What will it take to cure childhood disease?

Innovative collaborations are helping scientists at Seattle Children's Research Institute create a healthier future for all children.

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Research Institute

Marketing Supplement

Creating Tomorrow's Cures, Today

Collaborations bring Seattle Children's Research Institute closer than ever to curing childhood diseases and disorders.

Dr. Jim Hendricks, president of Seattle Children's Research Institute, and Dr. Bruder Stapleton, Seattle Children's chief academic officer.

Seattle Children's Research Institute's goal is to create a healthier future for all children.

Curing cancer without chemotherapy or radiation. Rewriting the blueprints of genes to cure diseases in children. Making heart surgery obsolete. These goals used to seem like science fiction. Today they are within reach.

But the process of developing cures and better treatments is so complicated that no one can do it alone. Experts in genetics, biology and other areas must work together to unravel how different factors conspire to cause medical problems – and to design the drugs or treatments that solve them. Sometimes those experts work under the same roof. Sometimes they are thousands of miles apart.

Collaborations spur advances

Every year, Seattle Children's Research Institute launches collaborations that break down the walls and bridge the gaps between scientific disciplines and between academic and commercial institutions. The research institute partners with biotechnology companies, private foundations, pediatric doctors, researchers, patients and families. Collaborations allow the healthcare community to accomplish more together than any one organization could on its own.

That means accelerating progress toward cures for some of the deadliest childhood diseases. It means developing new drugs for children faster than ever before. It means making existing treatments more effective with fewer side effects. It means answering behavioral health questions so better therapies can be created.

Most important, it means giving hope to children who wake up every day wondering if their condition will flare up – and bringing peace to parents torn by worry. It means creating a healthier future for all children. ■

Research Champions

Research Champions is a group of donors dedicated to supporting Seattle Children's work to discover new treatments and cures and create a healthier future for all children. The group's sponsors support the research institute's top priorities, including promising research initiatives and recruiting outstanding investigators from around the country. For more information, email ResearchChampions@seattlechildrens.org. Sponsors, as of July 31, 2014, include:

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Game-changing Medications

Seattle Children's Research Institute is teaming up with a biotech company to develop a new generation of treatments for children – starting with pediatric lupus.

Dr. Anne Stevens of Seattle Children's and Dr. Ernesto Muñoz of Kineta are joining forces to develop the first treatment for lupus designed specifically for children.

Most treatments weren't designed for – or tested in – children. This means doctors must give adult medicines to children, sometimes without knowing exactly what dose to use or what the side effects might be.

"Children metabolize medications differently than adults and are more vulnerable to side effects because their bodies are still developing," says Dr. Anne Stevens, a physician at Seattle Children's and one of only a handful of pediatric rheumatologists in the country who study autoimmune diseases. "But we use what we have."

To address this problem, Seattle Children's Research Institute recently launched a collaboration called the Alliance for Children's Therapeutics (ACT). ACT unites the research institute with Seattle biotechnology company Kineta, Inc. to develop a new wave of treatments specifically for children, starting with a potentially game-changing drug for lupus.

Turning discoveries into real-world treatments

Because most children are healthy and so few are sick, the market for pediatric treatments is too small for most pharmaceutical companies to spend millions of dollars developing them.

Kineta specializes in developing drugs in the early translational space. That makes it a perfect partner for researchers like Stevens, who makes discoveries about childhood diseases but doesn't have the expertise – or the funding – to bring new treatments to market.

Devastating side effects of current treatments

Autoimmune diseases like lupus strike when immune cells attack a patient's organs and tissues. The best current treatment is a combination of chemotherapy and steroids that help control lupus, but also increase the risk that patients will get cancer, diabetes and other serious side effects.

"Imagine being a teenage girl and having to take medications that make your face swell up and force you to worry about whether you'll ever be able to have a baby," Stevens says. "It can be devastating."

