

A close-up photograph of a baby with blue eyes, wearing a light-colored hat with a dark blue stripe and a light-colored short-sleeved shirt with a pocket. The baby is sitting on a bed with a white patterned blanket. In the background, there is a wooden headboard and a nightstand with a blue vase and a lamp.

JUST SUPPOSE
AIDAN'S STORY

THE PEDIATRIC CANCER PROGRAM AT THE
SIDNEY KIMMEL COMPREHENSIVE CANCER CENTER AT JOHNS HOPKINS

AIDAN ROGER DUPUCH CARRON

ENTERED THE WORLD A HEALTHY BABY BOY ON NOVEMBER 25, 2015. EVERY BIRTH BRINGS THE JOY AND PROMISE OF AN UNFOLDING STORY, FIRST SEEN THROUGH THE HOPES AND DREAMS OF PARENTS, AND AS THE JOURNEY CONTINUES, THROUGH THE LIFE-LONG ACTIONS AND DEEDS OF THE PERSON.

AIDAN'S JOURNEY IS NO DIFFERENT EXCEPT THAT HIS EARTHLY TIME ENDED MUCH TOO SOON, ON CHRISTMAS EVE 2017, BUT IT DID NOT BRING AN END TO HIS STORY. AIDAN'S LIFE, THOUGH BRIEF, HAD PURPOSE. WHAT HE TAUGHT THE WORLD ABOUT MEDICINE, COURAGE AND HOPE IS TIMELESS.

HIS PROMISE IS UNFOLDING NOW AS DOCTORS AND RESEARCHERS USE THE LESSONS THEY LEARNED FROM AIDAN TO TRANSFORM CANCER TREATMENT FOR PATIENTS ALL OVER THE WORLD.

AIDAN'S STORY



A LESSON IN MEDICINE

Families come to the Johns Hopkins Kimmel Cancer Center with hope that its physicians and scientists can help them in the most desperate times of their lives. It is not unusual for our doctors to see very difficult cancer cases. Families come here because of the Cancer Center's recognized expertise in understanding the causes and drivers of cancers and developing treatments that make the unmanageable manageable.

This was the reason the Carron's brought their precious Aidan to see Dr. Patrick Brown, one of the world's leading pediatric leukemia experts.

The uncharacteristic complexities of a relentless cancer proved too much for even the best doctors and the most heroic little warrior, but the ultimate victory belongs to Aidan. What his cancer taught Dr. Brown has inspired new research that could change the way

rare and difficult cancers are managed, saving lives and sparing others the unimaginable loss endured by Robert and Lizzy Carron and family.

Hemophagocytic lymphohistiocytosis (HLH) is a disease usually caused by a gene mutation, but in Aidan's case it was triggered by an improperly administered vaccine. The disease caused his own immune cells to begin attacking his body. The treatment for the disease involves using cancer drugs to calm and reset the immune system back to normal.

Aidan was just six months old when he developed a life threatening immune disease called hemophagocytic lymphohistiocytosis (HLH). The disease is usually caused by a gene mutation, but in Aidan's case it was triggered by an improperly administered vaccine he received in the Bahamas, where his family lives. The disease caused his own immune cells to begin attacking his body.

The treatment for the disease involves using cancer drugs to calm and reset the immune system back to normal. One of these drugs, called etoposide, can cause leukemia. It is a very rare complication and usually occurs one to two years after receiving the drug.

In Aidan's case, it seemed that everything that could go wrong, did go wrong and all at once. An unusual vaccine complication initiated a life-threatening immune disease. And treatment of the immune disease caused a rare form of leukemia.

This final complication of leukemia was what led the Carron family to Dr. Brown, director of the Kimmel Cancer Center's pediatric leukemia program.

At the Kimmel Cancer Center and through national leadership roles with the Children's Oncology Group, Dr. Brown has researched and developed treatments for some of the most intractable cases of leukemia. Throughout his career he has seen and treated some of the most severe complications but never had a case where they occurred at the same time, resulting in a leukemia that was virtually uncontrollable.

"I have never before seen the degree of resistance to chemotherapy that I saw in Aidan's cancer," says Dr. Brown.

These unusual characteristics made Aidan's cancer unique and deadly, but they also led Dr. Brown to look at leukemia in a different way.

The drug that cured Aidan's HLH caused an error in his DNA—the instruction manual that tells cells how to behave. In this case, it altered a gene called MLL.

"MLL leukemias are notoriously resistant to treatment. We knew we had to hit this cancer hard to get it under control," says Dr. Brown.

"Aidan was a courageous little warrior. He was an amazing child who lit up our lives every day. He was so brave and an inspiration to everyone he met. He was with us for a short time, but we will carry him forever in our hearts."

