In the largest, most comprehensive genetic analysis of childhood-onset inflammatory bowel disease (IBD), an international research team has identified five new gene regions, including one involved in a biological pathway that helps drive the painful inflammation of the digestive tract that characterizes the disease.

A research team led by Hakon Hakonarson, M.D., Ph.D., director of the Center for Applied Genomics, says the findings advance the scientific understanding of how IBD develops. The study appeared recently in *Nature Genetics*.

IBD is a painful, chronic inflammation of the gastrointestinal tract, affecting about 2 million children and adults in the United States. Of that number, about half suffer from Crohn's disease, which can affect any part of the gastrointestinal tract, and half have ulcerative colitis, which is limited to the large intestine.

Most gene analyses of IBD have focused on adult-onset disease, but the Center for Applied Genomics — one of the world’s largest pediatric genotyping programs — has concentrated on childhood-onset IBD, which tends to be more severe than adult-onset disease. The investigators performed a genome-wide association study on DNA from more than 3,400 children and adolescents with IBD, plus nearly 12,000 genetically matched control subjects, all recruited through international collaborations in North America and Europe.

In a genome-wide association study, automated genotyping tools scan the entire human genome seeking gene variants that contribute to disease risk.

The study team identified five new gene regions that raise the risk of early-onset IBD, on chromosomes 16, 22, 10, 2, and 19. The most significant finding was at chromosome locus 16p11, which contains the *IL27* gene that carries the code for a cytokine, or signaling protein, also called IL27.

“This cytokine acts on a biological pathway, the T-helper 17 pathway, which plays a key role in causing intestinal inflammation,” says Dr. Hakonarson. T-helper 17 cells, which were recently discovered, lead to severe inflammation and tissue injury in autoimmune diseases like IBD.

“There are many cytokines in our immune system, but our research strongly suggests that IL27 has a primary causative role in IBD,” adds Hakonarson. “This gene discovery makes sense in terms of our functional understanding of the disease.”

Some current IBD drugs are monoclonal antibodies that act on another cytokine, called tumor necrosis factor, which contributes to inflammation. Although much research remains to be done, the current study may provide a basis for developing drugs that target the cytokine IL27’s action in patients with the disease-causing *IL27* gene variant.

One strength of the current study, in addition to its large sample size, is the collaboration of many leading pediatric IBD research programs. In addition to The Children’s Hospital of Philadelphia, other centers with principal investigators who played key roles were the Hospital for Sick Children of the University of Toronto; the University of Edinburgh, UK; Cedars Sinai Medical Center, Los Angeles; Emory University, Atlanta; and the IRCCS-CSS Hospital, S. Giovanni Rotondo, Italy.

Children’s Hospital supported this research, along with the Primary Children’s Medical Center Foundation and grants from the National Center for Research Resources, a member of the National Institutes of Health. The researchers used data provided by the International HapMap Consortium and the Wellcome Trust Case Control Consortium.
A leading scientist at CHOP Research, Peter C. Adamson, M.D., has been selected to lead the Children's Oncology Group (COG) in their international efforts to find cures for children with cancer.

Dr. Adamson, an internationally recognized leader in pediatric cancer drug development, was elected to serve a 5-year term as the chairman of COG. He was selected by a nominating committee as one of two final candidates, and then elected by principal investigators of more than 200 COG sites. COG unites more than 5,000 experts in childhood cancer at leading children’s hospitals, universities, and cancer centers across North America, Australia, New Zealand, and Europe in the fight against childhood cancer.

Dr. Adamson’s previous roles at COG have included leading a 21-site phase 1 consortium that conducted initial evaluations of drugs being developed to treat cancer in children. During the eight years that Dr. Adamson led this effort, the collaborating sites conducted more than 25 studies designed to test the safety of novel anticancer drugs.

His experiences working with investigators from multiple disease areas and industry partners through his involvement with COG, his own research efforts, and his membership on key advisory committees for the National Cancer Institute, give Dr. Adamson a unique perspective on the nationwide challenges facing the cancer clinical trial system.

“Scientific discovery today is occurring at an unprecedented pace, but the clinical trial system that historically worked so well is showing a diminishing rate of return in our ability to cure children,” says Dr. Adamson. “This system was not designed to rapidly bring findings from the bench to the bedside, and a transformation of the system’s approach is needed to propel translational efforts on an international scale.”

COG is the preeminent collaborative research organization and was the first group to recognize the importance of collaboration in pediatric research, as even common childhood cancers are rare enough that no one center treats the number of children required for large-scale clinical trials. COG’s unparalleled collaborative efforts provide the information and support needed to answer important clinical questions in the fight against cancer. Today, more than 90 percent of the 12,500 children diagnosed with cancer each year in the United States are treated at COG institutions, with Children’s Hospital being one of the largest such centers in the world.

During his term as chair of COG, Dr. Adamson hopes to increase the collaborative efforts needed to create therapies for cancer that are more effective than existing treatment options. Emerging research shows that even the more common childhood cancers are actually a mix of different diseases, each potentially requiring a different specific therapy. Creating such disease-targeted therapies for children with cancer requires a better pathway for moving from the bench to the bedside, which Dr. Adamson will lead through expanding COG’s role at Children’s Hospital and fostering new and enhanced collaborations with COG sites throughout the world.