Kineta developed a drug candidate, called ShK-186, that is designed to target the immune cells that go haywire in lupus. The molecule has disarmed these cells in preclinical studies with minimal side effects. Stevens is working with Kineta's Dr. Ernesto Muñoz to see if the drug can do the same thing in children.

The first step is to study how ShK-186 interacts with immune cells taken from lupus patients experiencing nephritis, a complication that can cause kidney failure. Stevens and Muñoz hope to complete these early studies with patient cells within a year, then plan for a clinical trial. If ShK-186 is effective, it could be the first lupus therapy ever approved for children by the U.S. Food and Drug Administration.

And because ShK-186 targets cells that contribute to other autoimmune diseases, like multiple sclerosis and rheumatoid arthritis, it could someday improve millions of lives.

"We have a long way to go before we know if this drug will truly work, but we're really excited about its potential," Stevens says. "These kids deserve better." ■

> "Children metabolize medications differently than adults and are more vulnerable to side effects because their bodies are still developing. But we use what we have."
>
> – Dr. Anne Stevens

The medical challenges Dr. Anne Stevens sees in the clinic inspire her research to find better treatments for children and teens suffering from autoimmune issues like lupus, scleroderma and juvenile arthritis.

Revolutionizing Respiratory Care

What if a $20 device could save hundreds of thousands of babies' lives?

Dr. Skip Smith and research technician Tiffany Youngquist are part of the Neonatal Respiratory Support Technologies (NeoRest) team that is working to meet the global need for affordable, safe respiratory support technology that is easy-to-use and easy-to-maintain.

The lungs of infants born prematurely often aren't developed enough to work on their own. In the United States and other developed countries, these babies can be supported on ventilators or other machines until their lungs mature. But in the developing world, about one million infants die each year because breathing support machines like these aren't available – they are too expensive and require sophisticated training to use and maintain.

What if a $20 device could save these babies' lives?

A team of investigators at Seattle Children's Research Institute – including Dr. Skip Smith, Seattle Children's Chief Executive Officer Dr. Tom Hansen, Dr. Peter Richardson, John Walton and Chris Howard – have spent six years developing a simple device, called Seattle-PAP (Seattle Continuous Positive Airway Pressure). This device drives air through a nasal tube to maintain just enough pressure to keep infant lungs open. Their design spares babies from being intubated and placed on a ventilator.

Seattle-PAP features one key improvement over typical positive airway pressure devices: The air pressure oscillations it creates could make it even easier for premature infants to breathe. Preclinical studies suggest that the Seattle-PAP prototype works better than traditional devices that are expensive to buy ($6,000 to $60,000) and expensive to maintain.

"Most babies with breathing problems don't need to be on sophisticated ventilators to prevent lung failure – they just need something simple to support them," Smith says.

Helping the Bill & Melinda Gates Foundation fulfill a vision

The team's work was funded in part by an initial $2.3 million grant from the Bill & Melinda Gates Foundation, which supports experts like those on the Seattle-PAP team to develop concrete solutions to improve health in the developing world.

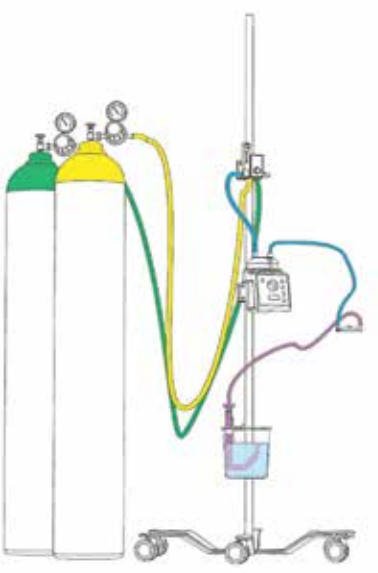
"Instead of fixating on big profits, the Bill & Melinda Gates Foundation's support has allowed us to position Seattle-PAP so we can charge a price that keeps it affordable in resource-limited countries," says Smith.