—Aidan's parents, *Lizzy and Robert Carron*



Aidan with his parents Lizzy and Robert, and hospital nurses

The approach was high doses of chemotherapy to kill as many of the leukemia cells as possible followed by a bone marrow transplant, replacing Aidan's diseased bone marrow with healthy marrow donated by his mother. Bone marrow is the factory for all blood and immune cells. The bone marrow transplant would provide a new, healthy factory for his blood and immune cells and also, since it was coming from another person, stimulate his immune system to attack the cancer. The immune-bolstering effect is called graft versus host disease, or GVHD, and occurs when the new donor cells recognize their host as a foreign predator. Doctors use medicines to keep the immune system from getting so aggressive that it permanently damages other tissues and organs, but unleash it enough to allow immune cells to seek out and attack any remaining leukemia cells.

"Aidan had GVHD, so we knew his mom's immune system was activated, but it was not killing the leukemia cells," says Dr. Brown. "I recognized that there was something different about his leukemia."

A LESSON IN COURAGE

Aidan was a warrior who waged a heroic battle. He spent most of his life—515 days of his brief two years—fighting for his life.

“He fought with every fiber of his being, and despite my best efforts I could not save him. The first time I saw him was in a video. He was singing and dancing in his hospital room. It was immediately obvious that this was a special little boy. The better I got to know him, I was strengthened by this joyous spirit that simply refused to be dampened by circumstances,” says Dr. Brown. “The best science and medicine we had failed Aidan, but he revealed to us new things about cancer. In his courageous suffering and struggle, Aidan taught us something new, something vitally important.”

Aidan’s tiny body was being attacked on three fronts. It acquired every bad characteristic possible. Through a complex and unusual set of molecular processes occurring simultaneously, the leukemia cells found a way to resist anti-cancer drugs, escape the bone marrow and survive in other places in his body, and hide from the immune system.

Cancer cells originate from our own cells, so they have at their disposal all of the processes and mechanisms of normal cells. They don’t reinvent the wheel because everything they need is already there. Cancer cells pull the programs they need from our DNA and use them to their advantage. Most cancers are able to exploit one program of survival to its advantage. In Aidan’s case, his cancer successfully selected three programs simultaneously to thwart every effort to kill it.

“Aidan’s cancer taught me that certain cancers are masters of escape,” says Dr. Brown.

Imagine Aidan’s leukemia as an astronaut going into outer space. The astronaut cannot survive on his own in that environment, so he uses special equipment to adapt and survive in the most hostile of conditions. That’s what Aidan’s cancer did.

The special equipment Aidan’s cancer used was a corruption of the very processes that our normal cells use. In scientific terms, we call these three processes epigenetic chemoresistance, adaptive resistance, and immune tolerance. “If any one of them had occurred independently, we may have been able to overcome it, but Aidan’s cancer somehow found a way to employ them all at the same time,” says Dr. Brown.

Epigenetics describes a chemical process used to turn genes on and off. Chemoresistance, or the ability of cancer cells to survive anticancer drugs, can result when cancer cells exploit this process to manipulate genes to maintain their survival. If DNA is our physical hardware, epigenetics can be thought of as a software package that, among other things, tells cells when to start growing and when to stop growing. Epigenetically altered cancer cells seem to maintain their ability to replicate, renew and divide even when being hit with anti-cancer drugs. This can be thought of as the astronaut using

tools to defend an attack directly on the spaceship.

Adaptive resistance is akin to the astronaut putting on a special suit that gives him the ability to survive outside of the spaceship and travel to distant places, while immune tolerance can be thought of as the astronaut disguising himself as a star to look like he belongs, causing potential threats to pass him by.

“Aidan’s cancer used all three of these evasion techniques simultaneously, allowing at least some leukemia cells to survive chemotherapy, find a new home in his skin, and trick mom Lizzy’s immune cells from



Patrick Brown, M.D.

attacking. It made it possible for a portion of leukemia cells to withstand every treatment approach and continue to rebound.

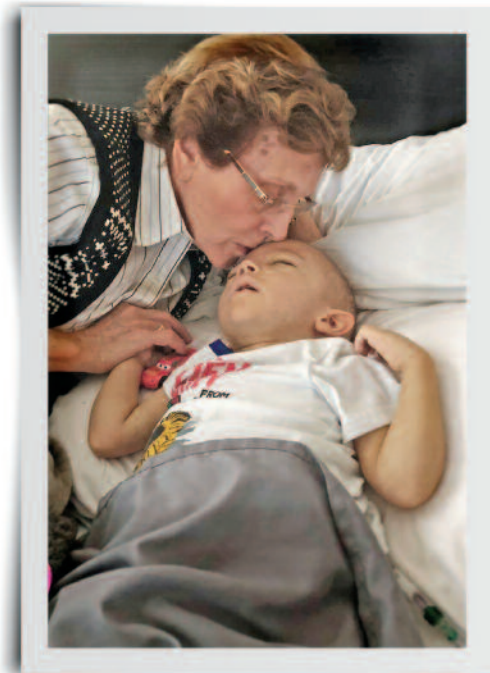
“The combination of these three things ultimately caused Aidan’s death,” says Dr. Brown. “But as his physical body weakened, his spirit became stronger.”

