

Pediatric Immunotherapy Program

Help us

NEVER SAY NO

to a child with cancer.



**GEORGIA
CANCER CENTER**
AUGUSTA UNIVERSITY

**Children's Hospital
of Georgia**

Pediatric Immunotherapy: The Time for Yes

One of the most heartbreaking words a parent of a child with cancer can hear is “No.” No more treatment options to cure your child’s cancer. No more clinical trials to slow down the relapsed cancer. No more hope.

Here at the Georgia Cancer Center, our heart’s desire is to Never Say No. We are striving to offer a complete array of clinical trials to families looking for immunotherapy options for their child with relapsed cancer. And, as some of the world leaders in helping the immune system control cancer in children, who better to lead the way?

Help us say Yes. It’s time.



IDO is the abbreviation for the enzyme at the heart of the discoveries that started the pediatric immunotherapy program at the Georgia Cancer Center. Immunotherapy is a treatment approach to cancer that harnesses the power of the patient’s own immune system to attack the cancer.

In the 1990s, Dr. David Munn and his colleague, Dr. Andrew Mellor, discovered the role of IDO in protecting a fetus from being attacked by the mother’s immune system during pregnancy. Dr. Ted Johnson was involved as an MD/PhD student at the time. They realized that many tumors also use IDO to fool the immune system into tolerating rather than attacking the growing cancer; so, they developed drugs that block IDO. Augusta University obtained a patent on the findings - so that the drugs could be developed for clinical use - and partnered with the NewLink Genetics Corporation to speed up drug development.

One of those IDO-blocking drugs, Indoximod, is now in cutting-edge clinical trials for children with brain tumors at Augusta University. The use of Indoximod in brain tumors is based on Dr. Johnson’s work combining this drug with conventional cancer therapy (chemotherapy and radiation) to target brain tumors.

Clinical Trials for Children with Brain Tumors

Based on preclinical laboratory results, the clinical trials are designed to test the concept that this class of drugs (IDO-inhibitor drugs) creates a synergy with standard treatments that:

-  Makes the combined treatment work **MORE POTENTLY** against the brain tumor and
-  Requires lower doses of chemotherapy and radiation to achieve the more potent effect; therefore, the treatment may be **LESS TOXIC** and the children may have fewer side effects and **BETTER QUALITY OF LIFE**.



Dr. Johnson and Dr. Munn have the following goals for quality-of-life-features in all of their immunotherapy trials:

- Use oral medications whenever possible and focus on moderate doses of chemotherapy
- Have as much of the treatment as possible taken at home (keeping hospital stays to a minimum) and work closely with the referring centers to decrease the amount of travel for long-distance patients
- Use immunotherapy to help out the chemotherapy and radiation so that ultra-high doses can be avoided (important for minimizing side effects like nausea, vomiting, hair-loss, etc.)
- Focus on maintaining a good quality of life — the goal is to have children returning to school, playful and happy, not wiped-out and miserable



“We have been able to design regimens that produce an excellent quality of life, with minimal well-tolerated side effects, yet still access the tumor-killing power of chemotherapy and radiation,” says Dr. David Munn. “Our ultimate goal is to achieve ten times the potency at one-tenth of the side effects.”



An important goal for the Georgia Cancer Center pediatric immunotherapy clinical trials is to use oral medications whenever possible. Here, Coulter takes his oral immunotherapy treatment, Indoximod, for the first time as his mother, Courtney, looks on.

Meet Coulter Hnatt

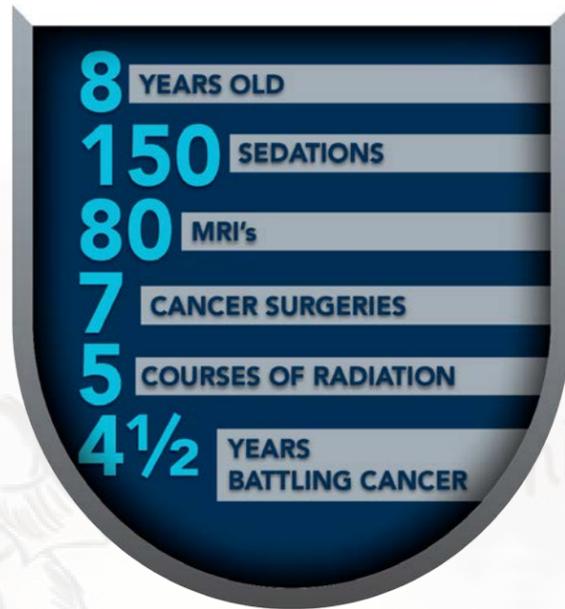
As a knight in shining armor fending off his princess sister's kisses, Coulter Hnatt might look like a typical 8-year-old (well, on Halloween anyway), but his story is extraordinary. His numbers tell the tale: 4 and ½ years battling cancer, enduring countless tests, numerous needle pokes, and many surgeries, radiation therapies, chemotherapies, sedations, and more holidays in hospital beds and medical facilities than any child – or adult – could possibly withstand.

