The Children's Hospital *of* Philadelphia®
RESEARCH INSTITUTE

Bench to Bedside

RESEARCH AT THE CHILDREN'S HOSPITAL OF PHILADELPHIA February 2010

Investigators Challenge Prevailing Assumptions in Interpreting Genome-Wide Studies

In the decade since the Human Genome Project produced the first map of DNA sequences in the human genome, scientists throughout the world have combed through genome data to identify genes and gene variants that cause human disease. A new study suggests that researchers may need to broaden their search farther afield to pinpoint rare but powerful disease-causing mutations.

Investigators from two large genome research centers at The Children's Hospital of Philadelphia and Duke University published a study recently in the online journal *Public Library of Science Biology* (PLoS Biology), describing what they call "synthetic genome-wide associations."

"We believe our analysis will encourage genetics researchers to reinterpret findings from genome-wide association studies, which will also enable all of us to generate more meaningful diagnostic results for patients," says co-author Hakon Hakonarson, M.D., Ph.D., director of the Hospital's Center for Applied Genomics.

Dr. Hakonarson and his colleague at Children's Hospital, Kai Wang, Ph.D., collaborated closely with the study leader, David B. Goldstein, Ph.D., of the Center for Human Genome Variation at Duke University. Both research teams had been working independently and simultaneously on a hypothesis that rare genetic variants had a larger role in disease than conventionally assumed.

When Dr. Goldstein presented his conceptual model last year to genetics researchers at the University of Pennsylvania, Drs. Hakonarson and Wang proposed a collaboration, subsequently supplying data from two genetic diseases — sickle cell disease and genetic hearing loss — that supported and validated the rare variant hypothesis proposed in the current paper.

To date, genome-wide association studies (GWAS) have detected many common gene variants associated with particular diseases, but those variants have shown only modest effects, accounting for a very small percentage of the genetic contribution to the disease.

"GWAS is a very powerful tool to identify disease genes, but for complex disorders, these common variants may not reflect true effect sizes," says Dr. Hakonarson. "We may need to look farther away from those common variants to find variants that are individually rare but have strong causative effects." The genetic variants being tested, also referred to as single-nucleotide polymorphisms (SNPs), are changes in a single chemical base of DNA that act as markers for a disease, without causing the disease.

In the current study, the researchers performed a computer simulation in which rare variants were distributed throughout 10,000 genotypes (models of DNA data simulating those collected from human study subjects). Their analysis yielded "synthetic associations"— statistical connections between the rare variants and the common variants that produced signals similar to those found in actual disease studies.

They then tested their approach on two large sample sets for well-characterized disorders, sickle cell disease and genetic hearing loss, in which causative genes were already known. They found a similar pattern of synthetic associations between rare and common gene variants. "Under conventional interpretations, GWAS found only modest contributions for associations with the gene that we know causes hearing loss," says Dr. Hakonarson. "Our study shows that conventional interpretation may undervalue the contribution of such gene variants in hearing loss, and we suggest that similar underrepresentation of effect sizes by common variants may occur in many other genetic disorders."

The usual assumption in GWAS is that disease-causing variants are located relatively close to the common variants that capture them (referred to as tagging SNPs). Researchers usually seek out causative variants that travel together with the common variant along the genome; in technical terms, the nucleotides are in relatively strong linkage disequilibrium. "Our study found the causative genes may be two to four times farther away than researchers tend to search, so their effect sizes are poorly captured," says Dr. Hakonarson.

Drs. Hakonarson and Wang are conducting follow-up studies, some in collaboration with Dr. Goldstein, to expand and refine the gene-hunting model using resequencing techniques. The immediate implications of this model, says Dr. Hakonarson, affect researchers more than clinicians. But eventually, he adds, this work may improve diagnostic evaluation for patients, furthering the goal of personalized medicine tailored to a patient's genetic profile. At the same time, technological advances in automated gene sequencing will enable researchers to work faster as well as smarter.