A LESSON IN HOPE

“Cancer never truly defeated him. Leukemia may have claimed Aidan’s physical body, but it did not claim his spirit and it does not own his story,” says Dr. Brown. “Aidan’s story is one of hope because what he taught us could lead to the defeat of the most relentless forms of cancer.”

Aidan’s unique case taught us that we must cut off every survival route and tool that cancer has—simultaneously.

The Kimmel Cancer Center is home to the leading experts in cancer epigenetics, genetics, bone marrow transplantation, and immunotherapy. Our experts are uniquely positioned to find a way to defeat these relentless forms of cancer through collaborative science that brings together the very best minds with a common purpose.



Aidan and grandmother Eileen Dupuch Carron

Cancer is good at doing bad things, but it needs certain things, and we have the expertise to figure out what cancers like Aidan’s need and securely block them off—from the very first day of therapy—sealing off every escape route and tool so there is no place for leukemia cells to turn or hide.

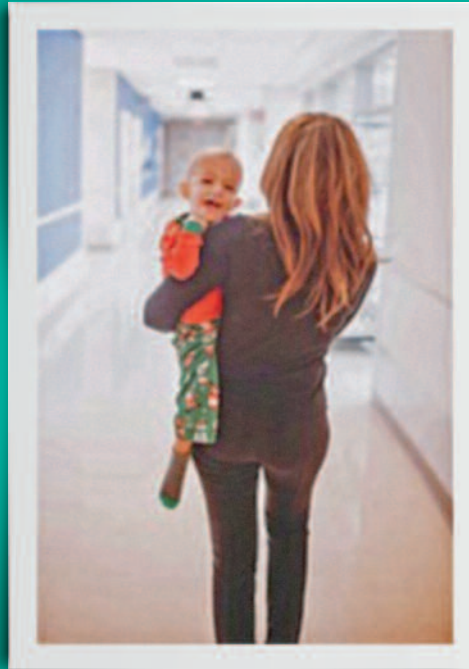
“Cancer never truly defeated him. Leukemia may have claimed Aidan’s physical body, but it did not claim his spirit, and it does not own his story.”

There are FDA-approved drugs that block off each of the escape routes and disable the survival tools Aidan’s cancer used. Our doctors helped decipher the mechanisms and develop the targeted therapies that turn epigenetic-silenced genes back on, immunotherapies that prevent cancer cells from hiding from the immune system and drugs that stop cancer cells from adapting to and creating new, friendlier environments.

“The ways we treat cancers today, always leaves at least one of these escape routes open or a survival tool available,” says Dr. Brown. “The next step is to study combinations of these drugs in the laboratory to see how they can be safely used together to separate leukemia cells from their survival tools and seal off every escape route. Laboratory studies would be followed by clinical trials, combining laboratory and clinical research to find a cure.

“Aidan inspired every member of his medical team,” says Dr. Brown. “If there is a way to treat patients and get better cure rates with lower toxicities, we should be doing the studies that make these treatments available to patients.”

“I believe we can do this, and if we do, we will cure leukemia and extend the approach to cure other types of resistant cancers,” says Dr. Brown. “When we do, it will all be because of Aidan and what he taught us.”



“Cancer beats us sometimes, but it has limits. What Aidan, Lizzy and Robert teach us all is that the power of love is without limits. This love is so strong that it brings new meaning to Aidan’s short time with us and offers hope for a cure to others who battle cancer.”

—*Dr. Patrick Brown*

GIVE HOPE

WORKING TOGETHER TO CHANGE THE STORY OF PEDIATRIC CANCER

Aidan's story illustrates the promise of discovery. Patients, families and doctors from all over the world turn to us for answers, and experts like Dr. Brown will not give up until every child is safe from the threat of cancer.

This challenge is too great for any one of us to take on alone. Consider that less than 5 percent of the National Cancer Institute's budget supports pediatric cancer research, and fewer than 5 cents of every dollar raised by the American Cancer Society is directed to cancers affecting children and adolescents. Pharmaceutical companies, which fund about 60 percent of adult cancer drug discovery, provide no support to pediatric cancer drug development.

Despite limited federal support, Dr. Brown is an international leader in pediatric leukemia and developed the promising new treatment combination described in this booklet. Imagine what he and our other pediatric cancer experts could do with more support.

Together, we can advance research and rewrite the story of childhood cancer so that every child's story has a happy ending.

For more information on how you can support
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