Coulter's fight began when he was 4 years old and doctors discovered a brain tumor near his brainstem. Surgeons at Texas Children's Hospital removed the entire tumor and then began the first round of radiation to help keep it from growing back: 33 proton therapy treatments at the MD Anderson Cancer Center in Houston. One year later, the cancer reoccurred. Despite additional treatment over the years from the nation's finest cancer centers, to also include St. Jude Children's Research Hospital, the cancer continues to return – bigger and badder than ever.

"It (the cancer) has come back every year," says Mike Hnatt, Coulter's father. "And it comes back worse and spreads and it has spread into the spine." He adds, "We have been no stranger to bad news. It feels like 8 out of 10 times each MRI he has done every month is a mixed bag or negative."

"But he keeps on prevailing," says Courtney Hnatt of her son, Coulter. "He really is amazing." She adds, "We had doctors actually turn from 'why don't you take him home for a couple of months because this is it,' to, 'wow, I can't believe how good he is doing.'"

October of 2015 was one of the dark periods. The Hnatts were living in Houston, Texas with Coulter and his younger sisters, Audrey, 5, and Codey 4. Coulter's spinal tumor was back and they needed to find new answers. Just as she had done successfully in the past, Courtney turned to the Internet and its network of cancer parent forums and posting of clinical trials. She had been following Dr. Ted Johnson at the Georgia Cancer Center in



Augusta, Ga and his upcoming Indoximod pediatric immunotherapy clinical trial for the last six months. It was time to make contact.

"We were out of all options," remembers Courtney. "This was our only hope."

After meeting with Dr. Johnson, the Hnatts were convinced by his sincerity and Coulter became the first person enrolled. On December 9, 2015, Coulter swallowed the Indoximod pill on the first day it was available as part of the pediatric immunotherapy clinical trial.

For nearly a year now, the Hnatt family have lived in the Ronald McDonald House just steps away from the Children's Hospital of Georgia where Coulter receives his comprehensive treatment, which includes chemotherapy and daily physical therapy. He also received gamma knife radiation at Augusta University Medical Center, and recently returned to Texas Children's Hospital for a course of radiation therapy. They couldn't be happier with their decision to come to Augusta.

"Dr. Johnson gave us the time we needed when so many doctors are in a rush," says Mike. "He continues today to spend every minute not in a hurry. He is there listening

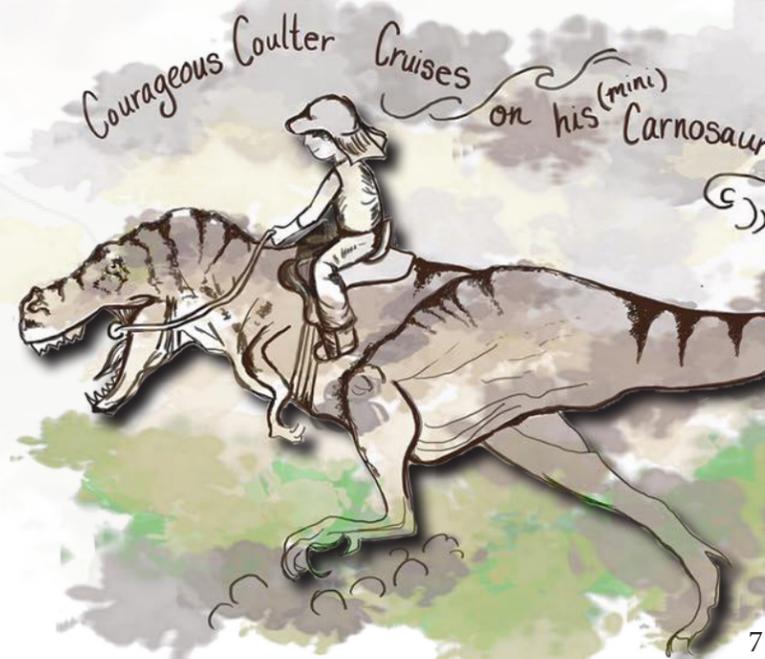
to us, talking, explaining everything as if he's got tons of energy and patience."

"And then on top of that we have this phenomenal take-home," adds Courtney. "The end result is Coulter is better today than he was 11 months ago. His quality of life is better."

