

Bench to Bedside



RESEARCH AT THE CHILDREN'S HOSPITAL OF PHILADELPHIA

April 2012

CHOP Researchers Pinpoint Genes Associated with Childhood Obesity

Genetics researchers at The Children's Hospital of Philadelphia have identified at least two new gene variants that increase the risk of common childhood obesity.

"This is the largest-ever genome-wide study of common childhood obesity, in contrast to previous studies that have focused on more extreme forms of obesity primarily connected with rare disease syndromes," said lead investigator **Struan F.A. Grant, Ph.D.**, associate director of the **Center for Applied Genomics** at The Children's Hospital of Philadelphia. "As a consequence, we have definitively identified and characterized a genetic predisposition to common childhood obesity."

The study, by an international collaborative group, the Early Growth Genetics (EGG) Consortium, appeared in the journal *Nature Genetics*.

As one of the major health issues affecting modern societies, obesity has increasingly received public attention, especially given a rising prevalence of the condition among children. Research indicates that obese adolescents tend to have higher risk of mortality as adults. Although environmental factors, such as food choices and sedentary habits, contribute to the increasing rates of obesity in childhood, twin studies and other family-based evidence have suggested a genetic component to the disease as well.

Previous studies have identified gene variants contributing to obesity in adults and in children with extreme obesity, but relatively little is known about genes implicated in regular childhood obesity.

"The Center for Applied Genomics at The Children's Hospital of Philadelphia has recruited and genotyped the world's largest collection of DNA from children with common obesity," said Grant. "However, in order to have

sufficient statistical power to detect novel genetic signals, we needed to form a large international consortium to combine results from similar datasets from around the world."

The National Institutes of Health partly funded this research, which analyzed previous studies supported by many other European, Australian and North American organizations.

The current meta-analysis included 14 previous studies encompassing 5,530 cases of childhood obesity and 8,300 control subjects, all of European ancestry. The study team identified two novel loci, one near the *OLFM4* gene on chromosome 13, the other within the *HOXB5* gene on chromosome 17. They also found a degree of evidence for two other gene variants. None of the genes were previously implicated in obesity. "The known biology of three of the genes," added Grant, "hints at a role of the intestine, although their precise functional role in obesity is currently unknown."

"This work opens up new avenues to explore the genetics of common childhood obesity," said Grant. "Much work remains to be done, but these findings may ultimately be useful in helping to design future preventive interventions and treatments for children, based on their individual genomes."

The co-first author of the paper, Jonathan P. Bradfield, is from The Children's Hospital of Philadelphia. Two senior investigators from Children's Hospital, **Hakon Hakonarson, M.D., Ph.D.**, director of the Hospital's Center for Applied Genomics, and **Robert I. Berkowitz, M.D.**, director of the Weight and Eating Disorders Research Program, were also among the study co-authors.

New Stem Cells Provide Safe, Prolific Source for Studies

Investigators at Children's Hospital have generated a new type of human stem cell that can develop into numerous types of specialized cells, including functioning pancreatic beta cells that produce insulin.

Called endodermal progenitor (EP) cells, the new cells show two important advantages over embryonic stem cells and induced pluripotent stem cells: they do not form tumors when transplanted into animals, and they can form functional pancreatic beta cells in the laboratory.

"Our cell line offers a powerful new tool for modeling how many human diseases develop," said study leader **Paul J. Gadue, Ph.D.**, a stem cell biologist in the **Center for Cellular and Molecular Therapeutics at Children's Hospital**. "Additionally, pancreatic beta cells generated from EP cells display better functional ability in the laboratory than beta cells derived from other stem cell populations."

In addition to producing beta cells, the researchers also directed EP cells to develop into liver cells and intestinal cells — both of which normally develop from the endoderm tissue layer early in human development.

Gadue and his colleagues published their study April 6 in the journal **Cell/Stem Cell**.