Children's Hospital and the Institute for Genome Sciences and Policy at Duke University provided funding support for this study. Co-authors with Drs. Goldstein, Hakonarson, and Wang were Samuel P. Dickson, of the Center for Human Genome Variation at Duke University; and Ian Krantz, M.D., of the Division of Human Genetics at Children's Hospital, an expert in genetic hearing loss.

NIH Grants Will Advance Novel Stem Cell Treatments for Blood Disorders

The new decade may herald an era of cell therapy — treating human diseases by delivering highly specific beneficial cells. In the wake of a National Institutes of Health (NIH) decision late last year permitting federally funded researchers to use new lines of human embryonic stem cells, the door has opened more widely to stem cell research.

Anyone who has ever undergone a bone marrow transplant has received a type of cell therapy, but current progress in stem cell research holds the potential of precisely controlling cell development for a broader variety of clinical treatments than ever before.

Two large federal grants recently awarded to Children's Hospital will advance the frontiers of research into cellular therapies. Both programs aim to engineer human cells into new generations of cells and tissues for patients suffering from blood diseases, cancer and, likely, a greater range of other disorders.

One grant focuses on developing human embryonic stem cells (hESCs) to improve platelet supplies for hematology and oncology patients, as well as using platelets to deliver customized proteins to injured blood vessels. The other grant concentrates on creating induced pluripotent stem cells (iPSCs), a type of stem cell that researchers would use to better understand a variety of diseases, and eventually channel into producing healthy replacement tissues for sick patients. Both programs exemplify 21st century cellular therapy.

"Having a larger and higher-quality supply of platelets will benefit many patients," says Mortimer Poncz, M.D., chief of Hematology at Children's Hospital, and co-principal investigator of the $16.8 million, seven-year grant titled, "Embryonic Stem Cell-Derived Platelets as Cellular Therapeutics." The National Heart, Lung, and Blood Institute (NHLBI), part of the NIH, issued the grant under a new initiative, the NHLBI Progenitor Cell Biology Consortium.

Platelets are naturally occurring blood cells that help control bleeding and assist in wound healing. Patients receiving chemotherapy and bone marrow transplantation depend on transfusions of platelets to restore levels depleted by their treatments. However, the donor supply is limited, and after multiple transfusions, patients may develop antibodies that attack the donated platelets.

Under the platelet grant, awarded jointly to Children's Hospital and the Fred Hutchinson Cancer Research Center/University of Washington Cancer Consortium, investigators will pursue a novel approach — generating platelets from human embryonic stem cells (hESCs). These cells are derived from human embryos fertilized in *in vitro* fertilization clinics and donated for research purposes and are capable of developing into every type of tissue in the body.

In seeking to control the fate of these hESCs, the two research centers in this collaboration are pursuing complementary approaches. The Children's Hospital group, under Dr. Poncz, will focus on generating platelets and their precursor cells from hESCs in laboratory studies. The University of Washington team, under co-principal investigator Beverly Torok-Storb, Ph.D., will rely on its expertise in stem cell transplants and animal studies to develop reagents that can be administered to patients to stimulate their existing precursor cells to develop into platelets.

At Children's Hospital, two project leaders are prominent stem cell researchers recently recruited to the Hospital's Center for Cellular and Molecular Therapeutics, directed by gene therapy pioneer Katherine A. High, M.D. Paul J. Gadue, Ph.D., and Deborah L. French, Ph.D., will lead important components of the overall program. Another project leader of the platelet grant, Mitchell Weiss, M.D., Ph.D., also leads the second NIH-funded grant for stem cell research, described below. Children's Hospital has established a new core facility, the Human Embryonic Stem Cell Core, to supply cells for their studies.