Accelerating clinical trials

The team is now collaborating with Texas Children's Hospital to launch clinical research studies to prove the device works in babies.

Texas Children's has the nation's largest neonatal intensive care unit – and therefore a lot of babies who need simple breathing support for a few days or weeks. Doctors there will test the device and deliver data to the Seattle Children's Research Institute team, which recently received a second Gates grant for $3 million to fund the studies.

"The Texas Children's collaboration means we can get the trials done faster and get this device in the hands of caregivers throughout the world as quickly as possible – hopefully within three years," notes Smith. ■



The Seattle-PAP device routes pressurized gas through nasal prongs and into an infant's lungs, delivering a constant stream of air to babies who cannot yet breathe on their own. The pressure of the gas is controlled by adjusting a tube that is submerged in the water reservoir.

1 million

Approximate number of infants in the developing world who die each year because simple breathing support machines aren't available.

Closing In on Cancer Cures

A research Dream Team is developing innovative treatments for the deadliest childhood cancers.

Dr. Mike Jensen and Dr. Rebecca Gardner are part of a Dream Team of national experts in genomics and cancer immunotherapy who are improving treatments for leukemia, neuroblastoma and other cancers.

Last year, Milton Wright III, then 20, came to Seattle Children's for a last chance to beat acute lymphoblastic leukemia (ALL). His cancer had relapsed for the second time and there was little reason to believe that traditional therapies could stave it off. So he joined Seattle Children's clinical research study of a therapy that reprograms T cells (the white blood cells that find and fight infections) to detect cancer cells and destroy them.

The immunotherapy treatment eradicated the leukemia cells in Wright's body in just two weeks and freed him to plan his life again. And it marked another leap forward in the search for more effective, less toxic cancer therapies.

Now the researcher at Seattle Children's Research Institute who developed this therapy, Dr. Michael Jensen, is part of a pediatric cancer research Dream Team that unites national experts in genomics with top immunotherapy researchers to accelerate progress against leukemia, neuroblastoma and other cancers that often leave children with little hope. The project was created in 2013 by two nonprofit organizations, Stand Up to Cancer and St. Baldrick's Foundation, which together gave $14.5 million to fund the team for four years.

"The geneticists know how to find potential weaknesses in cancer cells and we can reprogram immune cells to attack those targets," Jensen says. "Working in concert lets us move toward cures faster."

> "Normally we would all just try to figure this out on our own, but the Dream Team pulls us out of our silos."
>
> – Dr. Rebecca Gardner

Seattle Children's is one of just a handful of pediatric institutions with a cell production facility that meets the U.S. Food and Drug Administration's "good manufacturing practice" requirements for manufacturing biologic therapies for people.

Potential cures for fatal cancers

Every cell has receptors that receive signals from other cells. The Dream Team's geneticists are identifying receptors that are present on cancer cells but not on healthy cells. Once identified, Jensen's team inserts new genetic instructions into T cells, telling them to attach to those receptors and destroy the cancer cell – without chemotherapy or radiation.

It's an approach Jensen believes can carry over to many other cancers.

"We can modify T cells to target new receptors pretty quickly and test them in our lab," he says. "That helps the geneticists on the team know which receptors to focus on and which ones are dead ends."

The Dream Team includes renowned physicians and researchers from seven top hospitals and research institutions, including Children's Hospital of Philadelphia, Texas Children's Hospital and the National Cancer Institute. The team aims to launch clinical research studies of new immunotherapies within four years. These studies will be open to patients at hospitals and research centers throughout the nation, helping the team quickly fill the trials and identify which therapies are effective.

Game-changing leukemia therapies

The Dream Team also helps Jensen and his colleagues refine leukemia immunotherapies like the one that helped save Wright's life. So far, these therapies haven't caused any major side effects – a huge improvement over today's treatments, which can trigger everything from learning disabilities to increased risk of future cancers.

