

# Bench to Bedside



RESEARCH AT THE CHILDREN'S HOSPITAL OF PHILADELPHIA

May 2012

## “Exciting” Complete Responses Seen in Neuroblastoma, Lymphoma Trial

A drug designed to target abnormal genes that drive specific cancers has produced highly encouraging early results in children with two aggressive forms of cancer, lymphoma and neuroblastoma.

A phase 1 clinical trial of crizotinib achieved complete responses — an absence of detectable cancer — for some patients in a collaborative national study carried out by the multicenter Children's Oncology Group. The results were “an exciting proof-of-principle” for the targeted treatment, said the study leader, Yaël P. Mossé, M.D., a pediatric oncologist at The Children's Hospital of Philadelphia.

Dr. Mossé presented the findings at a recent press program organized by the American Society of Clinical Oncology (ASCO) in advance of its annual meeting in June. In addition, the society selected the research for its Best of ASCO program following the meeting, and has announced that Dr. Mossé will be the first recipient of its James B. Nachman ASCO Junior Faculty Award in Pediatric Oncology.

In 2008, Dr. Mossé led a team at Children's Hospital that discovered that mutations in the anaplastic lymphoma kinase (*ALK*) gene are present in 10 to 15 percent of cases of neuroblastoma, the most common solid cancer of early childhood. The same gene is disrupted in some cases of anaplastic large cell lymphoma (ALCL), a cancer of the lymph cells, and in non-small cell lung cancers (NSCLC).

Because drug manufacturers had already developed crizotinib for use in adult lung cancer clinical trials, Dr. Mossé and her colleagues were able to bypass an early development stage and obtain it for their pediatric trial. Crizotinib was approved in late 2011 to treat late-stage NSCLC in patients who express the *ALK* gene.

“We are entering a new era of cancer therapy, in which we use knowledge of basic biology to design very specific drugs that target cancer cells with few side effects on healthy tissue,” Dr. Mossé said. “In addition, as we concentrate on targets in

molecular pathways, we move away from an exclusive focus on one form of cancer to customizing treatments according to biological activity.”

The current trial was not restricted to patients with known *ALK* abnormalities, but was open to children with refractory or relapsed cancers. There were 62 patients enrolled who could be fully evaluated for drug toxicity. And even though many of the dosages were relatively high, toxic side effects were minimal.

For eight children with ALCL and confirmed *ALK* abnormalities, none had to be removed from the trial because of disease progression. In fact, 7 of the 8 patients had complete responses — no cancer could be detected with imaging scans. Within days of taking the oral medication, their fevers and chills stopped, and the children's pain diminished or disappeared. Another seven patients had inflammatory myofibroblastic tumors, a rare sarcoma (solid cancer), and found the therapy sufficiently beneficial that they were able to remain in the trial.

Twenty-seven patients enrolled in the trial had neuroblastoma, of whom eight had an *ALK* mutation identified in the molecular diagnostic lab at Children's Hospital. Two of those patients have germline mutations — a mutation occurring in every cell in their body — and both children achieved complete responses and remain on therapy. Of the 19 neuroblastoma patients in the trial whose *ALK* status was unknown, one has had a complete response and remains in the study, while six have stable disease and also remain on study. Ongoing lab studies are being done to analyze whether the patients' tumors have *ALK* mutations.

The trial findings may imply that children who did not respond to crizotinib did not have *ALK* abnormalities, although further studies are needed, even as the phase 1 trial helps define dose levels for a phase 2 study. Nonetheless, “the current study represents a major opportunity to personalize treatment for children with this high-risk form of neuroblastoma,” Dr. Mossé pointed out.

## Erectile Dysfunction Drug May Benefit Cardiac Function in Young Patients with Heart Defects

Sildenafil, also known as the erectile dysfunction drug Viagra®, may give a boost to underdeveloped hearts in children and young adults with congenital heart defects. CHOP researchers recently reported that sildenafil significantly improved echocardiographic measures of heart function in children and young adult survivors of single ventricle heart disease palliation.

“Although researchers will need to evaluate clinical benefits over a longer period with a larger number of patients, this finding offers a potential advance in the management of patients with these types of heart defects,” said study leader David J. Goldberg, MD, a pediatric cardiologist at Children’s Hospital.

The study appears online recently in the journal *Pediatric Cardiology*.