In addition to boosting the supply of platelets to carry out their usual biological roles, the researchers also seek to customize them as drug delivery vehicles. In mouse studies, for instance, Dr. Poncz's team previously treated the bleeding disorder hemophilia by loading platelets with the clotting factor that is deficient in that disease. "In addition to investigating platelets for treating hemophilia in people, we will investigate their potential role in delivering other bioactive proteins to sites of vascular injury," says Dr. Poncz. "For instance, platelets might deliver an enzyme called urokinase to selectively disintegrate blood clots."

Second grant will investigate induced pluripotent stem cells.

The second grant from the NHLBI also supports stem cell research, but focuses on a more recently discovered type of cell. This two-year, $997,000 grant was awarded to hematologist Mitchell Weiss, M.D., Ph.D. The Grand Opportunity (GO) Grant, funded by the American Recovery and Reinvestment Act, is part of an NHLBI program to support novel research designed to quickly advance an area of biomedicine in significant ways.

Scientists demonstrated in 2007 that they could reprogram human somatic cells (the vast majority of cells that are not sperm or egg cells) into a pluripotent state —the capacity to develop into other types of human cells. In this project, Dr. Weiss and his colleagues will manipulate induced pluripotent stem cells (iPSCs) into becoming hematopoietic, or blood-forming, cells.

"These cells represent a potentially remarkable tool for custom-fitting new tissue to an individual patient," says Dr. Weiss. "Because they originate from an individual patient's cells, they will not be rejected as foreign by the patient's immune system." But much work remains to be done in fully characterizing how iPSCs develop, and in understanding how they may differ from both hESCs and from typical blood cells.

Weiss will also investigate iPSCs as a powerful new model system for understanding how blood disorders develop. "Many blood diseases are difficult to study in patients, in terms of the exact mechanisms by which cells develop abnormally," says Dr. Weiss. "We will investigate iPSCs in models of two pediatric disorders, with the goal of using our improved knowledge of cell biology to devise treatments."

Dr. Weiss's group will focus on blood diseases associated with Down syndrome. Children with Down syndrome are at higher risk for transient myeloproliferative disorder, a precursor of leukemia, as well as for acute megakaryoblastic leukemia. Using animal models, the researchers will stimulate iPSCs to mimic disease processes seen in Down syndrome, in hopes of discovering ways to prevent these forms of leukemia.

A third goal of Dr. Weiss's project is to collect tissues from patients, then reprogram their cells into iPSCs and develop them into tissue banks for specific diseases. In this effort, his team will concentrate on a genetic blood disorder called Diamond Blackfan anemia.

Dr. Weiss's team at Children's Hospital will partner with scientists at two other institutions in the region: Pennsylvania State University, in State College, Pa., and the Coriell Institute for Medical Research, in Camden, N.J.

"The successful completion of these grants was in large part based on the recent establishment of the Human Embryonic Stem Cell Core at Children's Hospital," says Dr. Poncz. "These two grants illustrate the promising future that stem cell biology holds, not only for research purposes and for hematologic and oncologic disorders, but for a wide range of diseases that presently have suboptimal therapies. The future of stem cell therapy may be limited only by our imagination."

Special Bypass Procedure Used During Infant Heart Surgery Does Not Impair Later Neurological Outcomes in Children

Congenital heart defects (CHD) are the most common birth defects, affecting 8 per 1,000 live births with one third of affected children requiring intervention in early infancy. Increasing numbers of survivors combined with developmental expectations for independence, behavioral self-regulation, and academic achievement have led to a growing identification of neurobehavioral symptoms in some survivors.

A study now suggests that a cooling technique often used in heart operations does not impair neurological outcomes.

Congenital heart disease and its treatment were originally thought to potentially increase neurologic injury in these patients. The technique of deep hypothermic circulatory arrest (DHCA) is used in order to repair these congenital cardiac defects by providing a bloodless surgical field, which may facilitate completion of the best physiologic repair, and decrease the duration of blood exposure to the bypass circuit. However, it involves a period of reduced blood flow in the brain. Cooling is a protective mechanism to reduce metabolism of the brain and other organs during periods of low blood flow.

