According to new research from The Children’s Hospital of Philadelphia and the University of Pennsylvania, two children with an aggressive form of childhood leukemia achieved a complete response after being treated with an innovative cell therapy. In the study, both patients’ immune systems were reprogrammed to rapidly multiply and destroy leukemia cells.

The study appears in the April 18 issue of The New England Journal of Medicine.

Both patients were treated for acute lymphoblastic leukemia (ALL), an aggressive childhood leukemia. The most common form of leukemia found in children, ALL is largely curable, with a roughly 85 percent cure rate. However, the remaining 15 percent of ALL cases resist standard therapy.

The research team used a relatively new approach in cancer treatment: immunotherapy, in which the immune system is manipulated to increase its cancer-fighting capabilities. The investigators engineered T cells — the workhorses of the immune system, which recognize and attack invading disease cells — to selectively kill another type of immune cell called B cells, which had become cancerous.

One of the patients treated, 7-year-old Emily Whitehead, was the subject of a media frenzy last year when the experimental therapy led to her dramatic recovery after she relapsed following conventional treatment. Eleven months after receiving bioengineered T cells, Emily remains healthy and cancer-free.

The other patient, a 10-year-old girl who also had a complete response to the same treatment, suffered a relapse two months later when other leukemia cells appeared that did not harbor the specific cell receptor targeted by the therapy.

“This study describes how these cells have a potent anticancer effect in children,” said the study’s co-first author Stephan A. Grupp, M.D., Ph.D., the Center for Childhood Cancer Research’s director of Translational Research. “However, we also learned that in some patients with ALL, we will need to further modify the treatment to target other molecules on the surface of leukemia cells.”

The current study builds on Dr. Grupp’s ongoing collaboration with Penn Medicine scientists — led by the study’s senior author, Carl H. June, M.D. — who originally developed the modified T cells as a treatment for B-cell leukemias in adults. The Penn team reported on early successful results of a trial using this cell therapy in three adult chronic lymphocytic leukemia patients in August of 2011. Two of those patients remain in remission more than 2½ years following their treatment, and as the Penn researchers reported in December 2012 at the annual meeting of the American Society of Hematology, seven out of ten adult patients treated at that point responded to the therapy.

“We’re hopeful that our efforts to treat patients with these personalized cellular therapies will reduce or even replace the need for bone marrow transplants, which carry a high mortality risk and require long hospitalizations,” Dr. June said.

Though early results have been promising, the research team continues to refine their use of this new technology and to explore why some patients may not respond to the therapy or may experience a recurrence of their disease.

“The emergence of tumor cells that no longer contain the target protein suggests that in particular patients with high-risk ALL, we may need to broaden the treatment to include additional T cells that may go after additional targets,” said Dr. Grupp. “However, the initial results with this immune-based approach are encouraging, and may later even be developed into treatments for other types of cancer.”

For more information about this exciting, groundbreaking study, see the full press release.
A new report on teen driver safety by The Children’s Hospital of Philadelphia and State Farm shows encouraging trends among teen passengers. In 2011 more than half of teen passengers (54 percent) reported “always” buckling up, and from 2008 to 2011, risky behaviors of teen passengers (ages 15 to 19 years) declined: the number of teen passengers killed in crashes not wearing seat belts decreased 23 percent; the number of teen passengers driven by a peer who had been drinking declined 14 percent; and 30 percent fewer teen passengers were killed in crashes involving a teen driver.

Overall, the report measured a 47 percent decline in teen driver-related fatalities over the past six years. Still, as recent high-profile multi-fatality crashes illustrate, crashes remain the leading cause of death for U.S. teens.

“When most people think about those affected by teen driver crashes, they think of teens behind the wheel. This report includes encouraging news about teen passengers, who are often left out of the teen driver safety picture,” says Dennis Durbin, M.D., M.S.C.E., co-scientific director of the Center for Injury Research and Prevention at CHOP, and lead author of the report.

“When you see the needle move, as we have in this report, it’s time to apply the gas on programs that encourage safe passenger behaviors, as well as those that address what causes teens to crash,” Dr. Durbin added.

Based on recent research which identified specific behaviors or factors associated with teen driver crashes, Dr. Durbin offers key areas he thinks have the greatest potential to further drive down the teen crash rate: reduce distraction from passengers and technology, increase skills in scanning, hazard detection, and speed management, and increase seat belt use to improve a teen’s chance of survival in a crash.

Although the report indicates progress for teen driver safety efforts, risky behaviors — such as texting or emailing while driving, driving after drinking, and low seat belt use — remain serious problems. According to the report, “Miles to go: Focusing on Risks for Teen Driver Crashes,” a third of teens say they have recently texted or emailed while driving, a proven deadly distraction, especially for teen drivers. Speeding remained a factor in more than half of fatal teen driver crashes — nearly the same percentage as in 2008 — while the percentage of teens dying in crashes with a blood alcohol level > 0.01 increased slightly, from 38 percent to 41 percent.