“We are proud of this research discovery, and are glad to see it receive this recognition,” says Philip R. Johnson, M.D., chief scientific officer at The Children’s Hospital of Philadelphia Research Institute. “It provides a starting point for translating biological knowledge into future autism treatments.”

The autism gene research, which included two studies in the same issue of Nature, received extensive news coverage, including the CBS Evening News, ABC World News Tonight, BBC, Reuters, the Chicago Tribune, the Philadelphia Inquirer, and other news outlets in the U.K., India, Australia, Germany, and China. Dr. Hakonarson’s main collaborator was neuroscientist Gerard D. Schellenberg, Ph.D., of the University of Pennsylvania School of Medicine, with other scientists participating from 14 additional centers.
**Immunology Expert Receives American Philosophical Society Prize for Patient-Oriented Research**

Immunologist Jordan S. Orange, M.D., Ph.D., has received a prestigious annual award for his contributions to research and treatment of inherited immune deficiency diseases. Dr. Orange received the Judson Daland Prize for Clinical Investigation on Nov. 13 from the American Philosophical Society, an organization founded in 1743 by Benjamin Franklin.

The Judson Daland Prize recognizes outstanding achievements in patient-oriented research. Honorees are nominated by chairs of clinical departments at U.S. medical schools or hospitals and selected by a distinguished committee of biomedical researchers.

Dr. Orange's work involves the innate immune system, the body's first defense against life-threatening infections and diseases. His particular research focus is natural killer cells, a major component of the innate immune system, which have an inherent ability to destroy cancer or virus-infected cells. While in graduate school at Brown University, he discovered that natural killer cells produce cytokines, secreted immune signaling molecules that participate in defending the body against viruses.

Dr. Orange has continued his research in natural killer cells as a pediatrician and is defining the field of human diseases caused by inherent deficiencies of natural killer cells, including diseases in which only natural killer cells, or both natural killer cells and other components of immunity, are defective.

One example is Wiskott-Aldrich syndrome, a difficult to treat, life-threatening, immune-deficiency disease. Dr. Orange discovered a natural killer cell defect and its mechanism in this disease, which make patients especially vulnerable to herpesvirus infections and blood cell cancers. He used this knowledge to develop a novel therapy that bypasses the cellular defect, and has begun a unique clinical trial of the treatment at Children’s Hospital.

In addition to his laboratory research at Children’s Hospital, Dr. Orange evaluates and cares for children with primary immunodeficiency diseases, a varied and complex group of disorders resulting from a congenital defect in a component of the immune system. Though it results in recurrent or severe infections, the child’s underlying disease may go undiscovered for years until he or she receives an accurate diagnosis and appropriate treatment. Establishing an accurate diagnosis and providing therapy can dramatically improve outcome in these diseases and often provides a child with a relatively normal childhood and adult life.

Dr. Orange received the Daland Prize, including a $10,000 honorarium, during an award presentation on Nov. 13 at the American Philosophical Society's headquarters in center city Philadelphia. The prize commemorates Judson Daland, a prominent Philadelphia physician and medical researcher, who left a bequest to the society to support clinical research. As part of that fund, the society has awarded Judson Daland Fellowships since 1938, and established the annual prize in 2001.

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**Heart Function Improvements Using Drug for Erectile Dysfunction, Pulmonary Hypertension**

Heart function significantly improved in children and young adults with single ventricle congenital heart disease who have had the Fontan operation following treatment with sildenafil, a drug used to treat erectile dysfunction and pulmonary hypertension, according to a recent study at Children's Hospital.

Single ventricle defects are a collection of cardiac malformations that impair the heart’s ability to pump blood. Examples include tricuspid atresia, pulmonary atresia/intact ventricular septum, and hypoplastic left heart syndrome.

The Fontan operation redirects systemic venous blood directly to the pulmonary arteries, bypassing the heart. It is the third surgery in a staged palliation for single ventricle heart defects.

Investigators hypothesized that sildenafil may help cardiac performance by directly improving the squeeze of the heart muscle and by allowing for better filling of the heart.

In this study, the investigators randomized 28 children and young adults who had undergone the Fontan operation to receive placebo or sildenafil 3 times a day for 6 weeks. After a 6-week break, they were switched to the opposite treatment course. The investigators found significant improvement in heart performance during treatment with sildenafil.

“The enhanced heart performance may improve exercise performance and quality of life in these children and young adults,” says David J. Goldberg, M.D., a pediatric cardiologist at Children’s Hospital who presented an abstract on these findings at the American Heart Association Scientific Sessions in Orlando, Fla.

Grants from The Mark H. and Blanche M. Harrington Foundation and from Big Hearts to Little Hearts provided funding for this study.
The Hospital has unveiled a new social media program that supports several enterprise-level Facebook and Twitter sites, including Research Institute sites on Twitter and Facebook that were launched in September as part of a pilot social media program.