Stephanie Fuller, M.D., a cardiothoracic surgeon at Children's Hospital, presented these research findings in the prestigious J. Maxwell Chamberlain Lecture at the annual meeting of the Society of Thoracic Surgeons in Fort Lauderdale, Fla. According to the study, DHCA does not impair language skills, attention, and other neurocognitive abilities in school-age children.

Dr. Fuller and colleagues from Children's Hospital and the University of Washington assessed the use of DHCA as a predictor of neurodevelopmental outcomes in children who had cardiac surgery as infants. The infants were enrolled in a prospective study of apolipoprotein-E (APOE) polymorphisms and neurodevelopmental outcomes after cardiac surgery and underwent formal neurodevelopmental testing at 4 years of age.

Neurodevelopmental testing was completed in 238 out of 307 eligible patients. The surgeons used DHCA in 92 of those infants as deemed necessary to provide better operative exposure with a bloodless and less cluttered surgical field and therefore a shorter total cardiopulmonary support time. Use of DHCA was not predictive of worse performance for any neurodevelopmental outcome. Significant predictors of worse outcome included lower socioeconomic status, preoperative mechanical ventilation, and babies that were younger and smaller at the time of first operation. Neurodevelopmental assessment included cognition, language skills, attention, impulsivity, executive function, social competence, and visual-motor and fine-motor skills.

"Selective use of DHCA during cardiac surgery in infancy may facilitate operative repair and is not associated with impaired neurodevelopmental outcomes," says Dr. Fuller." Despite added risk factors, the selective use of DHCA during infancy for repair of congenital heart disease without an obstruction in the aorta was not predictive of worse performance at 4 years of age."

Dr. Fuller adds "use of DHCA as a support technique during cardiac surgery in infancy has many advantages, it is not necessary to sacrifice these advantages merely to avoid use of DHCA. Our study adds to the growing literature showing no adverse influence of limited periods of DHCA. New support techniques must be carefully evaluated prior to wide-spread acceptance to confirm they are not inferior to conventional management strategies."

Consultation Sessions Now Available for Social Media

The Research Social Media Support Group is now available for consultation sessions with investigators, research groups, and programs wishing to use social media to facilitate and share the results of the research endeavors at Children's Hospital.

Under the Hospital-wide program, employees are expected to have full onsite access to Facebook and Twitter in March, with access to other social media instances in the future. Until then, employees are encouraged to participate in social media and blog about their research activities from home in collaboration with the Research Social Media Support Group.

The support group consists of representatives from the Department of Research Communications, the Center for Biomedical Informatics (CBMi), and the Department of Research Information System's Web Services Team, who collaborated to move social media for research forward through an extensive pilot program.

The consulting team will provide the following services for owners of social media instances:

- Consulting with investigators on development and maintenance issues
- Assisting with site building
- Providing technical support
- Marketing social media instances
- Maintaining a central registry of Research Institute social media instances
- Assisting in triaging responses to inappropriate posts or comments
- Helping to navigate compliance, ethical, and business issues
- Serving as an advocate of research-specific social media issues within the Hospital Social Media Task Force

Please contact Jennifer Long, director of Research Communications, at longj@email.chop.edu if you would like to set up a consultation. Please visit the Social Media section of the CHOP Research intranet at https://intranet.research.chop.edu/display/SMT/Home for additional information.

PolicyLab Launches New Site

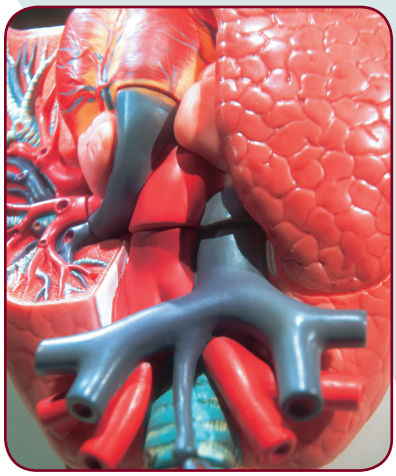
PolicyLab: Center to Bridge Research, Practice, and Policy at CHOP Research Institute recently announced the launch of its new Web site.