Both Courtney and Mike describe Coulter's "full capabilities" that he actively engaged during a family vacation in Wyoming this summer. "He was out there kayaking, horseback riding, whitewater rafting, doing ropes and challenge courses, and zip-lining amongst the grizzly bears." Adds Mike, "He is not in any pain at all."

The Hnatts are quick to point out, however, that Coulter is not out of the woods and Dr. Johnson doesn't "powder puff things." In fact, because Coulter's cancer was "outsmarting" the original chemotherapy, Coulter is now beginning a new kind of chemotherapy with the same immunotherapy treatment, a regimen that required Dr. Johnson to seek additional FDA approval (and internal IRB approval). The Hnatts appreciated and understood the work required to extend this arm of the clinical trial.

"We have chosen to stay here because Dr. Johnson has been so attentive to Coulter's needs," says Courtney. "He is here for the patient."



Treating More Pediatric Cancers

The Georgia Cancer Center is the first – and currently only – program integrating chemotherapy, immunotherapy and radiation to treat children with relapsed brain tumors. We have plans for even more children to benefit from the promise of pediatric immunotherapy by:

- Increasing the number of children in the existing Indoximod trial for brain tumors
- Starting clinical trials using an infant-friendly (liquid) formulation of Indoximod
- Expanding the existing Indoximod trial into Phase II and adding especially difficult-to-treat brain tumors such as pontine gliomas (DIPG)
- Adding more participating Centers around the country
- Beginning a first-in children trial of IDO-inhibitor in pediatric solid tumors (neuroblastoma, osteogenic and Ewing's sarcomas, rhabdomyosarcoma, and others)
- Beginning a first-in children trial of IDO-inhibitor in relapsed/refractory AML (acute myeloid leukemia)
- Developing a new class of immunotherapy drug (PTEN-inhibitor agents) that will let us take chemotherapy to the next level of effectiveness
- Developing a continuing pipeline of powerful new drugs through discovery research
- Pioneering new ways of monitoring a child's immunity against their cancer
- Ultimate goal: offering a treatment option for every child with cancer that incorporates some component of immunotherapy to harness the power of the patients' own immune system.

Be Nimble, Be Quick

These additional clinical trials are ready and waiting to open. But we can't enroll new patients without the resources we need for success. There is a pent-up demand for this exciting program – these discoveries and drugs are not available anywhere else in the world. We are receiving referrals from major cancer centers around the country and many families fly to Augusta for treatment.

Yet, we have had to turn children away because we do not have enough staff and other resources to handle the demand for even our existing brain-tumor trials. With more resources, we could significantly increase the number of children who could have access to these promising treatments.

We have the science ready and waiting to quickly offer additional clinical trials for other kinds of pediatric cancers; but, again, we need staff and other resources to implement them.

Pediatric "Piggyback" Model

Nationwide, children almost always lag many years behind adults in gaining access to new drugs and treatments. Through the Pediatric Immunotherapy Program at the Georgia Cancer Center, we have developed an innovative model to rapidly bring forward promising new immunotherapy drugs from