The investigators randomly assigned 27 children and young adults at Children’s Hospital to receive either sildenafil or a placebo for six weeks. After a six-week break in treatment, the subjects were switched to the opposite treatment course. The study team used echocardiograms to measure myocardial performance index (MPI), an indicator of the heart’s overall ability to pump blood.

The patients in this double-blind, short-term study, who had a mean age of 14.9 years, had undergone a Fontan operation in early childhood, a mean of 11.3 years previously. The Fontan surgery redirects blood circulation in patients born with a severely underdeveloped ventricle, one of the heart’s two pumping chambers. The operation is the third in a staged series of surgeries for life-threatening single-ventricle defects.

Although surgical advances over the past 20 years have dramatically improved survival for single-ventricle defects, patients with the condition continue to have long-term illness and risk of early death. The staged surgeries do not recreate normal heart circulation, but instead redirect blood flowing from the veins directly to the lungs, bypassing the heart. However, blood vessels in the lungs develop resistance to this blood, often reducing a patient’s ability to tolerate exercise.

Sildenafil, which reduces blood vessel resistance to the flow of blood, is already used to treat pulmonary hypertension (high blood pressure in lung vessels), as well as erectile dysfunction. Because sildenafil has also

shown promise as a treatment for adults with heart failure, the Children’s Hospital researchers are exploring whether it may benefit younger patients with certain types of congenital heart disease.

The current study is part of a broader phase 2 clinical trial at Children’s Hospital, the Sildenafil After the Fontan Operation (SAFO) trial. A previous study from the same research team, published in March 2011, found improvements in exercise performance, as measured by ventilator efficiency, in children and young adults with single-ventricle disease who took sildenafil compared to those who took placebo.

The current study was the first to show that sildenafil improved echocardiographic measures of ventricular performance in children and young adults with single-ventricle physiology. The biological mechanisms that affect ventricular performance are not fully understood, said Goldberg, but he noted that studies in other patients with heart disease suggest that inhibiting the abnormally high levels of the enzyme phosphodiesterase E5 (PDE5) may produce the physiological benefits seen in the single-ventricle patients.

Dr. Goldberg cautioned that further research should be pursued to determine if the observed improvements in ventricular performance persist beyond the short term and if they provide clear quality-of-life benefits. “If sildenafil is safe over the medium and long-term, and if it produces durable functional improvements, patients with single-ventricle heart disease could have their first effective long-term treatment,” he added.

Dr. Goldberg’s co-authors were Anita L. Szwast, MD, Michael G. McBride, PhD, Nicole Mirarchi, MA, Brian D. Hanna, MD, PhD, Gil Wernovsky, MD, and Jack Rychik, MD, all from Children’s Hospital; Benjamin French, PhD, from the Perelman School of Medicine at the University of Pennsylvania; and Bradley S. Marino, MD, MSCE, of Cincinnati Children’s Hospital Medical Center.

Grants from the Mark H. and Blanche M. Harrington Foundation and from Big Hearts to Little Hearts provided funding for this study. In addition, Goldberg received support from a National Institutes of Health grant.

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## Science Center’s QED Program - Spring 2012 Announced

The latest Round of the Science Center’s QED Proof-of-Concept Program (QED Spring 2012) has been announced.

The QED Proof-of-Concept Program provides commercialization advice and bridge funding to life science technologies that are still being developed within an academic setting, and that require one or more critical research steps before they are ready for transfer to the private sector. The program is open to researchers at 21 academic institutions throughout Delaware, New Jersey, and Pennsylvania (please consult the Science Center website).

The Request for Proposals is available [here](#).

Application forms, instructions, and other materials are available here:

- <http://www.research.chop.edu/forms/comm/QEDWhitePaperApplication.pdf>
- <http://www.research.chop.edu/forms/comm/WhitePaperFAQ.pdf>

Completed applications should also be uploaded via the [Science Center website](#). The final submission deadline is Friday, July 20 at 5 p.m., and applicants submitting by June 22 will have an opportunity to receive individual feedback and revise their applications before the final submission date.

If you are considering applying for the program, please contact Ellen Purpus or Greg Baker in the Office of Technology Transfer as soon as possible. Questions about the QED Program itself may also be directed to the QED Program Manager at [qed@sciencecenter.org](mailto:qed@sciencecenter.org).

## Tom Curran, Ph.D., Elected to the American Academy of Arts and Sciences

Tom Curran, Ph.D., FRS, an expert in childhood brain cancer at The Children's Hospital of Philadelphia, has been elected to the 2012 class of the American Academy of Arts and Sciences. One of the nation's most prestigious honorary societies, the Academy is a leading center for independent policy research.