PolicyLab aims to improve child health and well-being by engaging in research and intervention projects that are responsive to community needs and relevant to policy priorities.

A relatively new Center of Emphasis at Children's Hospital, PolicyLab was founded on the beliefs that research should be informed by community needs and priorities and that evidence should inform the decisions of policymakers.

The new Web site, located at www.research.chop.edu/policylab, contains extensive information on current projects, recent publications, and upcoming events.

In Early Heart Development, Genes Work in Tandem



Studying genes that regulate early heart development in animals, scientists have solved a puzzle about one gene's role, finding that it acts in concert with a related gene. Their finding contributes to an understanding of how the earliest stages of heart development may go awry, resulting in congenital heart defects in humans.

Peter J. Gruber, M.D., Ph.D., a cardiothoracic surgeon at Children's Hospital, led a study published in the Jan. 15 issue of the *Journal of Biological Chemistry*. Occurring in approximately 1 in 200 children, congenital heart defects represent the most common human birth defect.

"We uncovered a role for the *Gata5* gene, a role that has been unappreciated in vertebrate cardiac development," says Dr. Gruber. "*Gata5* is a gene that is essential to heart development in other animals, such as frogs and zebrafish, but contrary to expectations, deleting this gene seemed to have no effect on the hearts of mammals. We found, however, that in mice, this gene cooperates closely with other genes to affect heart development. It may work similarly in humans."

The *Gata5* gene expresses the protein GATA5, which is a member of a family of zinc-finger transcription factors — proteins that act as switches to turn gene activity on or off. Transcription factors regulate how DNA carries its instructions into messenger RNA, and RNA in turn helps produce a specific protein with particular functions in biological processes. The GATA transcription factors carry out important tasks during an organism's development.

Dr. Gruber's study team genetically engineered mice in which *Gata5* genes were inactive, and found the animals were healthy, with normally functioning hearts. They did find, however, that those mice showed increased expression of another gene in the same family, *Gata4*, which suggested that *Gata4* might compensate for the loss of *Gata5*.

When they bred a new group of mice in which *Gata5* was inactive and had only one functioning *Gata4* allele (each gene has two alleles) those mice all had profound cardiac defects and died before birth. Mice with a normal *Gata 5* gene and only one functioning *Gata4* allele were normal.

"Our research suggests that *Gata5* has a previously unsuspected role during cardiac development, acting cooperatively with *Gata4* to direct the heart to form normal structures," says Dr. Gruber. "If the same process occurs in humans, that tells us something new about prenatal heart development. The research also shows that studying a single gene in isolation may not be sufficient. Here one gene buffers the effects of losing another gene."

In people, genes in the GATA family regulate the development of heart muscle in particular structures that divide the left and right sides of the heart. Gruber's team is carrying follow-up studies, investigating how the genes seen in mice may be analogous to genes involved in embryonic heart development in humans. "Although a long way off, a greater understanding of biological mechanisms during early heart development may eventually provide useful targets for more accurate diagnosis or personalized treatment of children with congenital heart disease," adds Gruber.

Grants from the National Institutes of Health and the Pliezowicz Family Foundation supported this study.

Type 2 Diabetes Gene Predisposes Children to Obesity

Researchers have found that a gene implicated in the development of type 2 diabetes in adults also raises the risk of being overweight during childhood. The finding sheds light on the genetic origins of diabetes and may present an avenue for developing drugs to counteract the disease, which has been on the upswing in childhood and adolescence.

Researchers from Children's Hospital and the University of Pennsylvania School of Medicine published the study recently in the online version of the journal *Diabetes*.

"It has been a bit of a mystery to scientists how or even if these adult diabetes genes function during childhood," says study leader Struan F.A. Grant, Ph.D., a researcher and associate director of the Hospital's Center for Applied Genomics (CAG). "This finding suggests that there may be genetic activity during childhood that lays the foundation for the later development of type 2 diabetes."