The researchers manipulated two types of human stem cells — embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) — to become EP cells. Because both stem cell populations proliferate in great numbers and potentially generate all types of tissue, they offer enormous promise for scientists to precisely control cell development, both for the study of basic biology and for future cell-based treatments.

ESCs are derived from human embryos, typically unused embryos from fertility treatments that are donated for research purposes, while iPSCs are engineered from human somatic cells, such as skin cells or blood cells. Researchers have learned how to reprogram somatic cells to become pluripotent. Like ESCs, iPSCs are able to develop into many other types of human cells. However, when undifferentiated ESCs or iPSCs are transplanted in animal studies, they form teratomas, tumors containing many different cell types. Therefore, it has been critical that any cell

type generated from ESCs or iPSCs and used for transplantation is stringently purified to exclude undifferentiated cells with tumor-forming potential.

In the current study, the researchers used signaling molecules called cytokines to steer ESCs and iPSCs into becoming EP cells, committed to developing into endoderm, one of the three tissue layers found in early human development. The EP cells have nearly unlimited potential for growth in the laboratory.

Both in cell cultures and when transplanted into animals, the study team showed that EP cells can differentiate into multiple cell types, representing those found in the liver, pancreas, and intestine. Importantly, undifferentiated EP cells did not form teratomas in the team's transplantation studies.

In cell culture, the researchers differentiated the EP cells into beta cells — insulin-expressing cells similar to those found in the pancreas. Those engineered beta cells passed an important test — when stimulated by glucose, they were able to release insulin, a function that is impaired or absent in patients with diabetes. While the cells achieved only 20 percent of normal function, this result is an improvement over that seen in similar cells derived directly from ESCs or iPSCs, which typically respond very poorly or not at all to glucose.

Dr. Gadue stressed that these promising early results are only the first steps in researching EP cells. Further work may focus on taking cells from individual patients with genetic forms of diabetes or liver disease to derive EP cell lines. The EP cell lines can then be used to model the development and progression of the patient's disease and discover new therapies for that particular disease.

Finally, although applying this science to cell therapy is years away from practical clinical use, EP cells may offer a powerful starting point for developing tissue replacement treatments, such as supplying beta cells for diabetes patients or hepatocytes (liver cells) for patients with liver disease.

"While more work is needed to characterize EP cells, they may offer a potential source of safe, abundant cells for future diabetes treatments," Dr. Gadue said.

Scientific Symposium Scheduled for May 2012

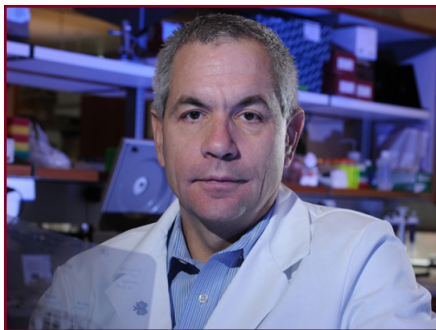
We are pleased to announce the return of the CHOP Research Institute Scientific Symposium. The event is scheduled for Friday, May 4, 2012 from 7:30am to 6:30pm in the Colket Translational Research Building, 1st Floor. The entire CHOP community is invited to attend, so please mark your calendars!

The symposium is a celebration of the important strengths of CHOP in basic, clinical, and translational research. The daylong

Symposium will include talks from faculty and an expo of our cores and administrative groups. The event will include a keynote address by Alan E. Gutmacher, M.D., director, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

Visit [The Office of Responsible Research Training's intranet site](#) to learn more about the event.

Children's Hospital Oncologist Featured at Annual Cancer Meeting



John Maris, M.D., director of the **Center for Childhood Cancer Research** at The Children's Hospital of Philadelphia, was recently featured in a series of videos prepared for the American Association for Cancer Research's annual meeting. Dr. Maris is the first pediatric expert to be

included in the Association's annual meeting videos.