Dr. Curran joins a select group of artists, scholars, scientists, and leaders that includes winners of a variety of awards, including the National Medal of Science, the Lasker Award, the Fields Medal, and the Pulitzer Prize.

Dr. Curran's research concentrates on the molecular biology of the brain's growth and development, with the goal of finding new treatments for childhood brain tumors. He has been awarded grants from the National Cancer Institute and the National Institute of Neurological Disorders and Stroke, as well as from private foundations. In addition to being an elected member of the Institute of Medicine at the Academy of Natural Sciences, Dr. Curran is a member of the Royal Society in the United Kingdom.

Currently deputy scientific director of The Children's Hospital of Philadelphia Research Institute, Dr. Curran is also a professor

of Pathology and Laboratory Medicine and professor of Cell and Developmental Biology at the Perelman School of Medicine at the University of Pennsylvania. He is a former president of the American Association of Cancer Research.

Born in Scotland, Dr. Curran received his Ph.D. from University College London. He was the founding chairman of the Department of Developmental Biology at St. Jude's Research Hospital in Memphis, Tenn., before joining Children's Hospital 2006.

Founded in 1780 by John Adams, John Hancock, and other scholar-patriots, the American Academy of Arts and Sciences elects leading "thinkers and doers" from each generation. Past members have included George Washington, Benjamin Franklin, Daniel Webster, and Albert Einstein.

The Academy announced its newest members on April 17. They will be honored in an induction ceremony on Oct. 6, at the Academy's headquarters in Cambridge, Mass. Among the 220 members of the 2012 Academy class are cancer researcher Brian Druker, astronomer Debra Ann Fischer, Secretary of State Hillary Clinton, and musician Paul McCartney.

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## CHOP Patients, Researchers Participate in Major Study of Type 2 Diabetes

Because type 2 diabetes is especially challenging to treat in young people, working to prevent the condition is more important than ever. That may be the biggest takeaway from a recent national clinical trial of treatments for type 2 diabetes in youths, one in which patients and staff members of the Diabetes Center for Children at The Children's Hospital of Philadelphia were heavily involved.

"Type 2 diabetes progresses more rapidly in young people than in adults," said pediatric endocrinologist Lorraine E. Levitt Katz, M.D., who added that the disease may require more aggressive early treatment in young patients. Dr. Levitt Katz was the project leader at the Children's Hospital center that joined the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) study. TODAY enrolled nearly 700 patients aged 10 to 17 across the U.S. from 2004 to 2009, including 69 patients from Children's Hospital.

In type 2 diabetes, a patient produces insufficient insulin or becomes unable to properly use the insulin his or her body does produce, and the result is an inability to control blood sugar. Although the disease has been increasing in recent years among young people, the best treatment for this population remains unknown.

The TODAY study divided participants into 3 treatment groups. One group received only metformin, a pill that is the standard drug for young people with the disease, while a second group took both metformin and another drug, rosiglitazone. A third group took

metformin and made lifestyle changes, such as adopting healthier eating behaviors and keeping active. Children and adolescents from diverse racial and ethnic background participated in 15 centers throughout the U.S.

The researchers evaluated how well participants were able to control their blood sugar. Overall, treatment succeeded in only 54 percent of the 699 participants. The treatment was effective in 53 percent of those in the group that combined metformin with lifestyle changes, compared to 48 percent success in those taking metformin without the lifestyle program, a difference that was not statistically significant. The group that combined both medications had 61 percent success, significantly better than taking metformin alone. However, rosiglitazone's use has been restricted since 2010 because of heart problems reported in adult patients. None of the young people in the study's treatment groups experienced serious side effects.

In 2011, Dr. Levitt Katz and her colleagues published a study showing that glycemic control in youths with type 2 diabetes declines as early as two years after diagnosis. Data from this study and from the TODAY study show that the disease progresses quickly in children and adolescents. TODAY study researchers plan to present their results in a symposium on June 9 at the 2012 Scientific Sessions of the American Diabetes Association in Philadelphia.

## CHOP Researchers Explore How Bacteria in Gut Regulate Broader Immune System

CHOP researchers have been studying how bacteria in the intestine play important roles in regulating the immune system, with possible implications for antibiotic use.

Corresponding author Junjie Mei, Ph.D., and senior author G. Scott Worthen, M.D., both of whom are researchers in the Division of Neonatology, recently published a study in the *Journal of Clinical Investigation* focusing on neutrophils, white blood cells that are important components of the innate immune system.