“Texting or emailing while driving is especially dangerous for teen drivers. We are encouraged that abstaining from cell phone use while driving is currently the norm for teens — most are not doing this dangerous behavior,” says Dr. Durbin. “To reach the teens that still do text or email while driving, messages should focus on teens’ positive safety beliefs about refraining from cell phone use while driving, rather than turning to scare tactics that always emphasize the negative consequences.”

The report provides evidence to support stronger Graduated Driver Licensing (GDL) programs, which allow teens to gain experience under lower-risk conditions. A comprehensive GDL program includes at least 50 hours of adult-supervised practice under varied conditions, limits teen passengers for the first year of independent driving, restricts unsupervised nighttime driving, requires seat belt use for the driver and all passengers, and prohibits cell phone use while driving.

“Since 2005, State Farm and CHOP have been working together to improve teen driver safety. While this report highlights the gains we are making, we still can do much more to reduce teen driver crash-related injuries and deaths,” says Chris Mullen, director of Technology Research, Strategic Resources at State Farm.

For the complete report and more information, including an infographic about the research, visit http://www.teendriversource.org.

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**ASCI Honors Four CHOP Physician-Scientists**

Four junior investigators from the Children’s Hospital of Philadelphia’s Department of Pediatrics have been chosen to receive the prestigious 2013 Young Physician-Scientist Award by the American Society for Clinical Investigation (ASCI).

The ASCI, established in 1908 and one of the nation’s oldest and most respected honor societies, recognizes physician-scientists with superb records of scholarly achievement in biomedical research. The Physician-Scientist Award honors outstanding early-career researchers who are funded by NIH career development awards.

The following CHOP investigators received the award:

- **Edward Behrens, M.D., Division of Rheumatology**, was acknowledged for his research on the immunopathology of macrophage activation syndrome, as well as signal transduction mechanisms acting as novel regulators of toll-like receptor 9 function.
- **Alexander Fiks, M.D., M.S.C.E.**, co-medical director of CHOP’s Pediatric Research Consortium and a PolicyLab faculty member, was selected for his research focused on improving the health of ambulatory patients through collaborative practice-based research. He is leading a series of studies using quantitative, qualitative, and informatics methods to explore the role of health information technology in improving medical decision making and child health outcomes.
- **Neal J. Sondheimer, M.D., Ph.D., Division of Genetics**, was acknowledged for studies of mitochondrial transcription and mutagenesis. His laboratory has developed genome-wide approaches to the analysis of mitochondrial variation in common disorders.
- **Jason Z. Stoller, M.D., Division of Neonatology**, was selected for his work to elucidate the molecular mechanisms controlling heart development. He has identified a critical signal in the transcription factor, TBX1, that when missing results in DiGeorge syndrome.

To learn more about the groundbreaking research being performed and the services offered at CHOP, see the Hospital’s website.
Almost exactly ten years after the successful completion of the Human Genome Project, President Obama recently unveiled another large, government-backed research project: the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) initiative. Calling the brain “an enormous mystery waiting to be unlocked,” President Obama laid out broad plans for the project, which will devote more than $100 million to brain-related research in 2014, and has the potential “improve the lives of not just millions, but billions of people.”

Once known as the Brain Activity Map, President Obama first mentioned the project during the 2013 State of the Union address. After claiming that every “dollar we invested to map the human genome returned $140 to our economy,” he noted now “is the time to reach a level of research and development not seen since the height of the Space Race.”

According to the White House, the broad goals of the initiative are to accelerate the development of new technologies to inform improved treatments for a variety of diseases like Alzheimer’s disease and epilepsy, reduce language barriers, “prevent, treat, or reverse” post-traumatic stress disorder and traumatic brain injuries in veterans, and create jobs.

Over the next few months, a “high-level working group” led by Rockefeller University’s Cornelia Bargmann, Ph.D., and Stanford’s William Newsome, Ph.D., will “articulate the scientific goals of the BRAIN initiative and develop a multi-year scientific plan for achieving these goals, including timetables, milestones, and cost estimates,” according to the NIH.

“We still haven’t unlocked the mystery of the three pounds of matter that sits between our ears,” the president said during his address.

### The Funding to Fuel the Initiative

Because large-scale research endeavors don’t come for free, a significant portion of the president’s address dealt with the financial aspects of the initiative. The project will launch with an initial investment of $120 million split up between three government agencies. The Defense Advanced Research Projects Agency (DARPA) will allocate $50 million of its 2014 budget to the initiative, while the NIH and the NSF will contribute $40 million and $20 million, respectively.

Several private institutions have also promised to support the project. The Allen Institute for Brain Science will spend $60 million a year to fund BRAIN-related projects at the Institute, and the Howard Hughes Medical Institute plans to spend $30 million annually. For its part, the Kavli Foundation has pledged $4 million a year for the next ten years.