The American Association for Cancer Research (AACR) videos highlighted Dr. Maris' **neuroblastoma research** and the **impact his work had on one young patient**. Neuroblastoma, a cancer of the peripheral nervous system, usually appears as a solid tumor in the chest or abdomen. It accounts for 7 percent of all childhood cancers, but because it frequently appears in an aggressive form, it causes approximately 12 percent of all childhood cancer deaths. In high-risk forms of neuroblastoma the cancer tends to return after initial treatment, usually with lethal results.

In 2010 Dr. Maris co-authored a study that examined the effects of immunotherapy — biologic agents that stimulate the body's immune

system — on neuroblastoma. The study showed patients receiving immunotherapy experienced a 20 percent improvement in survival two-year survival rates.

"That is about as much of a home run as you can expect in a large, randomized Phase III clinical trial, and something that overnight changed the way that we approach the disease, and has led to the implementation of immunotherapy as now as a standard way to treat neuroblastoma to improve survival by preventing relapse," Dr. Maris said.

The Cancer Center at CHOP has been using immunotherapy as part of standard treatment for children's with high-risk neuroblastoma since 2009. Children have arrived from around the world to receive this treatment at Children's Hospital, which has a long-established research and clinical program in neuroblastoma.

"Pediatric cancer research in many ways has played a leading role in the history of cancer research," Dr. Maris noted. "Many of the early discoveries of how chemotherapy can work to cure cancer were first seen in children with cancer.

More information about the AACR and the 2012 annual meeting can be found on the Association's **website**.

To Drive Infection, a Hijacking Virus Mimics a Cell's Signaling System

New research reveals how an invading virus hijacks a cell's workings by imitating a signaling marker to defeat the body's defenses. By manipulating cell signals, the virus destroys a defensive protein designed to inhibit it. This finding may represent a broader targeting strategy used by other viruses, and could lay the groundwork for developing more effective treatments for infectious diseases.

"Learning details of how cells respond to viruses helps us to understand key cellular machinery better," said study leader **Matthew D. Weitzman, Ph.D.**, of the **Center for Cellular and Molecular Therapeutics** at The Children's Hospital of Philadelphia.

Biologists have long known that viruses hijack cellular processes to replicate themselves, and that host cells have evolved defense systems to resist viral invasion. To replicate, viruses must deliver their own DNA into a cell's nucleus, so a viral infection entails a conflict between two genomes — the DNA of the host cell versus the foreign DNA of the virus. When viruses attacked, they do so by interacting with specific cell proteins as a way of penetrating the cell's defenses.

The study team, formerly based at the Salk Institute for Biological Studies in La Jolla, Calif., published their current findings online March 8 in *Molecular Cell*.

This study focused on herpes simplex virus type-1 (HSV-1), a common human virus that results in recurrent infections alternating with inactive periods. Like other viruses, HSV-1 is known to manipulate

cellular processes in order to infect cells, but the specific mechanisms by which it acts on the DNA repair pathway were previously unknown.

Dr. Weitzman's study team was studying a viral protein called ICP0 that overcomes host defenses by targeting cellular proteins for destruction. They found that ICP0 exploits phosphorylation, a chemical mark that is often used in cells to promote interactions between proteins, especially as part of the cellular signaling response to DNA damage. In HSV-1 infection, the phosphorylation signal on ICP0 attracts a cellular DNA damage response protein, RNF8, which binds to the false signaling marker and is then degraded. Because RNF8 normally inhibits viral replication, its destruction leaves the cell vulnerable to HSV-1 infection, as the virus takes over the cell's machinery.

The researchers also found that ICP0 exploits the same phosphorylation signal to bind to other cellular proteins in addition to RNF8, a hint that it may play a broader role in defeating antiviral defenses and manipulating cellular machinery. "By describing the mechanism of this particular interaction between a virus and a cell protein, we have pinpointed key regulators of a cell's processes, and shed light on how a cell regulates its defenses," Dr. Weitzman noted.