Neutrophils are “first responders” in the immune system, attacking invading microorganisms during an acute infection. However, an excessive number of neutrophils can increase inflammation and damage tissues, so the body needs to closely regulate the quantity of neutrophils. In studying genetically engineered mice, the research team analyzed how signaling proteins, cell receptors and other biological entities interact to regulate neutrophils and keep their numbers in balance.

The researchers also found that bacteria that normally live in the gut also participate in regulating neutrophils. When the scientists treated the mice with antibiotics, those antibiotics killed gut bacteria and also reduced neutrophil levels.

“We are carrying out further studies to investigate what these effects may mean for other organs, such as the lungs,” said Dr. Worthen. “For instance, altering bacteria in the intestine may reduce how well the lungs respond to pneumonia,” he added.

Dr. Worthen cautioned against drawing too many conclusions about human biology from studies in mice, but he noted that the current findings may increase understanding of how antibiotic use in patients may harm their immune responses in specific organs.

To see the abstract of this study, click here:  
<http://www.ncbi.nlm.nih.gov/pubmed/22326959>

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## Change to National Study Impacts The Children’s Hospital of Philadelphia

Under recently announced changes in the federal contract for The National Children’s Study (NCS), The Children’s Hospital of Philadelphia and six other sites across the U.S. will no longer be affiliated with the NCS as of September 2012. Launched locally in Montgomery County, Pa., in 2009, the NCS is part of the first and largest long-term study of children’s health ever conducted in the U.S. The Study’s goal is to track the health and development of children from before birth through age 21.

Children’s Hospital has spent the last seven years preparing for and implementing the NCS in Montgomery County, one of the original seven Vanguard sites of the NCS.

Many childhood diseases and unhealthy conditions have been on the rise over the past two decades and contribute to pediatric illnesses. The National Children’s Study was created by Congress in the Children’s Health Act of 2000 to address these concerns.

“Community participation has made the project tremendously successful. To date, almost 300 Montgomery County women have agreed to participate in the NCS and almost 200 children have been born,” said Jennifer Culhane, Ph.D., M.P.H., principal investigator of the Montgomery County site. “We extend our deepest appreciation and thanks to all our partners: the Montgomery County Health Department, more than 30 hospitals in 7 counties delivering babies

in the NCS, maternal-child health physicians and nurses, healthcare professionals, community leaders and organizations, and especially the Study participants and children.”

In late February, all seven original Vanguard Centers were notified by the National Institutes of Health that contracts would not be renewed. This was not the result of lack of performance by the Vanguard Centers but rather a change in the method of participant recruitment. Unlike the door-to-door recruitment conducted by the original Vanguard Centers, recruitment of women through obstetrical providers that participate in large health plans is being considered by the NIH. Effective September 3, 2012, Research Triangle Institute, a national research consulting firm, will be responsible for following the current Montgomery County participants.

While this change currently affects only the original seven Vanguard Centers, it is likely that the 30 other Vanguard sites will undergo the same change in the future, which would include the Children’s Hospital study site in Schuylkill County, Pa.

The fate of the NCS remains unclear as the number of sites participating in the study could decrease dramatically from the original 105 counties. It is also uncertain if CHOP will have the opportunity to follow Montgomery County participants in the future.

# Behind the Scenes: Clinical Trials Office

In your day-to-day work supporting or conducting research at CHOP, you may not see the multiple teams behind the scenes working to make sure research runs more smoothly and efficiently. What are these groups? What do they do? The “Behind the Scenes” series is designed to enhance the research community’s understand of the administrative support provided to investigators. Take a moment to learn about CHOP Research’s administrative resources and consider how they might benefit your research endeavors.

In this issue, Clinical Trials Office director Lisa Speicher, Ph.D., and associate director Nirmala Thevathasan give a look behind the scenes at what their group does to support CHOP Research.

## What is the overall goal of your department?

The Clinical Trials Office (CTO) is a core facility that provides clinical research personnel and resources to clinical investigators involved in all types of human subjects research at CHOP. Our staff has expertise in implementing and conducting clinical research studies and provides a variety of services from which both novice and experienced clinical researchers can benefit. We are available to help a clinical investigator navigate the complex regulatory and operational clinical research environment.

## What do you manage for the research community?

CTO provides nurse and non-nurse clinical research coordinators and project managers who are able to support any type of clinical research study including behavioral research, surveys, human tissue collection, retrospective chart reviews, and drug and device trials.

