

Research Champions

ANNUAL REPORT FOR CALENDAR YEAR 2010



Learn how your generous giving is helping our investigators prevent, treat and eliminate pediatric diseases.

Bridging a research funding shortfall

Your giving nurtures new ideas and life-changing discoveries

Dear Research Champion,

Less than half a cent of every healthcare dollar in the United States is spent on pediatric research. Put another way, 30% of the U.S. population is under the age of 21 — yet only 6% of the entire National Institutes of Health (NIH) budget is devoted to pediatric medicine and healthcare.

Breakthroughs in pediatric research will only come with support from Research Champions like you. With your help, Children's is building a world-class research organization designed to prevent, treat and eliminate pediatric diseases. In fact, Seattle Children's Research Institute has become one of the top five pediatric research institutions in the nation as measured by NIH funding.

Between 2003 and 2010, our federal funding increased from \$6 million to more than \$52 million, thanks in large part to philanthropic support that nurtured novel ideas from the pilot phase to federal funded studies — and the gifts that sustained ongoing research between grant funding cycles.

Half of our growth during the past two years has come from new dollars, and the remaining funds have enhanced existing programs — proof that not only are we bringing in great scientists, but our current investigators continue to excel.

Your generous support is integral to the growth and success of Children's research initiatives and our ability to discover new treatments and cures for childhood illnesses. This report demonstrates how research at



Children's is advancing science, enhancing medical care and improving the well-being of children and their families. It also highlights some remarkable investigators who exemplify the return on your investment in research. If you attended our Research Champions events during 2010, please reacquaint yourself with the work of these talented leaders. And if you missed any of our Research Champions events, I hope you will take this opportunity to read about our featured investigators' inspiring and innovative research.

Thank you again for your commitment to research at Children's.

A handwritten signature in black ink, which appears to read "James Hendricks". The signature is fluid and cursive, written over a white background.

James Hendricks, PhD
President, Seattle Children's Research Institute

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How Research Champions make a difference



Seattle Children's Research Champions provide vital support for initiatives to bring lifesaving cures and clinical advances to children in the Pacific Northwest and around the world. In 2010, the first year of the program, 454 Research Champions collectively gave \$13.8 million in support of research at Seattle Children's. This support was integral to a variety of key achievements at Seattle Children's Research Institute, including:

The Science Adventure Lab instructed 6,400 students from 54 different schools in every corner of Washington state. The 45-foot-long, custom-built mobile laboratory lets students interact with scientists and conduct experiments using real scientific tools. As one teacher wrote in a thank you to our staff, "The need for better science education is crucial... and the lab fills a gap that we cannot fill. It cannot be expressed strongly enough how important this is as we work to inspire children to become scientists."

The Treuman Katz Center for Pediatric Bioethics at Seattle Children's hosted its sixth annual international conference, which focused on ethical issues in prenatal and neonatal care.

By featuring nationally recognized speakers and drawing more than 250 participants, the conference advanced the Katz Center's mission of addressing the complex bioethical issues affecting families, healthcare institutions and society.

John Welsh, PhD, is leading a research team that is laying the foundation for a new generation of autism treatments. The team is testing drug compounds that build on Welsh's breakthrough insight that autism could fundamentally be a problem with brain speed. The new compounds enhance brain cells' ability to communicate and could play a key role in therapies that improve the lives of children with autism.

Dr. Tonya Palermo developed an online program that brings innovative pain management techniques to underserved areas. While an estimated 35% to 40% of children experience chronic pain, few hospitals have pediatric pain medicine programs, leaving many children without access to specialized care. Palermo's goal is to help them lessen pain's negative consequences.



Seattle Children's Research Institute: Committed to treatments and cures

Thanks in part to philanthropy, Seattle Children's is committed to giving researchers what they need to improve the health of children in our region and beyond. Our state-of-the-art bench research facility dedicated solely to pediatrics is a highlight of Seattle Children's Research Institute.

"Many pediatric research institutes are floors or wings of buildings cobbled onto something else, often a hospital or a research center focused on adults," explains Dr. Arnold Smith, interim director of the research institute's Center for Childhood Infections and Prematurity Research. "In this building alone, we have six floors of researchers and support staff who care about kids and are dedicated to finding cures for childhood diseases."