However, the government’s funding is subject to Congress’ approval, and House Republicans have already indicated a desire to sharply cut future spending. Nonetheless, a number of conservatives have already come out in support of the BRAIN initiative. House Majority Leader Eric Cantor indicated some measure of support for the project, albeit by saying that he favored “reprioritizing” money spent on “political and social science research into expanded medical research.”

Rep. Cantor’s comments bring up key questions about the BRAIN initiative’s funding: where the money would come from, and whether funding the project would constitute robbing Peter to pay Paul. Will the money be new, or would the funding be redirected from other projects already being supported by the NIH, DARPA, and the NSF?

### Questions About Feasibility, Goals

In addition to the questions about how the project will be paid for, the fact that BRAIN does not yet have clear goals — unlike the Human Genome Project, which aimed to provide an accurate sequence of the human genome — has led some researchers to be skeptical of the initiative. Whether a top-down approach to such a complicated project would be effective has also been an area of concern.

Indeed, during an “Open for Questions” session with Francis Collins, M.D., Ph.D., director of the NIH, and Arati Prabhakar, Ph.D., DARPA director, Twitter users questioned a number of aspects of the initiative.

While several questions were concerned with BRAIN funding, other questions about how the project’s findings would be made public, and whether brain-mapping should begin on organisms simpler than humans, were also posed. Users also brought up ethical issues associated with such research, and asked how the initiative’s findings might be translated into clinical or technological use.

Possibly in anticipation of such questions, in his introduction of the BRAIN initiative President Obama noted past returns on government investment in science and technology, pointing out that both computer chips and GPS technologies got their start with government funding.

“There is a great deal of exciting work going on in brain-mapping that has the potential to significantly impact the understanding, diagnosis, and treatment of childhood diseases such as autism,” said Tom Curran, Ph.D., F.R.S., deputy scientific director of CHOP Research. “President Obama’s announcement of an initial $100M investment in the BRAIN initiative is a great first step in mapping the human brain.”

To learn more about the BRAIN initiative, see the NIH’s page on the project.
John M. Maris, M.D., director of The Children's Hospital of Philadelphia's Center for Childhood Cancer Research has been chosen to lead the first-ever pediatric "Dream Team" solely focused on creating new treatments for the most challenging childhood cancers. Stand Up To Cancer (SU2C) and the St. Baldrick's Foundation, along with the American Association for Cancer Research (AACR), SU2C's scientific partner, recently announced the new Dream Team at the AACR Annual Meeting in Washington, D.C.

The pediatric Dream Team will have $14.5 million in funding over 4 years, provided by SU2C and St. Baldrick's. Crystal L. Mackall, M.D., chief of the Pediatric Oncology Branch of the National Cancer Institute (NCI), is the co-leader of the Dream Team.

The title of the research project, “Immunogenomics to Create New Therapies for High-Risk Childhood Cancers,” reflects the melding of two powerful disciplines that have historically functioned independently: immunotherapeutics and genomics. The goal of the project is to rapidly translate promising basic research into transformative, targeted treatments that will improve cure rates in children's cancer.

“The motivation for the creation of this collaborative research project is the realization that completely new strategies are needed if we are to have curative therapies for all childhood cancers,” said Dr. Maris. “Our Team hopes to rapidly develop more precise and effective treatments based on the unique characteristics of each child's tumor, here focusing on the genetic changes that make the cancer cells different from the rest of the child's body.”

At the press conference announcing the Dream Team, CHOP patient Emily (Emma) Whitehead provided dramatic evidence of the power of these scientific tools to treat cancer. Emily, age 7, had a dramatic recovery from a relapsed form of childhood leukemia following an experimental treatment that made use of her own immune cells. Researchers from CHOP and the University of Pennsylvania genetically engineered Emily's T cells to find and destroy leukemia cells, and nearly a year after receiving the highly innovative therapy Emily remains healthy and cancer-free.

The new pediatric Dream Team addresses a crucial need in treating children’s cancers. After dramatic progress throughout the last half of the 20th century, cure rates for pediatric cancers plateaued in the 1990s. In addition current therapies for childhood cancers often have severe side effects that reduce quality of life for survivors who enter adulthood. Hence, there is a need for new classes of treatments to improve both survival and quality of life.

Stephan A. Grupp, M.D., Ph.D., and Tom Curran, Ph.D., will lead the CHOP-based research programs. In collaboration with the University of Pennsylvania’s Carl H. June, M.D., Dr. Grupp developed the first highly effective childhood cancer immunotherapy, which ultimately resulted in Emily Whitehead's remarkable recovery.

The Dream Team will focus on the four most deadly pediatric cancers: malignant brain tumors, high-risk leukemias (such as the type of acute lymphoblastic leukemia that Emily Whitehead had), neuroblastomas (which affect the peripheral nervous system), and sarcomas (other tumors of bone and other tissue).