Our office also is available to: prepare IRB submissions for an investigator; collaborate with investigators and sponsors to determine study feasibility; assist investigators who are approached to participate in a clinical research study by industry or other academic centers with their study start up activities; facilitate the budget and contract negotiation process; obtain required regulatory documents; host site qualification and site initiation visits; attend investigator meetings, and assist an investigator with the development of a protocol that includes all aspects necessary for CHOP’s standard template.

The CTO is also able to develop a customized clinical research training program for both newly hired and existing study coordinators.

## How do you ease or improve things for investigators?

The CTO excels at matching top quality clinical research staff with clinical investigators and teams. Our highly trained and experienced staff members assist investigators by alleviating them of many of the regulatory and operational burdens that are encountered in the management and oversight of a typical clinical research study.

## How is the department structured?

The CTO is comprised of clinical research professionals with diverse backgrounds and various levels of education and experience, including registered nurses, respiratory therapists, and clinical research coordinators and project managers who hold advanced degrees in psychology, public health, business, education and clinical research. The CTO is managed by an administrative staff comprised of a director, associate director, clinical research educator, manager of business practices, clinical team supervisor, and resource coordinator, all of whom work diligently to ensure that the CTO delivers excellent service to our customers.

## How many people work in the department?

Approximately 35 to 40 people

## What types of projects does your group typically work on?

The CTO supports all types of clinical research studies, including behavioral health, tissue collection, data abstraction, interview/survey based, and all phases of drug and device trials, as well as investigator sponsored investigational new device (IND) and investigational device exemption (IDE) applications.

## Is there a special project the department is working on this year?

The CTO supports more than 100 studies of all types and varying complexities.

## What recent accomplishment is your group most proud of?

The CTO staff have supported several groundbreaking studies that have recently been featured in the news including Dr. Scott Azdick’s fetal surgery study (MOMS), Dr. Jordan Orange’s IL-2 study for Wiskott-Aldrich syndrome, Dr. Edwin Horwitz’s study of mesenchymal stromal cells in osteogenesis imperfecta, and the use of F-DOPA and positron emission tomography for hyperinsulinism, led by Drs. Lisa States and Charles Stanley.

While not every project reaches a high profile status, we are equally proud of the accomplishments of each and every member of our staff, each of whom are highly dedicated to the field of clinical research and continuously deliver excellence

## What do you want the research community to know about your work?

While the CTO is a fee-for-service-based core facility, our administrative staff members are available for consultation and will assist any investigator with navigating the complex aspects of conducting clinical research at CHOP. From facilitating budget and contracts negotiations for new clinical research studies, to assisting with assessing study feasibility and providing expert advice on hiring clinical research personnel, our staff are here to support all CHOP investigators.

## What does someone in your group tackle on a typical day?

People would be surprised to learn how much a clinical research coordinator (CRC) may have to tackle in one day. Many investigator responsibilities are delegated to a CRC, who may be juggling multiple protocols for multiple investigators! Additionally, protocols have become progressively more complex, and regulations intended to support research subject safety and study data integrity have continued to evolve. As a result, the CRC’s role has become more sophisticated and their responsibilities have expanded.

### A day in the life of a typical coordinator may include many of the following:

- Preparing an IRB submission
- Resolving billing issues
- Managing subject visits
- Processing samples
- Conducting informed consent
- Facilitating contract/ budget negotiations
- Preparing for and/or facilitating external audits (FDA, NIH, Sponsor)
- Reporting an adverse event
- Conducting study close out activities (final IRB notification, drug accountability disposition, file storage data clarification completion)
- Preparing an IND/IDE submission to the FDA

## What is a common misperception about your department?

That we only support drug and device studies.

## What is unique about what your department offers compared to similar departments at other institutions?

Many institutions have offices titled the “Clinical Trials Office;” however, CHOP’s office is unique because of the large pool of highly trained clinical research personnel who are available to support our investigators. There are very few institutions across the country that follow our model.

## How is your work influenced by the work of departments focused on supporting clinical care?

The ultimate goal of clinical research at the CHOP Research Institute is to improve the health of children. Clinical research and clinical care work hand in hand, you really can’t have one without the other. Data we acquire from our clinical research studies are translated into and guide our clinical care standard of practice. And the information we obtain from our patients receiving clinical care can be the catalyst for a new clinical research idea. This collaborative process is what ultimately leads to the improvement of human health.