Since 2003, we've grown from 20,000 to 350,000 square feet of research space. More than 500 investigators and staff conduct research in laboratory and associated support space located in the heart of Seattle's biomedical community. Future plans include expanding to nearly 2 million square feet of research space — every foot of it dedicated to finding innovative ways to treat and prevent childhood illnesses and injuries.

"We are developing the most advanced space so our research teams have the facilities and sophisticated technical resources they need to find solutions to some of the most daunting challenges in pediatric medicine," says James Hendricks, PhD, president of the research institute.

Collaborative work sparks growth

The growth of our research institute — which comprises nine interdisciplinary centers — is fueled by our affiliation with the University of Washington (UW) and the Fred Hutchinson Cancer Research Center — two of the largest recipients of federal research funding in the

nation. We are clinical, teaching and research partners with both UW and the Hutchinson Center. Our strong collaborations allow each organization to benefit from top-tier talent in a multitude of disciplines.

Other neighbors and collaborators include Seattle Cancer Care Alliance, Benaroya Research Institute, the Bill & Melinda Gates Foundation, PATH, the Pacific Northwest Diabetes Research Institute, Seattle Biomed and Virginia Mason Medical Center.

"We attract the highest caliber of researchers because of our partnerships," says Dr. Bruder Stapleton, Children's chief academic officer. "Our researchers stay at Seattle Children's because they have the opportunity to make significant contributions to child health in a place with a long-term financial commitment to research facilities and space."

Extraordinary community support

In addition to being located in a thriving city and region, Seattle Children's Research Institute is part of a financially stable, standalone children's hospital that is deeply committed to pediatric research.

"We have great support from Seattle Children's board of trustees and a commitment to curing kids," explains Hendricks. "We also benefit from a phenomenal level of philanthropic investment."

That support includes generous gifts from individuals, guilds, foundations and corporations with a stake in the health and well-being of children and teens. "At Children's, research is close to donors who are interested in seeing progress," says Dr. Mark Majesky, associate director of the Center for Tissue and Cell Sciences. "Donors are working directly with the researchers. This type of community support helps research move quickly from the lab to therapeutic testing."



Seattle Children's Research Centers

As one of the top five pediatric research institutions in the nation, we bring together the best minds in pediatric research to set new standards of care and find new cures for childhood diseases. Our nine interdisciplinary research centers address areas central to pediatric health and use an “open lab” format to foster a rich collaborative environment. Investigators draw from different departments and disciplines to find new cures for childhood diseases more quickly. Our discoveries in bench, clinical and outcomes research are recognized by scientists worldwide.

The Center for Child Health, Behavior and Development finds new ways to promote health and development so that all children can reach their potential. Investigators work with families, communities, schools, providers and healthcare organizations to translate research findings into actions that improve children's day-to-day lives.

The Center for Childhood Cancer translates new scientific knowledge and technologies into effective treatments that maximize the well-being of children with cancer and the quality of life for childhood cancer survivors.

The Center for Childhood Infections and Prematurity Research translates basic biology into strategies for the diagnosis, treatment and prevention of infectious diseases and conditions that impact children locally, nationally and globally.

The Center for Clinical and Translational Research advances laboratory discoveries toward new and innovative treatments that prevent and cure childhood illnesses and improve the quality of children's lives.

The Center for Developmental Therapeutics identifies and develops new drugs and treatments that will be safer and more effective for children.

The Center for Immunity and Immunotherapies brings together distinguished experts across multiple disciplines to solve some of the immune system's most complex problems. Investigators harness the power of the immune system to prevent, treat or cure life-threatening childhood diseases.

The Center for Genetics and Development improves diagnosis and treatment options for a broad range of diseases and conditions through research in human genetics and developmental biology.

The Center for Integrative Brain Research integrates knowledge at the genetic, molecular, cellular, network and behavioral levels to develop novel ways of preventing, treating and potentially curing pediatric neurological disorders.