Dr. Weitzman will continue to investigate HSV-1 infection in neurons and in animal models, and plans to extend his research into other viruses, which may act on different pathways than HSV-1 does. "Ultimately, better knowledge of molecular mechanisms in infection may suggest strategies to interrupt the viral life cycle and treat infections," he said.

Study Improves Understanding of Mitochondrial Transcription, Mechanics

A new study by Children’s Hospital of Philadelphia researchers answers a long-standing question about how mitochondrial DNA figures in the production of cellular energy. The study, which was led by Neal Sondheimer, M.D., Ph.D., director of the Sondheimer laboratory at Children’s Hospital, improves our understanding of how mitochondria work, and could eventually lead to new ways of treating mitochondrial diseases.

The mitochondrion is a key supplier of the energy needed for the multiple functions of our cells. These organelles, which are found each cell, play a pivotal role in human health, because when the mitochondrial power plants of our cells become damaged the energy output for the body’s cells and tissues progressively declines.

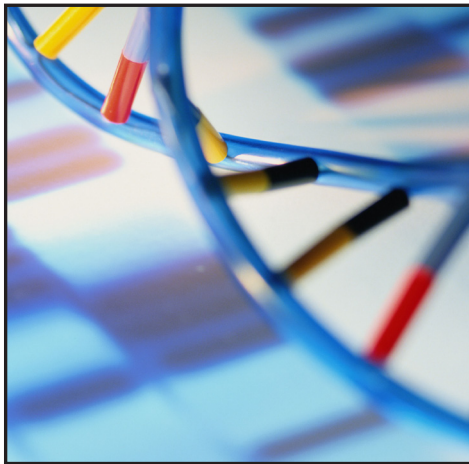
Mitochondria contain their own DNA, called mitochondrial DNA (mtDNA). While the DNA in a cell’s nucleus encodes the structure of both the cell and the mitochondria, mtDNA encodes key portions of the wiring diagram for the cellular power plants. The purpose of Dr. Sondheimer’s team’s study was to determine how mtDNA is used to create proteins used in the generation of cellular energy.

In order to make new proteins, mtDNA must be converted, or transcribed, into mitochondrial RNA (mRNA). But exactly how mtDNA does this has been a source of some controversy. While some investigators suggested the existence of a second heavy strand promoter — a specialized segment of DNA required for RNA synthesis, located on the “heavy” strand of mitochondrial DNA — some researchers doubted the second promoter’s existence because they couldn’t get it to work in the lab.

In addition to determining how to make the promoter, known as HSP2, work, Dr. Sondheimer and his team identified several of its

key features. The most important and “unexpected” feature of HSP2 is that a protein that normally activates mitochondrial promoters, transcription factor A (TFAM), acts to block transcription at HSP2. The study team’s finding “suggests that the cell may manipulate TFAM levels to change the genes that are expressed by the mitochondrion,” Dr. Sondheimer said.

Because determining the inner workings of the mitochondria could provide a major new approach to understanding and developing therapies for myriad rare and common diseases, the study’s findings could have significant repercussions.



“Although this finding has no immediate impact upon the care of our patients, it may have relevance in the future for patients who are unable to generate sufficient amounts of proteins encoded by the mitochondrial DNA to keep cellular function normal,” Dr. Sondheimer noted.

“If we are able to manipulate the pathways that control gene expression, it could form the basis of a new way of treating mitochondrial disease,” Dr. Sondheimer added.

The study was published March 26 in the Proceedings of the [National Academy of Sciences](#). In addition to Dr. Sondheimer, the study’s co-authors were Ornella Zollo, Ph.D., in the Division of Child Rehabilitation at Children’s Hospital, and Valeria Tiranti, Ph.D., of the IRCCS Foundation Neurological Institute in Milan, Italy.