## Is there anything your department does that might surprise people?

The breadth and variety of clinical research studies and therapeutic areas that we provide support to is astonishing. Also, we support more than clinical research; we support quality improvement initiatives, safety surveillance programs, and other clinical projects.

## What is the most satisfying part of your job?

Learning from one of my coordinators that a subject on a clinical research study has responded to an experimental treatment! That’s the gold ring for all the extraordinary efforts that the clinical research team makes.

## CHOP Neuroscientist Leading Project to Identify Novel Treatments for Stress Disorders in Military Personnel

A CHOP investigator is leading a collaborative, federally funded study to help veterans and active-duty service members better deal with post-traumatic stress disorder (PTSD) and other stress-related conditions.

The project, involving scientists from CHOP and Penn Medicine, aims to discover new treatments as well as to identify biomarkers—measurable biological substances such as hormone levels—that indicate a person’s resilience to stress. Their findings may also have the potential to benefit a broader group of patients, including children and families dealing with stress-related health problems.

Seema Bhatnagar, Ph.D., a neuroscientist in CHOP’s Department of Anesthesiology and Critical Care, is the principal investigator of a \$3.5 million grant from the Defense Advanced Research Projects Agency (DARPA), part of the U.S. Department of Defense. Dr. Bhatnagar is collaborating with scientists from the Perelman School of Medicine at the University of Pennsylvania in studying patients from the Philadelphia VA Medical Center and other military institutions.

Dr. Bhatnagar and her colleagues at CHOP’s Stress Neurobiology Division have researched how differences in

brain circuitry affect how animals react to stressful situations. They performed some of this preclinical work in earlier phases of the DARPA grant. Their new study aims to continue to validate their findings in animal models and to translate their basic science findings into human populations. For example, they are studying whether biomarkers may help predict which people are more likely to be resistant to developing PTSD when exposed to chronic stress.

“We are studying how to improve stress resilience in military personnel,” said Dr. Bhatnagar. “Our goal is to identify novel treatments for stress, particularly for PTSD. Our findings may apply to people in non-military situations as well.”

In addition to its Division of Stress Neurobiology, CHOP has clinical resources devoted to stress. For instance, multidisciplinary researchers at CHOP’s Center for Pediatric Traumatic Stress develop medical interventions for stress-related problems in children and families who have experienced car crashes and serious illnesses.

To read the Penn Medicine press release about this new stress resilience study, click here: <http://bit.ly/xidHoy>

## CHOP Physician and Vaccine Researcher H Fred Clark Passes Away

H Fred Clark, D.V.M., Ph.D., a retired research professor of Pediatrics at Children’s Hospital and the Perelman School of Medicine at the University of Pennsylvania, died on Saturday, April 28, after a protracted illness. Dr. Clark was 72.

Children’s Hospital recognized Dr. Clark in 2006 with its highest honor, the Gold Medal, which is awarded to those who have had a profound impact on children’s health in the United States and worldwide. The medal saluted Dr. Clark’s achievements as a co-inventor of the rotavirus vaccine, RotaTeq, along with fellow honorees Dr. Stanley Plotkin and Dr. Paul Offit. The three scientists carried out laboratory studies of the vaccine between 1980 and 1991 at Children’s Hospital and the Wistar Institute. Today, the vaccine they invented saves the lives of hundreds of thousands of children across our planet.

Dr. Clark received a degree in veterinary medicine from Cornell University and a Ph.D. in microbiology and immunology from the University of Buffalo. He studied and published extensively on both human and animal diseases, including rabies, tuberculosis, and hepatitis B, before joining Children’s Hospital in 1979, and concentrating on rotavirus research. In addition to his positions at CHOP and Penn, Dr. Clark also was an adjunct professor of the Wistar Institute.

Dr. Clark also devoted much of his time over the years to providing care and support to Haitians who suffered from poverty and injustice. He was one of those rare individuals whose life-saving scientific discovery and dedication to those less fortunate will live well beyond him. Dr. Clark is survived by his wife, Karen, and their children.

HAVE NEWS?

Contact Jennifer Long at ext. 4-2105  
or by e-mail at [longj@email.chop.edu](mailto:longj@email.chop.edu).

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online at <http://www.research.chop.edu/publications/>.

 The Children’s Hospital of Philadelphia®

RESEARCH INSTITUTE

34th Street and Civic Center Boulevard, Philadelphia, PA 19104-4399  
1-800 TRY CHOP [www.chop.edu](http://www.chop.edu)

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