The Center for Tissue and Cell Sciences seeks to restore children's health after injury through repair, regeneration or replacement of tissues, cells and organs. By understanding the body's response at the molecular, cellular, tissue and whole-organ levels, our researchers are developing innovative interventions that will ultimately help the body repair itself.



Investigating the impact of media exposure

Dr. Dimitri Christakis has devoted his career to investigating young children’s cognitive, emotional and behavioral development, including how media exposure impacts children — and helping parents take control of their family’s media habits. “My research is focused on developing pragmatic, actionable strategies for parents,” says Christakis, who directs the Center for Child Health, Behavior and Development at Seattle Children’s Research Institute.

Christakis has shown repeatedly that early TV exposure is associated with an array of child health and behavior problems. When screen time trumps parent-child interactions, it can cause delays in language development. Too much time spent viewing rapid-fire screen images can make real-time activities seem boring, causing attention problems when children enter the classroom. Christakis is especially concerned by the link between

screen violence and aggressive behavior, a connection he believes to be as strong as cigarette smoking and lung cancer.

“Repeated exposure to even cartoon violence desensitizes children and increases the likelihood that they will behave violently in real life,” he says. “Parents are surprisingly poorly informed about this, and in our studies we’re working hard to educate them. Parents need to know TV and other media have real and powerful effects on their kids.”

Christakis was pleased with Disney’s decision in 2009 to change how it markets its Baby Einstein videos, which are targeted at infants and young toddlers. Based largely on Christakis’ research findings, the company will no longer make educational claims on the videos. “This was a huge triumph,” he says. “I feel I’m making a tangible difference if parents are reducing the amount of TV their babies watch.”

A new approach to pediatric brain research

What distinguishes brain research at Seattle Children's from research at other centers? Dr. Jan-Marino "Nino" Ramirez is proud to answer this question. "Our integrative approach uniquely identifies us and reflects our vision for the future of brain research, which requires integrating knowledge at all levels — from gene to molecule to network to behavior to patient — to solve life-threatening neurological disorders," he says.

As director of the Center for Integrative Brain Research at Seattle Children's Research Institute, Ramirez is establishing programs that will lead to a better understanding of neurological, neurodevelopmental and neuropsychiatric disorders in children, including autism, Tourette's and seizure disorders. His own research focuses on the cellular basis of diseases that affect the autonomic nervous system. For example, one project aims to unravel the basis of erratic breathing, one of the most debilitating symptoms of Rett syndrome. "It's heartbreaking to see children struggling to breathe who are afflicted with Rett syndrome," says Ramirez. "Equally devastating are disorders in which children 'forget' to breathe or don't respond properly to challenges that require complex autonomic responses. There is currently neither a treatment nor a



cure for these disorders. Hence, as scientists with a mission to prevent, treat and someday eliminate pediatric disease, we have the enormous responsibility of developing new therapies and concepts to combat these neurological conditions."

Ramirez is also investigating the mechanisms underlying sleep apnea. "An astonishing number of children suffer from obstructive sleep apnea, which can cause poor school performance," notes Ramirez. "In order to understand sleep apnea and other neurological disorders, it is critical to investigate the problem from many different aspects — at the genetic, molecular, cellular, network and behavioral levels."

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— Dr. Jan-Marino "Nino" Ramirez



Exploring novel treatments for lupus

Life can be difficult for children with lupus today, but Dr. Anne Stevens is working toward a better future. “When my patients learn they have a chronic disease with no cure, it turns their lives upside down,” says Stevens, a pediatric rheumatologist and member of the Center for Immunity and Immunotherapies at Seattle Children’s Research Institute. “And even though today’s treatments save lives, the side effects take a considerable toll on patients and their families.”

Stevens is addressing these challenges in the laboratory, where her research has yielded some promising results. For example, rheumatologists know that patients with lupus develop antibodies to their own proteins, and that B lymphocytes make the antibodies with help from T lymphocytes. But the source of T lymphocyte reactivity has eluded scientists.

Stevens believes maternal cells — which are transported to a fetus during pregnancy and persist through a child’s lifetime — might

play a role in pediatric lupus. She’s leading a study of T lymphocytes in healthy children and children newly diagnosed with lupus to look for reactivity to maternal cells.