During a recent Dream Team "virtual lab" meeting (conference calls with researchers who investigate similar therapies around the country), participants traded ideas on how to ensure that cancer-fighting T cells stay alive after they're infused in patients. That way, they can fight the cancer if it ever comes back.

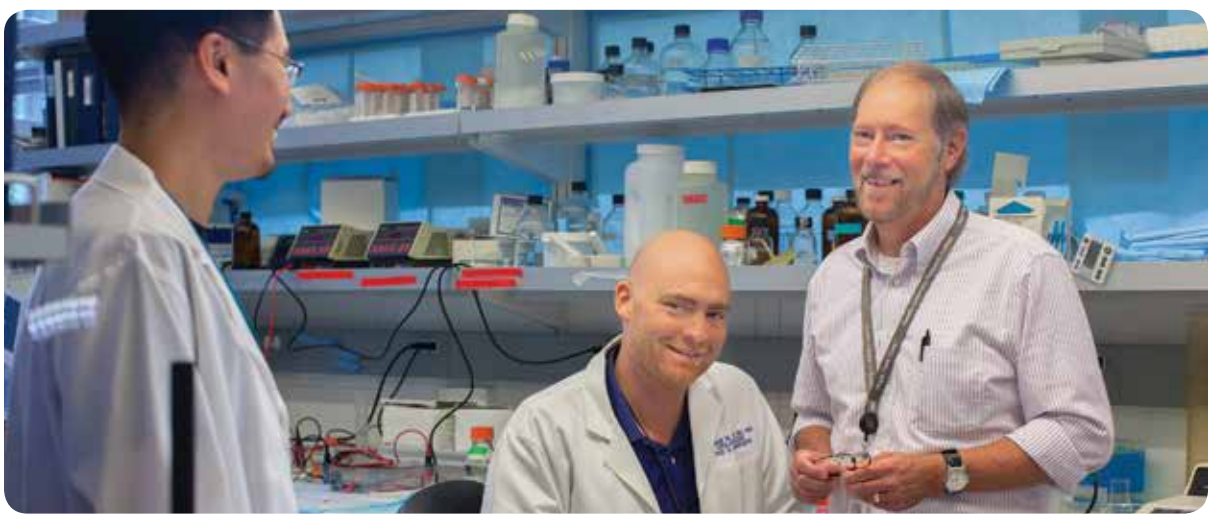
"Normally we would all just try to figure this out on our own, but the Dream Team pulls us out of our silos," says Dr. Rebecca Gardner, who is leading the leukemia immunotherapy clinical research studies at Seattle Children's. "That helps us work together toward answers, which means we can bring these treatments to children as fast as possible." ■

Common Tumors: Better Treatments

Seattle Children's researchers are uncovering why a blood pressure medication shrinks away infantile hemangiomas.

Before she took propranolol, hemangioma tumors covered Shakira Locke's face and neck – and blocked her esophagus and airway. After being treated at age 2, Shakira now breathes and eats normally.

Seattle Children's Dr. Jonathan Perkins was the first in the Pacific Northwest to use a blood-pressure medication to treat hemangiomas that otherwise would need to be surgically removed. He performs about 75% fewer surgeries since introducing this treatment.



Dr. Mark Majesky and his team are patenting a blood test using the biomarker they discovered to track whether propranolol shrinks a patient's hemangiomas.

Right after Lorene Locke gave birth to her daughter Shakira, she noticed what looked like a rash on the newborn's face. Three weeks later, doctors found an abnormal clump of vessels, called an infantile hemangioma, growing out of control inside Shakira's throat and on her neck, face and ear, blocking her airway and leaving her gasping for air.

While most hemangiomas go away on their own and don't cause problems, children like Shakira need multiple surgeries and procedures to remove the growths. Dr. Jonathan Perkins, an otolaryngologist and researcher at Seattle Children's, has spent years studying hemangiomas in search of a less-invasive approach. When French researchers discovered that a blood pressure medicine called propranolol could shrink away hemangiomas, Perkins found the breakthrough he was waiting for.