Douglas C. Wallace, Ph.D., director of the Center for Mitochondrial and Epigenomic Medicine at Children’s Hospital, acted as the article’s editor. Support for the study was provided by an NIH grant as well as the Children’s Hospital of Philadelphia Pediatric Development Fund.

Latest Issue of *Discovery to Innovation* Now Online

The most recent issue of *Discovery to Innovation* is now [available online](#). The issue features research revealing factors that contribute to disease, findings that may one day lead to new therapies, funding that will make continued investigations possible, and much more.

Visit www.research.chop.edu/discovery_to_innovation/ to read the issue or explore the archives.

From a Researcher to a Patient to a Champion for a Cause

During the day, postdoctoral fellow Jacquelyn Roth, Ph.D., can be found in the Abramson Pediatric Research Center, conducting laboratory research on brain tumors and working toward her board certification in clinical cancer cytogenetics.

Her work on cancer genetics at Children's Hospital, as part of the team led by Jackie Biegel, Ph.D., is an extension of the research she did while in the doctoral program in Genetics at Thomas Jefferson University. While at Jefferson, Jackie studied cancer, particularly looking for new genes involved in breast cancer.

Then, in 2010 at the young age of 28, "Little Jackie," as she has come to be called in Dr. Biegel's group, went from being the researcher to being the patient. She was diagnosed with breast cancer.

"I never thought I would be fighting breast cancer in two ways at once," she said.

But fight she did, through rounds of chemotherapy and radiation and the first of several surgeries to come. She now shares her spirit, knowledge, and insight helping others understand and handle the emotional and physical toll that comes with a breast cancer diagnosis – in essence, to help them become a "survivor" like her.

Jackie said that she pursued volunteer organizations after her diagnosis to connect with people in similar circumstances and share her story. With her background in research, she also hoped to bring her unique perspective and knowledge to the groups, get and give support, and find a way to become involved.



She ultimately became involved with Susan G. Komen for the Cure and caught the attention of the Philadelphia Affiliate CEO Elaine Grobman. Jackie said she stood out as the youngest at a breast cancer support meeting and was actively in treatment at the time.

Grobman subsequently asked Jackie to speak at the Race for the Cure Kickoff Party as the Survivor Speaker, which was held in February. For this event, Jackie filmed a video running through the Italian Market and up the steps of the Philadelphia Art Museum to the chants of "Little Rocky!"

"I knew that sharing my story would be healing, and I hoped in the process I could not only make other women aware of the disease, especially young women, but I hoped to show them that they are not alone." Jackie said in her speech for the Komen Race for the Cure kick-off event.

In addition, Jackie recently attended the Conference for Young Women Affected by Breast Cancer, for which she wrote a welcome letter and served as the "face" of the event. And this fall she will be one of three survivors honored at the "Butterfly Ball," the annual fundraiser for the organization Living Beyond Breast Cancer.

"I know that I've gained an appreciation for things that I just never understood before. I don't sweat the small stuff, it just seems like a waste of time now," she said. "Along this journey, I've gained independence and I am stronger than I ever thought I could be."



Images of Jacquelyn Roth courtesy of Sudarshan Phani and Joshua Pelta-Heller.

Behind the Scenes: Office of Postdoctoral Affairs

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, **Office of Postdoctoral Affairs** director Wendy Williams, Ph.D., gives a look behind the scenes at what her group does to support CHOP Research.

What is the overall goal of your department?

The Office of Postdoctoral Affairs (OPA) is committed to supporting the next generation of research scientists at Children’s Hospital. The office provides programmatic support to all research trainees (including postdoctoral fellows, physician fellows, training grant fellows and CHOP-based UPenn graduate students), and maintains a specialized administrative infrastructure to support CHOP’s postdoc population.

What do you manage for the research community?