“Our preliminary research has shown that healthy kids’ immune systems are tolerant of their mothers’ cells, while kids with lupus seem to overreact,” Stevens explains. “But we need to study more patients before we can draw a definitive conclusion.”

If maternal cells prove to be a culprit, Stevens says scientists would have a great opportunity to develop targeted treatments for children with lupus. “Maternal cells are present in about one in a million cells,” says Stevens. “That’s a small number of cells. If we could develop a therapy that blocks reactivity to the maternal cells or eliminates them altogether, it could be very successful with few side effects — unlike today’s pediatric lupus treatments, which are extremely immunosuppressive and toxic.”



Understanding antibiotic resistance

Infections caused by bacteria resistant to usual antibiotics can pose significant challenges for sick children, including prolonged illness and even death. While much attention has been directed at understanding resistance in Gram-positive organisms, especially methicillin-resistant *Staphylococcus aureus* (MRSA), less is known about multi-drug resistance in Gram-negative organisms in pediatric settings.

Research conducted by Dr. Danielle Zerr has revealed worrisome increases in multi-drug resistance to the Gram-negative bacterium *Enterobacteriaceae*. “We are concerned about this scenario because it limits the antimicrobials available to treat infections and it creates a threat for rapid spread of resistance,” says Zerr. To better understand the problem and develop proactive solutions,

Zerr and her team are partnering with four children’s hospitals across the country to study antibiotic resistance in *Enterobacteriaceae* bacteria that produce urinary tract and bloodstream infections. The team will use a powerful set of molecular tools to identify key differences between resistant strains and still-susceptible strains.

“These data will fill a critical gap in the pediatric literature and provide the foundation for the design of future intervention studies to reduce the spread of this resistance,” says Zerr. “This information has the potential to inform treatment of serious bacterial infections in children. It will guide changes in treatment to reduce the incidence of these infections, prevent infection-related mortality and improve outcomes.”

Stem cell initiative aims to transform cardiac care

When diseases strike, stem cells may hold the power to regenerate new, healthy cells and tissues that can repair injured or defective areas of the body. Dr. Mark Majesky, associate director of the Center for Tissue and Cell Sciences at Seattle Children’s Research Institute, is developing new ways of repairing the heart and regenerating heart tissues through the Myocardial Regeneration Initiative.

“If we can develop new strategies and therapies that utilize existing cells to repair and rebuild damaged tissues, we can eliminate serious heart defects and save many kids’ lives in the process,” says Majesky.

Majesky and his team are conducting detailed studies of how heart and coronary vessels develop. Ultimately, it may be possible to create healthy heart cells in the laboratory and then transplant those cells into patients with chronic heart disease to repair the heart and coronary vessels without invasive surgery or a heart transplant.

Using the tools of developmental biology and developmental genetics, the research team is creating models that will help them learn how the heart and its vascular system — especially the coronary arteries — form during development. “We’re looking at key control genes that regulate the critical steps as the heart and coronary vessels are formed in the embryo,” Majesky explains. “Once we



understand how the tissues and cells form, and how the pathways for heart development take shape, we will have a framework that allows us to take the first step in prevention and repair of heart and valve defects.”

When fully assembled, the Myocardial Regeneration Initiative team will include experts in developmental biology, genetics, bioengineering, pathology and clinical pediatrics. “It takes an intellectual village to help children live healthier,” says Majesky. “We need a talented multidisciplinary team to accomplish our scientific goals and translate discoveries from the laboratory into treatments for children with heart conditions.”

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— Dr. Mark Majesky



Tackling the obesity epidemic

Today, with more than 15% of American children considered obese, it's feared that weight-related diseases will reach epidemic levels when those youth reach adulthood. Two Seattle Children's researchers who share a focus on childhood obesity are working to reverse this trend.

Brian Saelens, PhD, a health psychologist with Seattle Children's Research Institute's Center for Child Health, Behavior and Development, merges his clinical work with studying how a child's home and environment affect eating and physical activity. Saelens is investigating how the availability of parks, fast-food restaurants and grocery stores, along with a community's "walkability," impact kids' health. "We're hoping to influence policies that make healthy choices easy, convenient and fun," Saelens says. "Right now, most of our environments make it easier and cheaper to be sedentary and get unhealthy food."

