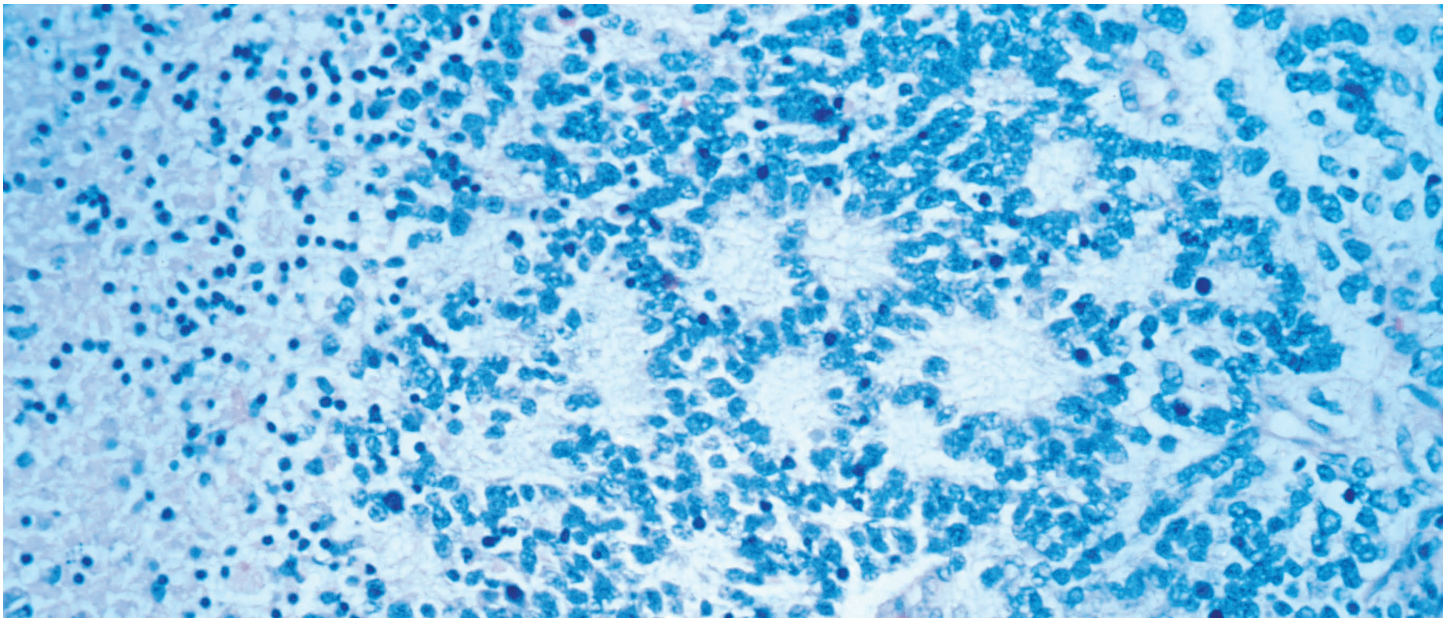
CHICAGO Stories
THE UNIVERSITY OF CHICAGO MEDICAL CENTER



Above: Microscopic view of a typical neuroblastoma with rosette formation Dr. Maria Tsokos, National Cancer Institute

UCMC Neuroblastoma Patient First in World to Receive Breakthrough Drug

A year ago, Anna O'Connor was at a low point in her seven-year battle with neuroblastoma, a pediatric cancer that grows slowly but relentlessly in teens and young adults. A promising new drug had stopped working, and the tumors in her bones, liver, and abdomen were multiplying faster than ever.

"I had tried pretty much all the things targeted to neuroblastoma," she recalled. "I was pretty much out of options."

University of Chicago Medical Center (UCMC) pediatric oncologist and neuroblastoma researcher Sam Volchenboum, turned to an old drug called thalidomide to keep Anna's tumors in check until a new drug emerged from research. Four decades ago, thalidomide caused horrendous birth defects when given to relieve nausea in pregnant women. Today it's used in combination with other oral medications to slow a tumor's growth by choking its blood supply.