The Office of Postdoctoral Affairs manages the support infrastructure for CHOP Research Trainees. For postdoctoral fellows, the office provides individual or small group welcome sessions and administers the annual postdoc review process, among a variety of other services. The OPA also supports the CHOP Research Trainee Advisory Committee (RTAC), a faculty led committee dedicated to maximizing the quality of the CHOP research trainee experience.

How to you ease or improve things for investigators?

The Office of Postdoctoral Affairs is available to provide input and support for all CHOP investigators, both in relation to trainee matters and in postdoc data collection for T32 training grant applications. The office strives to keep an open-door policy wherein trainees and investigators can reach out for assistance at any time.

How is the department structured?

Each team member serves a core function with specific expertise but we work as a team to support the research community.

How many people work in the department?

Five.

What types of projects does your group typically work on?

- General and programmatic support of all CHOP research trainees
- Specialized administrative support for CHOP’s postdoc population

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

General outreach to the trainee and mentor communities, program development

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

In FY2012, the OPA will review and update of the Annual Postdoc Review process and form to better assist in setting expectations between mentors/mentees and to better reflect the core competencies of a successful postdoctoral fellow.

What recent accomplishment is your group most proud of?

Completion of a Trainee Tracking Database and profile system, designed to collect trainee information for use in T32 Training Grant applications and for general administrative use.

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

We’re always available to answer questions related to the CHOP Research trainee community.

What is a common misperception about your department?

OPA maintains a specialized administrative infrastructure to support CHOP’s postdoc population which many assume is a CHOP Human Resources function. CHOP Human Resources handles all appointments and terminations of postdocs. OPA provides support once the postdoc arrives at CHOP.

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

Our support of a smaller trainee community allows us to perform more one-on-one and personalized support functions. We have also had a direct connection to the National Postdoctoral Association for over 3 years, with both the office Director and Academic Programs Officer having served on the organization’s Board of Directors.

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

We are continually expanding our support efforts to encompass physician fellows and to assist in their transition to research training, both through our support of RTAC and programmatic development.

Is there anything your department does that might surprise people?

We provide CHOP mentors with a wide range of support services including access to grant template language for such topics as minority recruitment, the responsible conduct of research, and postdoc training and support.

What is the most satisfying part of your job?

I have the support of leadership to: 1) find new opportunities to increase CHOP’s visibility as a premier place to come and train in research and 2) identify issues/challenges and propose solutions to improve the trainee experience at CHOP.

2012 CHOP Distinguished Research Trainee Awards Announced

The CHOP Research Institute has announced the winners of the 2012 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. Sixteen outstanding nominations were received among the three groups. Five winners, including two postdoctoral fellows, two physician fellows, and one graduate student, were selected after review and voting by members of the Research Trainee Advisory Committee, chaired by Michael Robinson, Ph.D.

Kelly Dougherty, Ph.D., Division of Gastroenterology, Hepatology and Nutrition, and **Susan Wood, Ph.D.**, Division of Research Anesthesiology, received the award in the Postdoctoral Fellow Category. **Utpal Bhalala, M.D.**, a pediatric critical care medicine fellow, and **Andrew Wood, M.D.**, a pediatric hematology-oncology fellow, were selected to receive the award in the Physician Fellow Category. **Amy Gleichman**, a graduate student at the University of Pennsylvania, received the award in the CHOP-Based Graduate Student category.

Dr. Dougherty's research focuses on randomized clinical trials addressing physical activity- and nutrition-related issues affecting growth and body composition in healthy and chronically ill children, including cystic fibrosis (CF) and sickle cell disease (SCD). Her clinical studies, performed under the mentorship of **Virginia A. Stallings, M.D.**, have provided evidence that the currently recommended doses of vitamin supplementation for affected children are often sub-optimal. Children with CF, for example, can benefit from two times the current recommended dose of daily vitamin K supplementation. This increase can dramatically improve the lives of these chronically ill children, a trend that Dr. Dougherty has also explored in SCD-afflicted patients taking a daily regimen of vitamins D3 and A supplementation. These findings, amidst her other honors and awards, are representative of her hard work and dedication. As Dr. Stallings relates, "occasionally there is a stellar postdoc who has the qualities that are needed to be a leader in complex, interdisciplinary pediatric research and who is committed to conducting clinical and translational research that actually will result in improved health of children and quality of life for the child and family, and Kelly is one of these young people." Dr. Dougherty's successes have led to her recent appointment as Research Assistant Professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania and Children's Hospital.

