OPTIMIST INTERNATIONAL
Friend of Youth

WORKING WITH JOHNS HOPKINS PEDIATRIC ONCOLOGY TO FIGHT PEDIATRIC CANCER

Giving Hope, Getting Hope, Sharing Hope

The collaboration between Optimist International and Johns Hopkins Pediatric Oncology is a natural one. Optimist's motto is "Friend of Youth." Cancer is the antithesis of this. So, joining the Johns Hopkins Kimmel Cancer Center to take on the disease that claims more time, young lives, and futures brings a unique and profound meaning to this motto.

Children and families around the world can be **Optimist*ic***. For the first time in the history of cancer medicine, the technology exists to quickly decipher the cellular causes of every cancer. With these Johns Hopkins-pioneered discoveries, we can begin to alter the course of pediatric cancers in ways we could only image a decade ago. "We're the ones leading the way—finding the genes, studying what they do in terms of the biology of a particular pediatric cancer, and developing molecularly targeted therapy against it," says Donald Small, M.D, Ph.D., Kyle Haydock Professor and Director of Pediatric Oncology at the Johns Hopkins Kimmel Cancer Center.

There is much to be hopeful about.

With help from organizations like Optimist International, which recently completed a $1 million legacy endowment for childhood cancer research, Johns Hopkins Pediatric Oncology researchers and clinicians, are making unprecedented progress. This vital support fuels the laboratory and clinical advances in pediatric cancer, ***giving hope*** to the more than 12,000 children diagnosed each year. By supporting the leaders in the field of pediatric cancer research and care, children from around the world are ***getting hope***, knowing they can come to Johns Hopkins and receive the best and most advanced care available anywhere. These organizations are successful through the tireless support of countless volunteers who ***share our hope*** and belief that we can conquer pediatric cancer.

Just suppose we could create a future free of childhood cancer. Together, we can.

Getting Hope: An Optimist*ic* Future

Securing a Cancer-Free Tomorrow for Children

Johns Hopkins Pediatric Oncology has embarked on a campaign to create a $30 million endowment that will ensure that these promising initiatives have the steady support they need to result in monumental leaps in knowledge, and ultimately cures for all children with cancer.

It will empower our faculty to purchase the sophisticated gene sequencing equipment and hire the research staff they need to develop aggressive research programs aimed at understanding the underlying causes of childhood cancer:

- find cures for those cancers we currently cannot cure.
- improve therapies, developing targeted therapies that kill the cancer without harming the child.
- use biology and laboratory discoveries to improve clinical trials.
- study the short- and long-term consequences of cancer and cancer therapy on the child to improve the quality of life during and after treatment.

Ensuring the Future of Pediatric Cancer Research

To ensure continued advances in pediatric cancer research and treatment, we must attract the best and brightest young investigators and clinicians. The **Optimist International Research Fellowship in Pediatric Hematology and Oncology** enables us to accomplish this. Most recently, it made it possible for the Kimmel Cancer Center to offer Eric Schafer, M.D., a permanent position in the pediatric oncology program. In addition to his clinical work, he will be doing laboratory research with Patrick Brown, M.D., to develop clinical trials for children with MLL gene-rearranged leukemias. Dr. Schafer also competed and earned a spot in the Johns Hopkins Graduate Training Program in Clinical Investigation.

Giving Hope: The Home of 21st Century Pediatric Cancer Medicine

A New Pediatric Cancer Hospital

The Charlotte R. Bloomberg Children's Center will open in 2012. This technologically advanced, but patient and family-friendly building will be home to our pediatric oncology inpatient unit and outpatient clinic.

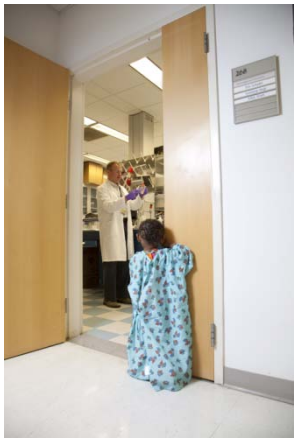
The inpatient unit will have 20 private rooms with the ability to expand to 22. It will include a playroom for children and a separate room for teenagers. Many amenities will be available for the comfort of families, including sleeper sofas in every room, lounges, showers, laundry facilities, and 24-hour room service.

The outpatient unit has eight exam rooms, four private infusion areas and a beautiful, two-story open infusion area with five additional chairs and beds, and an on-floor pharmacy. It has two waiting areas, separately and distinctively designed for the different interests and needs of children and teenagers.

Sharing Hope: Research that Makes a Difference

Milestones in Pediatric Oncology Discovery and Innovation

Genetic Culprits
Pediatric Oncology director Donald Small was the first to identify and clone the FLT3 gene. Mutations to this gene are linked to treatment-resistant types of childhood leukemia, including infant leukemia. Our pediatric oncology team has identified drugs that block or inhibit FLT3 function and are now directing multi-institutional clinical trials.



In a brand new discovery, our scientists became the first to decipher the genetic code of a pediatric cancer. Using sophisticated new gene sequencing technologies, the team mapped the genetic sequence of medulloblastoma, the most common type of pediatric brain cancer. Information like this, gained from gene sequencing technology, could potentially help our team change the course of some relentless childhood cancers.

