block it from getting into the spinal cord and from there having it leave the spinal cord to transit to the brain, where we perceive pain.

Unlike other current approaches that use heat, cold, chemicals, or surgery to non-selectively interrupt nerves to stop pain, RTX targets the specific sensory pathways of tissue damage pain and heat. Other sensory pathways, such as touch, pin prick, pressure, muscle position sense (known as proprioception), and motor function, remain intact. It is not a generalized numbing as occurs with local anesthetics.

"What makes this unique from all the other things that are out there is this is so highly selective," Mannes said. "The only thing it seems to take out is heat sensation and pain."

RTX is derived from the *Euphorbia resinifera* plant, a cactus-like plant native to North Africa. Euphorbia extract has been known for 2,000 years to contain an "irritant" substance, which NIH scientists identified how to use for patients through basic research on living cells observed through a microscope. Adding RTX to TRPV1-containing cells caused a visible calcium overload, which Iadarola and Mannes eventually translated into an early-stage human clinical trial.

The next steps include additional, larger clinical trials to move RTX toward eventual approval by the U.S. Food and Drug Administration and clinical availability.

This research was supported by the Intramural Research Program of the NIH Clinical Center and NIH's National Institute of Neurological Disorders and Stroke.

This [news release](#) was published by the National Institutes of Health on May 29, 2025.