Recent research in genomics, said Dr. Maris, has shown that pediatric cancers are fundamentally different from adult cancers. Children's cancers are less likely to arise due to recurring mutations that can be countered with small molecule drugs. Instead, this Dream Team will exploit the unique feature of molecules on cell surfaces of childhood cancer cells that are not present on normal cells, and thus offer targets for treatments employing bioengineered agents working through the immune system.

“The success of the program will ultimately be judged by the number of lives saved through our efforts,” said Dr. Maris.

2013 CHOP Mentor Award Winners Announced

The Office of Faculty Development recently announced the recipients of the 2013 Children's Hospital Mentor Award. The 2013 Chop Mentor Award winners are Mary Catherine Harris, M.D., Ron Keren, M.D., M.P.H., and Mitchell J. Weiss, M.D., Ph.D.

The annual CHOP Mentor Award is given to up to three faculty members who have “demonstrated extraordinary dedication to fostering the professional development of other members of the faculty,” according to the Office of Faculty Development. Covering activity over the past three years, the award honors faculty members’ dedication to and excellence in mentoring, and any innovations in designing mentoring activities.

Mitchell J. Weiss, M.D., Ph.D. has been a member of the University of Pennsylvania faculty since 1999, when he joined as an assistant professor; in 2011, he was made a full professor. Dr. Weiss studies developmental hematopoiesis and stem cell biology, studying “how transcription factors control blood cell development.”

Ron Keren, M.D., M.P.H., is the director of Children's Hospital's Center for Pediatric Clinical Effectiveness. After receiving his M.D. from the NYU School of Medicine, Dr. Keren went on to earn his M.P.H. from the Harvard School of Public Health in 2001. His work is focused on the “effectiveness and cost-effectiveness of treatments for common problems in general pediatrics,” and earlier this year Dr. Keren was awarded nearly two million dollars by the Patient-Centered Outcomes Research Institute (PCORI) to lead a study examining whether oral antibiotics are as effective at treating infection over an extended period as peripherally inserted central catheters.

A senior attending neonatologist, Mary Catherine Harris, M.D., joined Children's Hospital in 1985, after receiving her medical degree from Dartmouth University. In 1990 she was promoted to associate professor, with full professorship following in 2006. Her research interests include neonatal infectious diseases and immune system response.

“I am honored and at the same time humbled to have received this recognition. In my own past, have had the good fortune of having wonderful mentors — among them Drs. Stephen Ludwig and Steven Douglas,” Dr. Harris said. “It is my privilege to foster academic and personal success among my talented, junior colleagues.”

For more information about the Office of Faculty Development, please visit http://www.research.chop.edu/programs/facultydevelopment/index.php or contact Mary Field at fieldm@email.chop.edu.
CHOP Teams Up With Pfizer to Speed Pediatric Research and Development

The Children's Hospital of Philadelphia and Pfizer, Inc., are joining forces with the goal of translating biomedical discoveries into novel treatments. Children's Hospital is set join the Centers for Therapeutic Innovation (CTI) network, a novel collaboration model built by Pfizer that brings academic researchers together with Pfizer scientists to expedite the pace of innovation.

Children's Hospital is only the second pediatric center to participate in the CTI network, which has established partnerships with 21 academic medical centers throughout the United States, such as Rockefeller University, Beth Israel Deaconess Medical Center, and the University of California, San Francisco.

“We are excited to have this opportunity to accelerate the process of moving scientific insights toward therapies that healthcare providers can offer in the clinic,” said Philip R. Johnson, M.D., chief scientific officer and senior vice president of The Children's Hospital of Philadelphia. Dr. Johnson is one of CHOP’s representatives on a joint steering committee with Pfizer representatives that will direct CTI's activities in Philadelphia.

CTI will bring together scientists from Pfizer and Children's Hospital to identify preclinical research at CHOP with potential applications for innovative treatments. Pfizer will share with CHOP researchers an extensive collection of antibodies and other proteins, along with other proprietary research and drug-development tools. CHOP investigators will collaborate with Pfizer scientists at CTI laboratories in both Boston and New York City.

The goal is to advance a project into a Phase 1 clinical trial.

“Working with leading academic researchers is a key part of the CTI model,” said Anthony Coyle, Ph.D., CTI's Chief Scientific Officer. “CHOP’s world-class reputation as a leading research hospital means it is an ideal partner for CTI as we continue our determined efforts to translate exciting science into effective medicines for patients.”

40 Distinguished Years: Celebrating the Career of Beverly J. Lange, M.D.

As part of a celebration of her career, Beverly J. Lange, M.D., who recently retired after 40 years of pioneering research and leadership, delivered the third Anna T. Meadows lecture. In her talk, “Survival on the Yellow Brick Road,” Dr. Lange discussed her work with chemotherapy-related cognitive dysfunction while also highlighting some of the accomplishments of her time at The Children's Hospital of Philadelphia.