Social media can offer a powerful set of technologies to facilitate the practice of research in many ways. CHOP Research is taking positive steps to support the use of social media in research efforts at the Hospital, and to stimulate thought as to how social media can be effectively used for conducting, promoting, and sharing results of our research efforts.


Under the Hospital-wide program, employees are expected to have full onsite access to Facebook and Twitter in March 2010, with access to additional technologies expected later. Access to social media will further engage and connect our employees to one another and to colleagues at other institutions, spur greater collaboration, and effectively and efficiently disseminate valuable updates on our programs and investigators.

Our principal investigators and organizational leaders are the best source of information about how to use social media most effectively for specific research domains and we encourage those ideas to take shape.

Those who would like to use social media to further their own research and to maximize the value of this new opportunity will have access to a Research Social Media Support Group starting in January 2010. This group consists primarily of Research Communications, the Center for Biomedical Informatics (CBMI), and the Research Institute Web Services Team. Members of these groups, particularly Research Communications Director Jennifer Long and CBMI’s Pete White and Mark Porter, have been instrumental in leading the effort to move social media for research forward.

The Research Social Media Support Group will be available to conduct consultations with investigators and organizational leaders, with the ultimate goal of supporting viable social media venues.

The support group will provide the following services for owners of social media instances:

- Consult with investigators on development and maintenance
- Assist in building sites
- Provide technical support
- Market social media instances
- Maintain a central registry of Research Institute social media instances
- Assist in triaging responses to inappropriate posts or comments
- Help navigate compliance, ethical, and business issues
- Serve as an advocate of research social media issues within the Hospital Social Media Task Force

The support group has also provided a variety of resources on the intranet at https://intranet.research.chop.edu/display/SMT/Home.

Questions about research-related social media program should be directed to Jennifer Long, director of Research Communications, at longj@email.chop.edu. Stay tuned for more details about social media and the Research Social Media Support Group.
Patenting an invention is a lengthy and complex process. From start to finish, many factors must be considered, including the impact of prior art on the patentability of the discovery and identification of the correct inventive entity. In addition, the process involves drafting a fully detailed patent specification about the claims, the commercial potential of the invention, and the costs associated with the pursuit of patent protection both domestically and globally.

A special patent seminar hosted by the Office of Technology Transfer will address these and other issues on Jan. 5 from 10:30 a.m. to noon in Abramson Research Center, Room 123 ABC.

The seminar will feature Kate Rigaut, Ph.D., J.D., a partner and shareholder at the intellectual property law firm of Dann, Dorfman, Herrell and Skillman. Dr. Rigaut will outline the patent process and discuss each aspect of patent prosecution and enforcement. A question and answer period will follow the presentation.

Dr. Rigaut has experience in preparing freedom-to-operate opinions; analysis and resolution of inventorship disputes; patentability opinions; interference proceedings; and reexamination, patent prosecution, amendments, and responses to United States Patent and Trademark Office Official Actions on a variety of subjects including cancer genes, transgenic plants, RNA viruses, monoclonal antibodies, genetic alterations associated with disease, antisense technologies, and compositions involved in anti-inflammatory and anti-cancer responses.

Questions about the seminar may be directed to Technology Transfer Director Ellen Purpus, Ph.D., at purpus@email.chop.edu or Business Manager Jacquie Saporito at saporito@email.chop.edu.

**Patent Seminar Scheduled for Jan. 5**

Anne Kazak, Ph.D., Division of Oncology, has been selected to serve as the next editor of *Health Psychology*, a journal dedicated to furthering the understanding of the scientific relationship among psychological factors, behavior, and physical health and illness.

Dr. Kazak, who previously served as the editor of the Journal of Family Psychology from 2004 to 2009 and of the Journal of Pediatric Psychology from 1998 to 2003, will serve a six-year term as editor of *Health Psychology* beginning in July 2010. Pediatric research has historically been underrepresented in *Health Psychology*; Dr. Kazak is focused on encouraging pediatric submissions during her term.

*Health Psychology*, the scholarly journal of the American Psychological Association, is highly ranked among clinical psychology journals and has one of the highest Impact Factors among all psychology journals. The journal accepts original research with significant theoretical or practical importance and the potential to make an impact on current practices or policies.

**CHOP Research Investigator Named Editor of Leading Psychology Journal**

All principal investigators (PIs) on an Institutional Review Board or Institutional Animal Care and Use Committee protocol and investigators who have primary responsibility for a research grant, clinical trial, cooperative agreement, contract, or other internally or externally sponsored research agreement are required to complete PI Training, a brief review of essential information related to the regulatory environment in which sponsored projects are conducted.

Investigators must complete this training by Dec. 31. Beginning in January 2010, activation of new award accounts may be delayed if this requirement has not been met.

PI Training may be completed through an online module, via podcast, during an in-person session, or by printing and reviewing a manual. Please visit the Office of Responsible Research Training intranet site at [https://intranet.research.chop.edu/display/deptrtt/PI+Training](https://intranet.research.chop.edu/display/deptrtt/PI+Training) to access the training.

Questions may be directed to researchtraining@email.chop.edu.