Type 2 diabetes occurs either when the pancreas produces too little insulin, or when the body cannot efficiently use the insulin that is produced because the cells have become resistant. Formerly called adult-onset diabetes and still most common in adults, type 2 diabetes has been increasing sharply among children and teenagers.

Dr. Grant and study co-leader Hakon Hakonarson, M.D., Ph.D., CAG director, investigated 20 gene variants, known as single nucleotide polymorphisms (SNPs), previously reported to be associated with type 2 diabetes. The researchers drew on a cohort of nearly 7,200 Caucasian children, aged 2 to 18 years, in an ongoing genome-wide association study of childhood obesity at Children's Hospital. Dividing the cohort randomly in half allowed the team to follow their discovery study with a replication study.

Investigators continue to unravel the complicated role of different diabetes-related genes in influencing body weight toward both lower and higher ends of the scale. The risk of developing type 2 diabetes in adulthood is often influenced by factors in the first year of life, including lower birth weight, as well as by higher body mass index (BMI) during childhood. Obesity is a well-known risk factor for type 2 diabetes.

A study published earlier this year by the same study team found that another type 2 diabetes gene, *CDKAL1*, affects fetal growth and increases the likelihood that a baby will be underweight at birth.

The current study found that the gene *HHEX-IDE* does not affect birth weight, but makes it more likely that a child will become obese during childhood. The gene does not appear to predispose to obesity in adults, although by contributing to childhood obesity, it may set the stage for type 2 diabetes in adulthood.

Dr. Grant cautioned that *HHEX-IDE* accounts for only a small proportion of the genetic contribution to the risk of type 2 diabetes, so many other gene variants remain to be discovered. However, he adds, *HHEX-IDE* may represent an important underpinning of the disease.

"Previously we thought that this gene affects insulin production during adulthood, but we now see that it may play an early role in influencing insulin resistance through its impact on body size during childhood," says Dr. Grant. "One implication is that if we can develop medicines to target specific biological pathways in childhood, we may be able to prevent diabetes from developing later in life."

The National Institutes of Health, the Cotswold Foundation, and Children's Hospital supported this study.

Investigators, Staff Must Consider Federal Export Control Laws

The federal export control laws govern how certain information, technology, and commodities can be transmitted to anyone overseas (including U.S. citizens abroad) or to foreign persons here in the United States. These laws can affect an institution in many different and unexpected ways.

Like most federal regulations, there are definitions to consider.

Exports are any oral, written, electronic, or visual disclosure, shipment, transfer, or transmission of any commodity, technology (information, technical data, assistance), or software code to anyone, including U.S. citizens outside U.S. boundaries and non-U.S. entities or individuals regardless of location.

We may rarely be impacted by them but we need to be aware of — and abide by — these laws and regulations.

There are several situations in which the export control laws are likely to impact us:

- Travel abroad: travel to some locations and for certain purposes can be problematic and requires special consideration
  Where are you going? What will you be doing there? What are you taking with you?
- Shipping: sharing certain pathogens or biologics with colleagues outside the U.S. will usually require a license
  What are you shipping and to whom? For what purpose?

Much of the work at CHOP Research is covered by the "fundamental research" exclusion, which covers basic and applied research in science and engineering where the resulting information is ordinarily published and shared broadly within the scientific community. Fundamental research is distinguished from proprietary research and from industrial development, design, production, and product utilizations, the results of which ordinarily are restricted for proprietary and/or specific national security reasons.

Normally, the results of fundamental research are published in scientific literature, thus making it publicly available. Research that is intended for publication — whether it is accepted by scientific journals or not — is considered fundamental research. Therefore, a large segment of academic research is considered fundamental research.

Because the results of the research are publicly available (except for encryption object code and source code in electronic form or media), fundamental research is not subject to Export Administration Regulations and does not require a license.