Acute Lymphocytic Leukemia (ALL)
ALL is one of the most common types of pediatric cancers. By defining specific subtypes of the cancer and altering the administration of chemotherapy, Kimmel Cancer Center researchers improved cure rates to nearly 90 percent.

Brain Cancer Discoveries
Brain cancers are among the most common cancers in children. Johns Hopkins scientists in the Vogelstein/Kinzler/Velculescu laboratory of the Kimmel Cancer Center linked mutations two genes, IDH1 and IDH2, to nearly three-quarters of the most common types of brain cancers known as gliomas. Patients with certain tumors that carry these genetic alterations appear to survive at least twice as long as those without them. They believe further research on the genes could also lead to more precise diagnosis and treatments.

Kenneth Cohen, clinical director of Johns Hopkins Pediatric Oncology, and colleagues developed an “up-front” radiation therapy for pediatric brain tumors, now widely adopted by other cancer treatment facilities. Dr. Cohen also is studying the first use of arsenic given in combination with radiation therapy in children with high risk brain tumors. This treatment is part of an overall program to develop novel therapies for children with poor prognosis brain tumors.

Pilomyxoid Astrocytoma (PMAs) is a type of brain cancer largely seen in children and was first identified by Hopkins pathologist Peter Burger, M.D., and colleagues. To further advance

research and treatment of PMA, we invite adults or children who have been diagnosed with PMA to join the Johns Hopkins PMA Registry, a resource for patients and physicians alike supervised by Dr Cohen.

Pediatric Sarcomas

Treatment for pediatric sarcomas has not changed much since the 1980s. Future advances in the care of children with sarcoma will only come from a deeper understanding of the biology of these tumors, and the translation of this understanding into clinical trials. Our researchers are working to drive this progress. An exciting new area of research is in cancer stem cells. These cells represent a rare and stealth population of cells that often escapes the assault of anticancer drugs and drive the growth of tumors. Like the typical stem cell that helps form and regenerate tissue and cells, cancer stem cells are capable of limitless growth, self-renewal, and the generation of new tumors. Our team suspects that while chemotherapy destroys the bulk of the tumor, it does not get at the cancer stem cells. These resistant cells then eventually drive the growth of tumor cells, causing the cancer to return.

Ongoing work is now focused on identifying the Ewing's sarcoma cancer stem cell and using drugs that interfere with the metabolism of cancer stem cells as a way to kill them. Another therapy that targets a specific enzyme is being studied for its potential to kill Ewing's sarcoma and rhabdoymosarcoma cancer stem cells. With promising early laboratory data, the team is working to move quickly to clinical trials of the drug.

New Anticancer Drug

The Kimmel Cancer Center led a multi-institutional study of an experimental drug that blocks the cancer-associated hedgehog gene pathway. The drug showed impressive activity in medulloblastoma brain cancer and led to clinical trials of the drug in children with medulloblastoma.

Bone Marrow Transplant

Our Center was a pioneer in bone marrow transplant therapy. In 1995, we established one of the first pediatric bone marrow transplant programs. Today, we are again leading the field with development of haploidentical, or half identical, bone marrow transplants. This form of transplant allows patients who do not have an identical immune system match to undergo potentially curative bone marrow transplants with a half-matching parent or sibling has a marrow donor. Our investigators have learned how to manage immune complications—even making them work to their benefit against the cancer. Recent finding reveal half-identical transplants may actually produce better results than standard, perfectly-matched transplants. The Kimmel Cancer Center is the only cancer center performing half-identical bone marrow transplants.

Pediatric Oncology Fellowship Program

The fellowship program is a joint endeavor of Johns Hopkins and the National Institutes of Health. It is designed to provide clinical and research exposure to develop and train the next generation of specialists in pediatric cancer laboratory and clinical research and patient care.

Discoveries Pilomyxoid Astrocytoma (PMA) Registry

PMA, studied and defined by Johns Hopkins researchers as a distinct type of glioma, is a form of brain cancer most commonly seen in children. Despite its growing recognition, little is known

about the tumor. Researchers will use data gathered in the registry to help refine current therapies and to develop new ones.

Isolating Blood Stem Cells
Our researchers developed the technology to isolate the rare blood stem cell from within a sea of hundreds of billions of blood cells. The blood, or hematopoietic stem cell, controls the development of all other blood and immune cells. The discovery has led to better diagnostics in blood-born cancers such as leukemia and blood stem-cell based therapies.

Inducing Cancer Cell Death
Pediatric oncology researchers identified a gene, called PASG, that when altered causes cells to age prematurely and die. In order to grow and stay alive, cells depend on PASG to reduce the activity of other genes. Researchers are studying agents that block the function of the gene as a way to force cancer cells into an early death.

Preventing and Managing Late Effects
As cure rates improved for children with cancer, experts began to recognize treatment-related side effects. The Kimmel Cancer Center established one of the first childhood cancer survivors programs in the nation to study, monitor, treat, and develop methods to prevent long-term complications of cancer therapy. These late effects include infertility, cardiac toxicities, hyperthyroidism, and developmental and cognitive delays.