Dr. Susan Wood, nominated by **Rita Valentino, Ph.D.**, performs research designed to elucidate the neurobiological basis for vulnerability to stress-related diseases. In addition, she aims to identify the cellular mechanisms underlying stress-related psychiatric and medical comorbidities. These studies help us to understand why some individuals are more susceptible to stress-related pathological consequences than others. Dr. Wood's work has earned her much recognition, including the highly competitive National Alliance for Research in Schizophrenia and Affective Disorders Young Investigator Award and an American Heart Association Individual Postdoctoral Fellowship. She also excels as an instructor and mentor, with over 6 years of teaching experience. According to Dr. Valentino, "Susan has consistently distinguished herself among trainees

through her research, and her dedication to teaching and service." Dr. Wood aims to continue her high-impact work in academia following completion of her postdoctoral fellowship.

Dr. Bhalala is a researcher and physician with a particular interest in pediatric critical care medicine. In collaboration with his mentors, **Vinay Nadkarni, M.D.**, and **Robert Berg, M.D.**, Dr. Bhalala has conducted innovative clinical studies related to the use of Near-Infrared Spectroscopy as a means of early identification of low cardiac output syndrome. In addition, he has analyzed the effects of novel periodic acceleration forces (generated during a patient's ground or air transport to a hospital) on the endothelium and vasoactive mediators. Dr. Bhalala's success is also reflected in his clinical duties. As Dr. Nadkarni notes, Dr. Bhalala "is an outstanding and ethical physician, with a commitment to excellence in scientific discovery, translation, and clinical practice." Dr. Bhalala will be an Assistant Professor at Johns Hopkins University next year, where he will continue his career as a resuscitation scientist.

Dr. Andrew Wood, a physician fellow in the division of oncology, was nominated by **John Maris, M.D.**, for his exceptional achievements in translational research. According to Dr. Maris, "Andrew has limitless potential, and I think he will become a leader in the field of pediatric oncology with a focus on new drug development based on our understanding of the basic mechanisms of oncogenesis." This high praise stems from his work examining oncogene mutations and their effects on drug sensitivity. A somatic mutation of the gene *ALK*, for example, reduces the effectiveness of the anti-cancer drug crizotinib. Dr. Wood's research has shown that such drugs should be engineered to have increased drug-*ALK* affinity in order to overcome resistant mutations in children and adults. This work, and more, has earned him numerous awards and honors, placing him prominently among the most talented up-and-coming translational researchers.

Amy Gleichman, who is seeking her doctorate from the University of Pennsylvania under the mentorship of **David Lynch, M.D., Ph.D.**, is working to define the mechanisms involved in anti-NMDA receptor encephalitis. Specifically, she has identified the functional epitope on this receptor, an area where antibodies bind and change its conformation. This mechanism has significant implications for the function of the receptor and for various forms of encephalitis. Dr. Lynch credits Ms. Gleichman's keen interest and exceptional productivity for helping to focus his research efforts. As he remarked, "Amy retains an enthusiasm for science and particularly neuroscience that I have seen in few if any other investigators in my 30 years in science." Amy's excitement and passion will surely lead her to a successful and prolific scientific career.

All of our 2012 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 22, 2012. 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 December 2012. 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.

HAVE NEWS?

Contact Jennifer Long at ext. 4-2105
or by e-mail at longj@email.chop.edu.

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RESEARCH INSTITUTE

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