In 2008, he put Shakira on the drug, making her one of the first patients in the region to receive it. Within four months the tumors that obstructed her airway were gone. Today, Perkins estimates that he performs 75% fewer surgeries to remove hemangiomas because the blood pressure medication is so effective.

He's now teaming with Dr. Mark Majesky, a principal investigator at Seattle Children's Research Institute and an expert on how blood vessels form, to find out more about how propranolol works and to determine the best ways to use it in patients.

> "It was so clear I just about jumped out of my chair."
>
> – Dr. Jonathan Perkins

"I don't necessarily think like someone who studies these deep biological questions," Perkins says. "Mark knows which questions to ask and the fastest ways to answer them."

The "a-ha" moment

Propranolol works for about 60% of patients with hemangiomas, so one of the first goals is to identify who will respond to the drug. Perkins and Majesky started testing propranolol on hemangioma tissue and met every other week to discuss the results and plot their next steps. The a-ha moment came last year, when the researchers discovered a new biomarker and found that levels of it were dramatically higher in blood taken from patients with hemangiomas than in healthy patients' blood.

"It was so clear I just about jumped out of my chair," Perkins recalls.

The researchers are patenting a blood test that uses the biomarker to track whether propranolol is working in a particular patient. This will help doctors know if a hemangioma is shrinking even if it's inside a patient and out of sight.

Ultimately, Perkins and Majesky hope to develop a similar test that can predict whether propranolol will be effective, helping doctors quickly decide when patients need surgery and saving patients from the trial and error of taking a drug that may not be a good match for them.

Pursuing game-changing tumor treatments

Majesky and Perkins are getting set to apply for a National Institutes of Health (NIH) grant to keep studying propranolol and pursue similar treatments for many other tumors.

The project is a shining example of how questions and insights that arise when a doctor is caring for a patient can spark research that potentially improves that care. And its early success illustrates what is possible when collaborators within Seattle Children's align their strengths and work together to solve a problem.

"It's about making kids' lives better," Majesky says. ■

Fueling Puget Sound's Economy

Seattle Children's Research Institute is bringing new jobs and millions of dollars to Washington state's life sciences sector.

Seattle Children's Research Institute's Jack R. MacDonald Building at 9th and Stewart in downtown Seattle.

The economy was declining in 2010 when Seattle Children's took a risk and decided to renovate a vacant downtown building with laboratory space to house a new kind of pediatric cancer research center. It was a non-conventional, courageous but strategic move at a time when other institutions were bracing for a rough economy.

Four years later, that building, at the corner of Olive Way and Boren Avenue, is home to the Ben Towne Center for Childhood Cancer Research. This enterprise has received government grants and generous support from Seattle's philanthropic community, lured researchers from top institutions in San Francisco, Los Angeles and Atlanta, and developed therapies that use the immune system to eradicate cancer in children and young adults.

"Every day, about 50 people go to work in that building, and more than 1,100 people work for our research institute," says Dr. Jim Hendricks, president of Seattle Children's Research Institute. "We're not just creating innovative treatments and discovering insights that may improve pediatric healthcare – we're creating jobs that fuel the local economy."

A growing role in a booming sector

The life sciences sector – which includes everything from nonprofit research institutions to biotechnology companies – contributed $11 billion to Washington's economy in 2012 and Seattle Children's Research Institute plays a growing role.