While these regulations are manageable and most of the activities at CHOP Research are allowable, we still need to ask questions, determine what, if anything, needs to be reviewed for the purposes of these regulations, and record our decisions appropriately.

Therefore, if you are planning any overseas trips or will be shipping materials to colleagues elsewhere in the world, please contact Deb Barnard in the Office of Research Compliance and Regulatory Affairs at ext. 6-9367 or barnardd@chop.edu.

Young Investigator Receives Research Honors With Support of Hospital Mentor

Medical students at the University of Pennsylvania must complete a scholarly pursuit, a period of time prior to graduating medical school in which they conduct research with a faculty mentor and prepare a research paper. One such student, Jennifer Handzel, M.D., was recently recognized for her research titled "What Happens to Inner-City Youth Between Ages 8-19: Perceptions and Intentions vs. Reality?"

Dr. Handzel's research, conducted in collaboration with her research mentor, Hallam Hurt, M.D., Division of Neonatology, looked at factors associated with trajectory altering events (TAEs) — substance use, teen parenthood, school failure, and entering a juvenile system — in teenagers of low socioeconomic status between the ages of 16 and 19. The study team, who followed study participants from birth, looked at the relationship between TAEs and two sets of data: the teens' self-described intentions for the future at 8 to 10 years of age and information from the teens' early childhood.

The research showed that there was no correlation between the teens' intentions for the future and TAEs. Childhood environmental factors, specifically exposure to violence at age 7 and poor home environment at age 5.5, were the variables most significantly associated with a participant experiencing a TAE as a teenager.

Dr. Handzel was awarded the Young Investigator Trainee Award for her presentation of this research at the 2009 Eastern Society for Pediatric Research Annual Meeting. She was also one of three presenters to win an award at the College of Physicians of Philadelphia Annual Public Health Poster Session; this prize gave Dr. Handzel the opportunity to spend a day shadowing a Philadelphia Public Health official.

"This story exemplifies how integrating a young investigator, representing both Penn and CHOP, into research provided an opportunity that took her not only to academic presentations but also to an important forum for public health in our city," says Dr. Hurt.

Dr. Handzel is currently a pediatric resident at Children's Hospital and plans to publish these findings and continue research looking at the effects of poverty on inner-city children as they transition into adulthood.

"Almost daily, I see first-hand the effects that poverty has on our inner-city children," says Dr. Handzel. "As a first year resident, I am still not entirely sure which area of pediatrics I will eventually pursue; however, I do expect to incorporate research as a component of my future career."

New Research Policy Web Page Announced

Research Administration has announced the launch of its new Research Policies Library page. This page is located on the Research Institute's intranet site and has its own "Policies" tab in the intranet's tab-based navigation.

You may access this page from the main CHOP Research intranet (the 5th tab from the left) or you can access it directly from the link below.

Policies are organized by activity and some policies are reflected in more than one area. It is important to note that the this page serves as a portal and official link to the area of the intranet where the policies are maintained. We will be adding new policies to the Research Policies Library as they are written and approved.

The policy page is located at: https://intranet.research.chop.edu/display/rpl/Home.

Evaluation of New Research and Training Portal Announced

Children's Hospital has the opportunity to evaluate the new OpenHelix search and training portal at www.openhelix.com. OpenHelix offers tutorial suites (online tutorials and training materials) on a large number of bioinformatics and genomics resources available on the Web. OpenHelix also provides a search capability to find the right resource and training materials for your needs.