Dr. Lange “played many, many critical roles,” at CHOP and in the scientific community during her career, John M. Maris, M.D., director of the Center for Childhood Cancer Research, noted in his introduction to Dr. Lange’s lecture. Named for Anna T. Meadows, M.D., who retired from CHOP in 2010 after 38 years of service, and who was a leader in the field of cancer survivorship, the Anna T. Meadows lecture has been held annually since 2011.

After receiving her medical degree from Temple University in 1971, Dr. Lange began her research training at Children's Hospital under the husband and wife team of Drs. Werner and Gertrude Henle, working on Epstein-Barr virus (EBV), a common virus associated with a range of conditions, from mononucleosis to certain forms of cancer. After her work on EBV, in 1983 Dr. Lange shifted her attention to oncology and leukemia. In 1984 Dr. Lange was named associate professor of Pediatrics at Children's Hospital, with full professorship following in 1990.

During her career, Dr. Lange worked on many aspects of pediatric oncology, including acute myelogenous leukemia (AML). While AML is the second most common form of leukemia in adults, leading to roughly 15,000 new cases and 10,000 deaths every year in the United States, the disease is rare in children, with only 500 to 600 children diagnosed per year.

Since Dr. Lange began working on the disease, AML survival rates have greatly increased, with the 5-year survival rate now around 85 percent. Dr. Lange called her work with cancer and leukemia “the love of my life.”

She has also held a number of prestigious appointments outside Children’s Hospital. From 2002 to 2004, Dr. Lange was the president of the American Society of Pediatric Hematology and Oncology, and since 2003 has been a member of the Children's Oncology Group, serving on the organization’s Scientific Council and Executive Committee.

During her lecture, Dr. Lange focused on her recent work studying how cancer therapy impacts pediatric patients’ cognitive function. Chemotherapy-related cognitive dysfunction (CRCD) affects both children and adults, has been hampered by the high cost and inadequacy of available testing methods, Dr. Lange has said.

Sometimes referred to as “chemo brain,” CRCD can be especially hard on children. Because CRCD can lead to learning and memory deficits — as well as problems later in life — the condition is particularly worrisome in very young children who are still developing, Dr. Lange noted.

In addition to the need for improved assessments of CRCD, there is also a need for “more and more feasible trials,” to better understand CRCD’s effects, Dr. Lange said. “We need to make CRCD a priority for families.”

After officially retiring in late 2012, Dr. Lange is now emeritus professor of Pediatrics at the University of Pennsylvania, and splits her time between Philadelphia and Venice, Italy.

Dr. Lange’s experiences and accomplishments set “the standard for an academic career,” Dr. Maris noted.
Pediatric researchers, investigating the biology of brain tumors in children, are finding that crucial differences in how the same gene is mutated may call for different treatments. A new study offers glimpses into how scientists will be using the ongoing flood of gene-sequencing data to customize treatments based on very specific mutations in a child’s tumor.

“By better understanding the basic biology of these tumors, such as how particular mutations in the same gene may respond differently to targeted drugs, we are moving closer to personalized medicine for children with cancer,” said the study’s first author, Angela J. Sievert, M.D., M.P.H., an oncologist in the Cancer Center at The Children’s Hospital of Philadelphia.

The study, of which Dr. Sievert was a co-first author with Children’s Hospital’s Shih-Shan Lang, M.D., was published recently in the Proceedings of the National Academy of Sciences.

The study, performed in cell cultures and animals, focused on a type of astrocytoma, the most common type of brain tumor in children. When surgeons can fully remove an astrocytoma (also called a low-grade glioma), a child can be cured. However, many astrocytomas are too widespread or in too delicate a site to be safely removed. Others may recur. So pediatric oncologists have been seeking better treatment options — ideally, a drug that can selectively and definitively kill the tumor with low toxicity to healthy tissue.

The current study focuses on mutations in the BRAF gene, one of the most commonly mutated genes in human cancers. Because the same gene is also mutated in certain adult cancers, the pediatric researchers were able to make use of recently developed drugs known as BRAF inhibitors that were already being tested in adults.

Reaffirming Cancer’s Complexity

The current study provides another example of the complexity of cancer: in the same gene, different mutations behave differently. Dr. Sievert and her colleagues at Children’s Hospital were among several research groups who reported almost simultaneously in 2008 and 2009 that mutations in the BRAF gene were highly prevalent in astrocytomas in children.

“These were landmark discoveries, because they suggested that if we could block the action of that mutation, we could develop a new, more effective treatment for these tumors,” said Dr. Sievert.

However, follow-up studies in animal models were initially disappointing. BRAF inhibitors that were effective in BRAF-driven adult melanomas made brain tumors worse, via an effect called paradoxical activation.

Further investigation revealed how tumor behavior depended on which type of BRAF mutation was involved. The first-generation drug that was effective in adult melanoma acted against point mutations in BRAF called V600E alterations. However, in most astrocytomas the mutation in the BRAF gene was different; it produced a fusion gene, designated KIAA1549-BRAF. When used against the fusion gene, the first-generation drug activated a cancer-driving biological pathway and accelerated tumor growth.