"Obesity is beyond a medical problem—it's a symptom of a fundamental cultural problem," says Dr. Lenna Liu, an investigator with the research institute's Center for Child Health, Behavior and Development and pediatrician at Odessa Brown Children's Clinic, "and that problem is limited access to healthy foods and activities."

In the clinic, Liu works to correct this by promoting family-based lifestyle changes, like reducing the amount of soda and juice children drink. She also helps families stay motivated when basic needs like groceries, housing and employment compete with health concerns.

"What makes this issue even more challenging is that lower-income kids most impacted by this epidemic have the least access to resources," Liu said. Liu's research focuses on building programs to educate families about healthy choices, including the Actively Changing Together (ACT) program offered through YMCAs in King and Snohomish counties. In 2009, she helped organize the first-ever Washington State Childhood Obesity Summit, where an alliance of organizations, including Children's, laid the groundwork for shaping new legislation.

"I always have to remember that it will take a couple of generations for these cultural changes to occur, and it helps to keep that long-range view," Liu said.

A revolution against cancer

Dr. Michael Jensen, a principal investigator with Seattle Children's Research Institute's Center for Childhood Cancer, is pursuing a dramatic vision of how to eradicate cancer, without the debilitating side effects of chemotherapy and radiation. By developing therapies that use a child's own immune system to destroy cancer cells, Jensen believes we can usher in an era where cancer treatment lasts just a few days, and the experience of going through it is no worse than having a mild case of the flu.

His approach has already proved remarkably effective at eliminating cancer in mice. And his new lab at Seattle Children's is taking the final steps toward turning this research into real-world treatments that save children's lives. "I believe it's a matter of when, not if, these therapies will wipe out some of the most common cancers affecting children," Jensen says.

Jensen's approach starts by taking T-cells - specialized white blood cells that fight infections - from patients' blood. Then, recombinant DNA is inserted into these cells, instructing them to attach to cancer cells and kill them. Working together with partner organizations such as the Fred Hutchinson Cancer Research Center, the lab's team is preparing to guide a new generation of therapies from the lab to the clinic.

To propel Jensen's research, Seattle Children's is completing a multi-million dollar facility where the actual cell reprogramming



Above: Dr. Mike Jensen is developing revolutionary therapies that will use a child's own immune system to destroy cancer cells.

Facing page: Dr. Lenna Liu (left) is building and studying programs that educate children and their families about healthy lifestyle choices. Dr. Brian Saelens (right) is studying built environments to determine how home and neighborhood affect a child's eating and physical activity.

will occur. It will be one of a small handful of pediatric facilities in the United States meeting strict FDA requirements for manufacturing therapies.

When the facility is finished, Jensen's team will conduct clinical trials on T-cell therapies for leukemia and lymphoma, and also test similar treatments targeting many other cancers.

As the research progresses, Jensen expects these therapies to break the grip of cancers that affect children and make key contributions to treatments that also save adults.

"The science is already in place," he says. "Now we just need to refine it."

"I believe it's a matter of when, not if, these therapies will wipe out some of the most common cancers affecting children."

— Dr. Mike Jensen

Your generous giving transforms lives!

Individuals and family foundations join Research Champions by making a gift or grant of \$1,000 or more in one calendar year to support research. Gifts or grants at the \$2,500 level qualify organizations, including guilds, nonprofit organizations and corporations.

Contributions from Research Champions are directed toward areas of specific donor interest or research greatest needs, such as supporting highly promising research projects, training the next generation of research-scientists and acquiring cutting-edge lab tools and equipment.

As a Research Champion, you give hope for the future by investing in research today. With your continued support, Seattle Children's is setting new standards of pediatric care, revolutionizing how devastating diseases are treated and seeking to discover the breakthrough cures that will benefit people of all ages.

To learn more about Research Champions, or to make a qualifying gift for 2011, contact Brenda Majercin at 206-987-4979, brenda.majercin@seattlechildrens.org, or go to www.seattlechildrens.org/researchchampions.

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