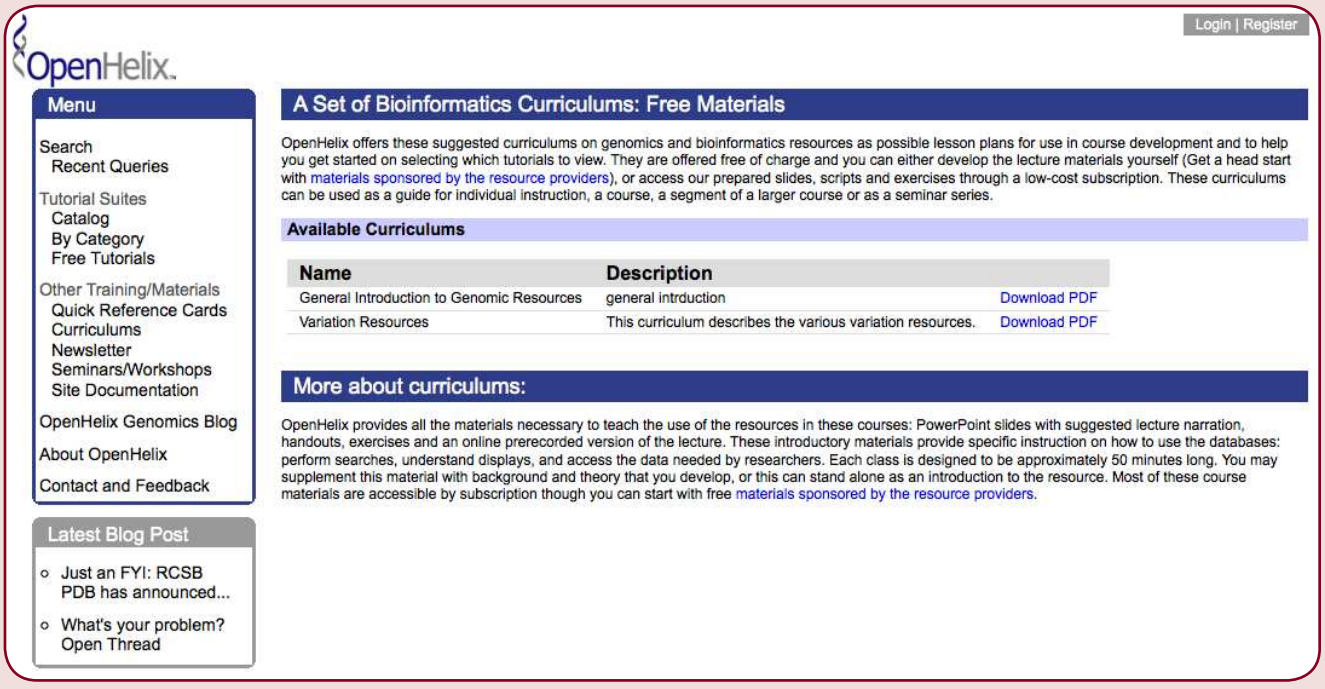
The online, narrated tutorials, which run in just about any browser, can be viewed from beginning to end or navigated using chapters and forward and backward sliders. The 30-to-60-minute tutorials highlight and explain all the features and functionality needed to start using the resource effectively. The tutorials also include a "movie," which walks the user through a sample exercise while the narrator explains and completes each step. You can use the tutorial to introduce yourself to a new resource, to view new features and functionality, or simply as a reference tool to refresh your memory of the resource.

In addition to the tutorials, you can also access training materials including the animated PowerPoint slides used as a basis for the tutorial, suggested scripts for the slides, slide handouts, and exercises, which can be used to create classroom content.

OpenHelix is asking is that you use the site, and occasionally fill out a very brief online survey about your experience.

Visit www.openhelix.com, register using the link to the top right, confirm your e-mail address, and you will have access to all the features and functions of their site. The site will recognize you as a evaluation subscriber through your CHOP IP address. If you have any difficulty or have questions and comments, contact Scott Lathe at slathe@openhelix.com or 425-401-1400.

Please note that access to OpenHelix at this time is for evaluation purposes only. Access should not be given to anyone outside of Children's Hospital or the University of Pennsylvania and all materials that have been downloaded will need to be deleted at the end of the trial period on April 14, 2010.



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

Read this and previous versions of *Bench to Bedside* 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

Produced by The Children's Hospital of Philadelphia Research Institute.