By examining the molecular mechanisms behind drug resistance and working with the pharmaceutical industry, the current study’s investigators identified a new, experimental second-generation BRAF inhibitor that disrupted the cancer-promoting signals from the fusion gene, and did not cause the paradoxical activation in the cell cultures and animal models.

This preclinical work result lays a foundation for multicenter clinical trials to test the mutation-specific targeting of tumors by this class of drugs in children with astrocytomas, said Dr. Sievert. As this effort progresses, it will benefit from CHOP’s commitment to resources and collaborations that support data-intense research efforts.

The direction of brain tumor research over the past several years reflects some of those data-driven advances, said Adam C. Resnick, Ph.D., the senior author of the current paper and principal investigator of the astrocytoma research team in the Division of Neurosurgery at Children’s Hospital.

“For years, astrocytomas have been lumped together based on similar appearance to pathologists studying their structure, cell shape and other factors,” said Dr. Resnick. “But our current discoveries show that the genetic and molecular structure of tumors provides more specific information in guiding oncologists toward customized treatments.”

“The better we understand the mutational landscape of tumors, the closer we’ll be to defining therapies tailored to a patient’s specific subtype of cancer,” added Dr. Resnick.
2013 CHOP Distinguished Research Trainee Awards Announced

The CHOP Research Institute has announced the winners of the 2013 CHOP Distinguished Research Trainee Awards, which provide institution-wide recognition for exceptional CHOP Research trainees, and create an avenue for mentors to show appreciation for their researchers-in-training.

The Office of Postdoctoral Affairs sought nominations for the award from faculty mentors in three trainee categories: Postdoctoral Fellow, Physician Fellow, and CHOP-based Graduate Student. Eighteen outstanding nominations were received among the three groups. Three winners were selected after review and voting by members of the Research Trainee Advisory Committee, chaired by Michael Robinson, Ph.D.

Yiran Guo, Ph.D., Division of Human Genetics and Molecular Biology, received the award in the Postdoctoral Fellow Category. Kosuke Izumi, M.D., Ph.D., a fellow in Human Genetics and Molecular Biology, was selected to receive the award in the Physician Fellow Category. Wulan Deng, Ph.D., a former graduate student at the University of Pennsylvania, received the award in the CHOP-Based Graduate Student category.

Dr. Yiran Guo, nominated by Hakon Hakonarson, M.D., Ph.D., performs research that focuses broadly on integrative genetic/genomic association tasks across multiple complex disease areas. His work, performed in association with CHOP’s Center for Applied Genomics and BGI (formerly the Beijing Genome Institute), includes managing a large-scale, 1,000 rare disease sequencing program that will identify causative genes for rare pediatric diseases by exome and whole genome sequencing. Isolating these genes will help researchers worldwide to better understand the etiology of rare disorders, a first step in developing novel diagnostic tools and treatments. Dr. Guo has also served as the lead analyst in a multi-site project exploring the genetics influencing body mass index. This line of research will have implications in studies of obesity, type 2 diabetes, and a number of associated disorders.

According to Dr. Hakonarson, “Dr. Guo is making excellent progress in preparing himself for an independent research career. His research is highly regarded, which speaks for his exceptional skills as a postdoctoral trainee.”

Dr. Kosuke Izumi is a researcher and physician with a particular interest in translational research as it relates to developmental genetics, including human developmental disorders and birth defects. In collaboration with his mentor, Ian Krantz, M.D., Dr. Izumi studies the chromosomal disorder Pallister-Killian Syndrome (PKS), caused by extra copies of the short arm of chromosome 12. Individuals with PKS exhibit distinctive developmental disabilities, including diaphragmatic hernias, heart defects and growth disruption. Dr. Izumi’s work on PKS will lead to the identification of the critical genes that contribute to the PKS phenotype as well as candidate downstream genes that may be directly causative of associated birth defects.

His focus and perseverance may also lead to the development of new pharmacologic approaches to treat this diagnosis.

Dr. Krantz praised his hard work, stating, “Dr. Izumi has been extremely productive academically. He has catalyzed projects in the lab, created new directions of investigation, and has initiated an academic career for himself that will make him a leader in the field of human developmental disorders.” Dr. Izumi recently joined the lab of a collaborator, Dr. Katsu Shirahige at the University of Tokyo, where he will continue to study the molecular basis of PKS and examine a new disorder related to a novel gene identified in the Krantz laboratory.

Dr. Wulan Deng, a recent doctoral program graduate at the University of Pennsylvania, was nominated by Gerd Blobel, M.D., Ph.D., for her exceptional research skills and passion for science. Her work has introduced major contributions in the fields of transcriptional regulation and chromatin function. According to Dr. Blobel, “Wulan's work on higher order chromatin organization has provided fundamental insights into gene regulation and opened the door for a new approach to manipulate globin gene regulation for therapeutic purposes.”