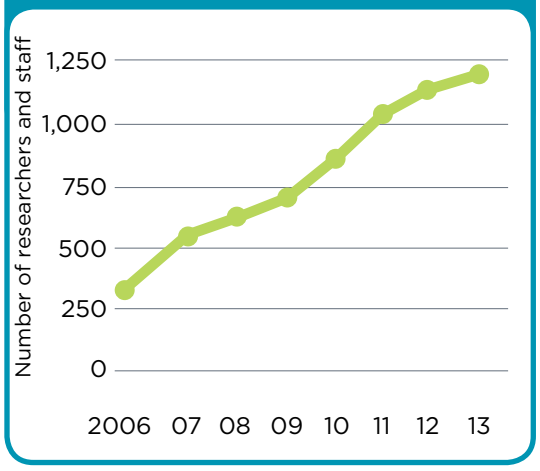
The research institute brought in approximately $76 million in grants and donations in 2013, more than double the research institute's 2008 total of $37 million. This funding moves through the economy via the research institute's collaborations with local companies and nonprofits, and is helping to grow its workforce. In 2012, the state's life sciences jobs yielded an average wage of $81,620, compared to $51,100 for Washington's other private sector jobs, according to the Washington Biotechnology and Biomedical Association.

"We've recruited some of the world's top researchers to Seattle and created a dedicated workforce that is highly motivated to solve some of medicine's most complex problems," says Dr. Bruder Stapleton, Seattle Children's chief academic officer. "That intellectual capital is vital to our quest to fulfill Seattle Children's mission to prevent, treat and eliminate pediatric disease, and adds to our local research sector's strong foundation."

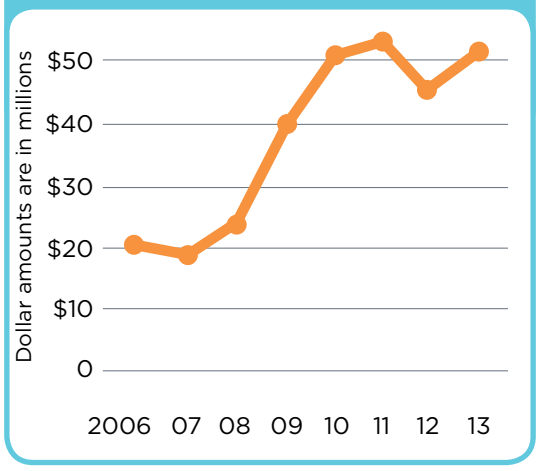
This foundation is part of what makes the Seattle area one of the nation's best places to start a biotechnology or medical research venture, fueling economic growth and keeping Seattle at the forefront of innovation. ■

Growth of Seattle Children's Research Institute

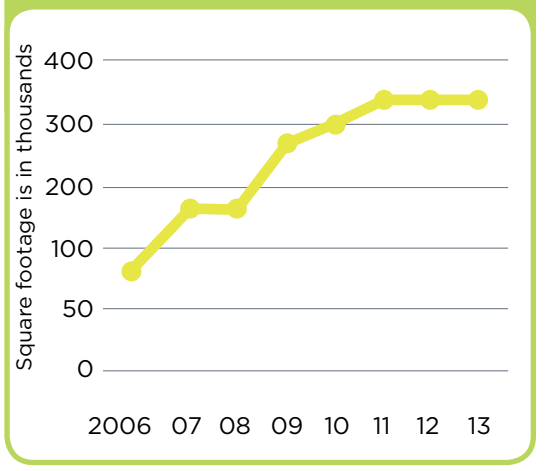
Research institute workforce



Amount of federal funding for our research efforts



Amount of research institute square footage



Research with a heartbeat.

At Seattle Children's, our Hospital and Research Institute work as one team—in the lab, at the bedside and in the community. By linking scientific research with clinical care, we are unlocking the mysteries of childhood diseases like cancer, cystic fibrosis and epilepsy. We are making a difference for children and families in our region and around the world. Families rely on our discoveries. And we rely on your generosity. To learn more or donate, visit seattlechildrens.org/research.

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What Will It Take to Cure Childhood Disease?

Curing cancer without chemotherapy or radiation. Using compounds found in nature to treat autoimmune diseases. Making surgery for life-threatening tumors obsolete. These goals used to seem like science fiction. Today they are within reach.

But it takes all of us, working together. Join Seattle Children's Research Institute and the Puget Sound Business Journal on Oct. 22 to learn more.

7 to 9 a.m., Wednesday, Oct. 22, 2014

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