What came next, however, excited neuroblastoma patients and clinicians worldwide. Researchers from several groups announced discovery of a gene mutation associated with the development of neuroblastoma. Within months, O'Connor became the first neuroblastoma patient in the world to receive a drug that targets that mutation.

A half year into therapy, the 24-year-old Wheaton, Illinois, resident's tumors have stopped growing for the first time in more than two years.

Events converge in O'Connor's favor

Three events following the gene discovery enabled the UCMC, known for providing patients with the best emerging treatments, to put O'Connor on the genomically targeted treatment so quickly.

Pfizer already had a drug against the mutation, in a gene called ALK (anaplastic lymphoma kinase), in its developmental pipeline as a lung cancer therapy. Secondly, an adult trial of the ALK inhibitor was under way at the Medical Center. Finally, a genetic test of a biopsied sample of O'Connor's tumor proved positive for the mutation.

Above: Patient Anna O'Connor and pediatric oncologist and neuroblastoma researcher, Sam Volchenboum, MD, PhD PHOTO BY: BRUCE POWELL

While the ALK inhibitor leaves her exhausted, O'Connor said she no longer suffers debilitating back pain. Heavy-duty narcotic pain relievers have thankfully been dropped from the regimen of 30 or so medications she takes for symptom relief.

O'Connor was diagnosed in summer 2002 after noticing a lump in her abdomen. A senior at Wheaton North High School, she was a swimmer and lifeguard who was also active in drama and music. Her biggest concern in those days was doing well in school. "I was a perfectionist before being diagnosed with neuroblastoma," she said. Since then, she has been enrolled in more than a dozen clinical trials.

> "The potential impact of research is huge because current cure rates for all patients are less than 50 percent"
>
> -Sam Volchenboum

2002 marked a turning point for Volchenboum, too. He was completing the "first grueling year" of a clinical fellowship in pediatric oncology at the Dana-Farber Cancer Institute in Boston, when he decided to treat and study neuroblastoma.

"My interest in caring for young adults with neuroblastoma started when I was a first-year fellow, and I met a lovely 12 year-old girl who had widespread disease," he said. "I ended up being her doctor until I left in 2007, and I continue to have a special interest in this small but wonderful group of patients."

While neuroblastoma can occur at any time from infancy through the teen years, the outcomes vary by age. Even massive tumors can spontaneously begin to shrink in babies, who have a 90 percent cure rate. In teens, neuroblastoma grows slowly, but, so far, research has not shown how to prevent teens from eventually dying of the disease.

Current treatments cure only half of neuroblastoma patients

Volchenboum came to UCMC two years ago because he saw it as the "place where I was going to be molded into a critically thinking scientist." He is one of a new breed of clinical researchers versed in systems biology, an emerging field that seeks to use computational models to understand complex disease processes with molecular precision. His particular interest is proteomics—the study of protein levels in complex systems—to individualize treatment and find cures. One of his main goals is to adapt mass spectrometry for rapid testing of protein samples in clinical settings.

"Although there are only a few thousand cases of neuroblastoma worldwide each year, the potential impact of research is huge because current cure rates for all patients are less than 50 percent," Volchenboum said. "It is becoming clear that we can cure only a subset of patients by using conventional chemotherapy, surgery, and radiation. To go further will require a paradigm shift in how we treat these kids."

O'Connor also sees neuroblastoma as her opportunity to have an impact. As one of the few adult patients, she can be one of its few effective patient advocates. Young patients from around the world email her for advice, and she has founded a non-profit company – Anna's Hope – to raise funds and awareness. A carnival fundraiser last summer drew a thousand supporters, including Volchenboum, who gave a talk.

"It sort of gives my whole cancer a purpose," she said of her advocacy.

Because the ALK inhibitor is targeted to a specific mutation proven to be present in her tumors, it has potential to be far more powerful than anything else she has taken. But that remains to be seen, and O'Connor is preparing for the future. A 2007 graduate of Wheaton College, she has enrolled in graduate school seeking a master's degree in psychology. In 18 months, if all goes as planned, she'll begin her career as a licensed counselor.