Dr. Deng’s discovery hinged on the use of synthetic zinc finger proteins engineered to create chromatin loops in vivo at the beta globin locus. This experimental system was intended to identify the cause-effect relationships of chromatin loops and gene expression. Indeed, these specially modified zinc finger proteins were highly active in producing chromatin loops and in activating beta globin gene transcription. Dr. Deng’s more recent studies revealed that the system may also be employed to reactivate embryonic or fetal globin gene expression in adult erythroid cells. This could potentially benefit patients with sickle cell anemia and certain forms of thalassemia. Dr. Deng is now leading efforts to engineer new zinc finger proteins targeted to the human fetal globin gene promoters in order to examine this novel therapeutic strategy. Dr. Deng has received a number of additional awards, and part of her work was recently published in the journal Cell.

Each of our 2013 award winners were presented with certificates of achievement by Philip Johnson, M.D., chief scientific officer, during the CHOP Research Poster Day award ceremony and reception on February 27, 2013. They also received a monetary prize and will be featured on the CHOP Research Trainee Web portal at http://training.research.chop.edu.

The next request for CHOP Distinguished Research Trainee Award nominations will be extended in mid-October 2013. All mentors are encouraged to consider nominating their exceptional trainees for this prestigious honor.

Please contact David Taylor at taylor@email.chop.edu with any questions you may have.

CHOP Ranked Top NIH-Funded Children’s Hospital

We’re pleased to announce that during the 2012 Federal fiscal year, The Children’s Hospital of Philadelphia Research Institute received more NIH funding than any other independent children’s hospital. Children’s Hospital received more than $125 million in NIH funds in 2012, beating out Boston Children’s Hospital.

This good news is the latest in a series of #1 rankings and honors. In its recent list of the 10 Best Children’s Hospitals, Parents magazine named CHOP the nation’s overall best pediatric hospital. The Children’s Hospital of Philadelphia also ranked in the top 3 in all 6 medical specialties included in the survey. Parents magazine ranked Children’s Hospital’s Cancer Center and emergency medicine first; the Cardiac Center tied for first; neonatology ranked second; and orthopedics and pulmonology ranked third.

In addition, U.S. News and World Report last month named CHOP the top pediatrics graduate program in the country. In the 2014 Best Graduate Schools rankings, Children’s Hospital, along with its academic affiliate, the University of Pennsylvania’s Perelman School of Medicine, garnered the #1 spot in Pediatrics. And last year, Children’s Hospital tied for first overall in U.S. News and World Report’s 2012-13 rankings of the top children’s hospitals in the country, while also ranking number one in six of ten specialties.
Tom Curran, Ph.D., F.R.S., Joins Fellows of the AACR Academy

A world-renowned cancer investigator at The Children's Hospital of Philadelphia was recently honored by the American Association for Cancer Research as it inaugurated the first class of the Fellows of the AACR Academy.

Tom Curran, Ph.D., F.R.S., deputy scientific director of The Children's Hospital of Philadelphia Research Institute, was formally inducted into the Academy on April 5 in Washington, D.C. He is one of 106 fellows from across the country to receive the honor of induction into the AACR Academy.

The Academy was created to recognize and honor distinguished scientists whose major scientific contributions have propelled significant innovation and progress against cancer. These Fellows have been selected through a rigorous peer review process that evaluates individuals on the basis of their stellar scientific achievements in cancer research.

“I am particularly honored to receive this recognition from my peers in the AACR,” said Dr. Curran. “The mission of the AACR is to prevent and cure cancer, and to be a member of the inaugural group of fellows of the AACR Academy is both inspiring and humbling.”

Dr. Curran, a past president of the AACR, studies brain development and pediatric brain tumors, with an eye toward identifying molecular changes and potential drug targets. He also investigates the mechanism of action of anticancer drugs in tumor cells and cancer models.

Specifically, Dr. Curran discovered the Fos oncogene and its binding partner from another oncogene called Jun. He later showed that these two oncogenes regulate gene expression associated with cell proliferation and differentiation, cell death and neuronal activation. This work illuminated the pathways that go awry in cancer cells, and initiated the use of Fos as a marker for activity-dependent changes in the nervous system.

Dr. Curran recently united his interests in cancer and neurobiology to study children’s brain tumors. He developed a high-incidence model of pediatric medulloblastoma that he used to demonstrate how orally-bioavailable, small molecule inhibitors of Hedgehog signaling rapidly eliminate even large tumors in mice. This work led to clinical development of inhibitors of Smoothened for the treatment of basal cell carcinoma and medulloblastoma.

Additionally, Dr. Curran considers among his greatest achievements his contribution to the development of a drug that is now in pediatric trials — Erivedge, which was recently approved by the FDA to treat cancer in adults.