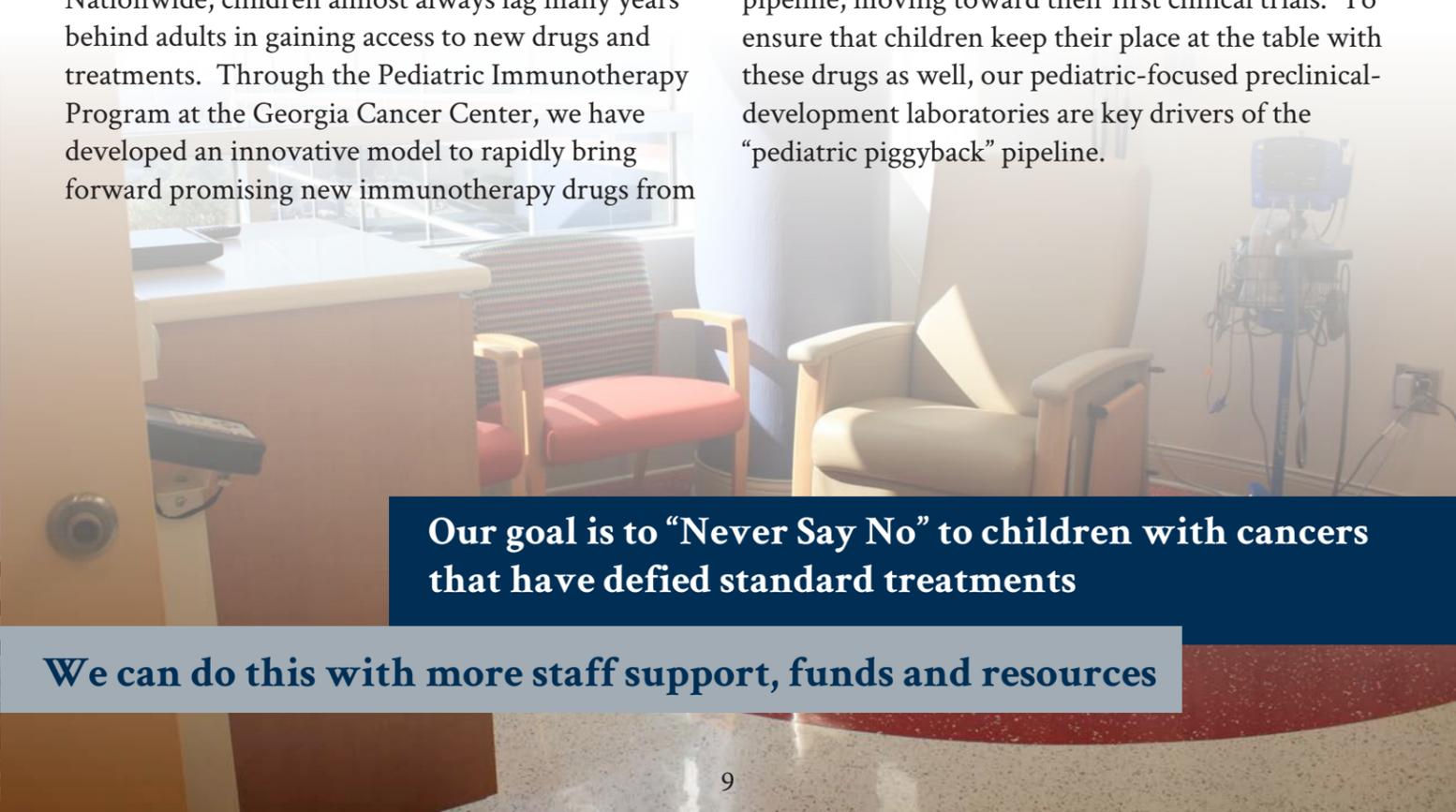
the pre-clinical pipeline into pediatric clinical trials. We call this the "pediatric piggyback" approach. Our goal is to begin a "piggyback" pediatric trial of a given immunotherapy drug just as soon as suitable safety data are available from a corresponding adult trial in the analogous tumor – without having to wait for the drug to eventually reach the commercial market in adults.

This "pediatric piggyback" strategy works because of the excellence in preclinical research and drug development in the Pediatric Immunotherapy program. Discoveries at Augusta University are moving the field forward, and this is being translated into a place at the table for children in the newest clinical trials.

But the immune system is capable of doing much more than we are currently asking it to do. One drug – no matter how good – is not enough to tap the whole power of the immune system. We have several other potent drugs in the development pipeline, moving toward their first clinical trials. To ensure that children keep their place at the table with these drugs as well, our pediatric-focused preclinical-development laboratories are key drivers of the "pediatric piggyback" pipeline.

Our goal is to "Never Say No" to children with cancers that have defied standard treatments

We can do this with more staff support, funds and resources



Turn the Tide

We have already achieved the greatest goal: we have the science and we have the vision. Now, we need the financial resources to put the science to work and make the vision a reality. We have determined that \$10 million is necessary to ensure a sustainable future for the Pediatric Immunotherapy Program at the Georgia Cancer Center and to create a program that never has to say “No” to a child seeking the option of immunotherapy.

Making an investment in the Pediatric Immunotherapy Program is making an investment in a child’s future.

How to make an Impact:

CONTRIBUTE

- Seed funding for clinical trials to support launch of early-phase immunotherapy trials in children (data collection, sample collection, x-rays, etc.)

\$3 million over 5 years (\$600,000/year)

GIVE

- Operating funds to continue nimble development of state-of-the-art new immunotherapy drugs for children, especially to quickly translate breakthroughs and opportunities into first-in-children trials in childhood cancer.

\$5 million endowment

PROVIDE

- Infrastructure support to add full-time, pediatric-focused personnel, including a pediatric nurse practitioner; oncology clinical-trials nurse-coordinator; data manager; and regulatory/compliance staff for first-in-children trials.

\$2 million over 5 years (\$400,000/year)

You can make a gift using cash, securities, estate gifts, real estate or other assets, payable to Georgia Health Sciences Foundation. You may also pledge an amount to be given over time.

Naming Opportunities are available.

Help us **NEVER SAY NO** to a child with cancer.

To learn more about how you can give hope to cancer families, please contact Eileen Brandon at 706-825-4779 or ebrandon@augusta.edu.

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