Dr. Curran has been honored with numerous awards and fellowships throughout his distinguished research career. Most recently, he was named a fellow in the prestigious American Academy of Arts and Sciences as well as the Royal Society, the oldest scientific academy in continuous existence that features the world’s most eminent scientists; and was elected a member of the Institute of Medicine.

In addition to serving as the Deputy Scientific Director at CHOP Research, Dr. Curran is a Professor of Pathology and Laboratory Medicine and Professor of Cell and Developmental Biology at University of Pennsylvania’s Perelman School of Medicine. He is also the associate director of Translational Genomics at the Penn Genome Frontiers Institute in Philadelphia.

2013 CHOP Research Institute Scientific Symposium to Promote Collaboration, Emphasize Discovery

On May 2 and 3, 2013, The Children’s Hospital of Philadelphia Research Institute will celebrate another year of scientific innovation and discovery at its annual Scientific Symposium. This event, taking place in the Colket Translational Research Building, will showcase the groundbreaking work of some of CHOP’s most successful researchers. Since its inception in 2004, the CHOP Research Institute Scientific Symposium has become one of the premier networking events at Children’s Hospital. By promoting an open discussion of research progress and novel techniques, this event has frequently fostered new collaborations and opened new avenues of scientific exploration for CHOP researchers.

For 2013, the Scientific Symposium has been restructured to take place over two days. This format will better showcase the institution’s strengths in pediatric basic, clinical and translational research while meeting the challenging schedules of our research community. Each of the two half-day sessions will consist of a keynote address as well as a number of brief faculty presentations, moderated panel discussions, and Q&A discussions, each with a focus on the CHOP Research Affinity Groups (RAGs). The CHOP RAGs showcase the diverse, cross-cutting and multidisciplinary work being performed at CHOP and demonstrate how basic, clinical, and translational research can be effectively integrated within a larger research program.

The Scientific Symposium will kick off on Thursday, May 2, 2013, at 12:00pm, with an opening address by Philip Johnson, M.D., chief scientific officer and executive vice president of the CHOP Research Institute. This will be followed by a series of scientific sessions and an external keynote speaker.

Leonard I. Zon, M.D., Grousbeck Professor of Pediatric Medicine at Harvard Medical School, Howard Hughes Medical Institute Investigator, and director of the Stem Cell Program at Children’s Hospital Boston, will present “Finding New Therapies for Blood Disease and Cancer Using Zebrafish.” A reception will be held immediately following this keynote address.

On Friday, May 3, 2013, the Scientific Symposium will continue with breakfast and additional scientific sessions, including an internal keynote speaker. Katherine High, M.D., William H. Bennett Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania, Howard Hughes Medical Institute Investigator, and director of the Center for Cellular and Molecular Therapeutics at CHOP will present “Gene Therapy and Genome Editing as Approaches to Treating Genetic Disease.” The day will conclude with a networking lunch for pre-registered attendees.

To learn more and register for the 2013 CHOP Research Institute Scientific Symposium, please visit http://www.research.chop.edu/programs/symposium/. Pre-registration is required for attendance at the event’s meals and reception. Please direct any questions you may have to researchtraining@email.chop.edu.
Announcing the 2013 QED Application Cycle

Since 2009, the QED Proof-of-Concept Program operated by the University City Science Center has supported life science technology development at universities across the Greater Philadelphia Region. Established in 1963 and headquartered in Philadelphia, PA, the Science Center runs QED within a suite of commercialization programs to help researchers turn their ideas into realities. In partnership with the Office of Technology Transfer, QED offers investigators the chance to become directly involved in the commercial aspects of their innovations.

The QED Program is launching its next application cycle in April 2013. Eligible investigators reside at participating research institutions, including The Children’s Hospital of Philadelphia. QED provides business and strategic guidance as applicants propose R&D projects to reveal the commercial potential of their innovations. The scope of technology broadly includes all life sciences and medical research plus a separate track for digital health technologies such as bioinformatics, mobile applications, electronic records, imaging platforms, educational tools, and software-embedded devices.

A panel of industry representatives makes recommendations for funding (up to $100,000 in cash for life science projects over 12 months – matched by the institution; up to $50,000 plus the match for digital health), to implement the selected projects and encourage follow-on investment from the private sector. QED Program Manager Adam Greenspan will be visiting campus to discuss the QED Program and answer questions for investigators who might be interested in exploring this opportunity.

Key dates for 2013:

- Request for Proposals released April 18
- Information Session May 8th
  - From 11:00 a.m. to 12:30 pm, the Science Center will host an information session in the Abramson Research Center, room 124
- Early submission deadline May 17
  - meetings (for early applicants) TBD, late May through early/mid-June
- Final submission June 17
- Finalist Invitations 1st week in July
- Finalist Roundtables 2nd week in July
- Finalist Orientation 3rd week in July
- Specialist Clinics TBD, early/mid-August
- Final proposal submission September 13
- Final presentation TBD, late October

For more information, please visit the main page www.sciencecenter.org/programs/qed.