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# NIEHS Spotlight

## Institute Honors Employee Achievements

*By Eddy Ball*

On the afternoon of December 14, NIEHS honored employee achievements at the 2006 Director's Annual Honor Awards Ceremony in Rodbell Auditorium. Director David A. Schwartz, M.D., addressed an unusually well-dressed audience of Honor Award Winners and colleagues. Along with other NIEHS leaders, Schwartz presented award plaques and cash prizes to scores of people whose individual and group efforts had helped NIEHS move forward and enjoy a highly successful year.

"This is really a time for us to celebrate our joint accomplishments and also our individual accomplishments," Schwartz told the audience. "I just want to tell you, as director of the Institute, how proud I am to lead the Institute and how thankful I am for the support that all of you have provided."

The NIH Merit Awards recognized individual and group accomplishments in the Office of the Director (OD), Office of Management (OM), Division of Extramural Research and Training (DERT) and Division of Intramural Research (DIR). In addition, employees won awards for collaborative efforts across divisions, accomplishments as unsung heroes and on the basis of peer nominations.



*Schwartz was joined on stage by (from left) Director of Clinical Research Perry Blackshear, M.D., Acting DERT Director Dennis Lang, Ph.D., Associate Director for Management Marc Hollander and Deputy Director Samuel Wilson, M.D. (Photo courtesy of Steve McCaw)*



*News Director Robin Mackar, shown with Schwartz, was the first recipient honored at the ceremony. (Photo courtesy of Steve McCaw)*

Thirteen post-doctoral fellows won stipends of \$1,000 each for professional development as part of the Fellows Award for Research Excellence (FARE) Awards, and a special category honored employees with the 2006 DHHS Secretary's Award for Distinguished Service for dedicated support for the health and safety of victims of Hurricanes Katrina and Rita along the Gulf Coast. Closing out the ceremony were the NIH Director's Award and awards to 17 employees for 30 years of Service Recognition.

OM Analyst Diane Crawford organized the annual event.

### **OD: NIH Director's Award Winners**

Individuals: Robin M. Mackar, Brenda Weiss, Ph.D., Sheila Newton, Ph.D., Davenport Robertson, M.S.L.S., Allen Dearry, Ph.D., Larry Wright, Ph.D., M.S.L.S., and Angie Sanders.

Collaborative Effort Across Divisions: Marc. S. Hollander, Allen Dearry, Ph.D., Steve Akiyama, Ph.D., Richard A. Freed, Nancy Stegman, Joseph Hughes and Mary Wolfe, Ph.D.

## **OM: NIH Director's Award Winners**

Individuals: Clarence Gibson, Dick Sloan and Rich Freed.

Groups: Scott Merkle, Christopher Hunt, Jr, Diane Crawford, William Fitzgerald, Deloris Anderson and Valeria Shropshire; Kimberly S. Peterson, Mitsue M. Parrish and Kathryn W. Woods; Mary E. Butts, Vicki T. Grigston, Laurie K. Johnson, Vanessa R. Knight and Susan H. Hart.

Collaborative Effort Across Divisions Richard A. Freed, Ellen Moul, Michael Spencer, Charletta Fowler, Margarita Roque, Bruce Wiggins, Stephanie A. Jones and Connie C. Riley.

## **DETR: NIH Director's Award Winners**

Individuals: Cindy P. Lawler, Ph.D.

Groups: Anne Sassaman, Ph.D., Dennis Lang, Ph.D., Janice Allen, Ph.D., Carol Shreffler, Ph.D., and J. Patrick Mastin, Ph.D.; Kimberly McAllister, Ph.D., Janice Allen, Ph.D., Jerry Phelps, Cindy Lawler, Ph.D., Kimberly Gray, Ph.D., David Balshaw, Ph.D., Jerry Heindel, Ph.D., and Claudia Thompson, Ph.D.; Elizabeth McNair and Michelle Owens.

## **DIR: NIH Director's Award Winners**

Individuals: Deborah McCarley; Lisa F. Rogers; Michael D. Shelby, Ph.D.

Groups: Mike Tyson, Roy Reter and John Grovenstein; Kristine Witt, Ph.D., Raymond Tice, Ph.D., and Cynthia Smith, Ph.D.

Collaborative Effort Across Divisions: Michael Humble, Ph.D., Liam O'Fallon, Paivi Salo, Ph.D., and Patricia Chulada, Ph.D.



*Schwartz recognized Patricia Chulada, Ph.D., Paivi Salo, Ph.D., Liam O'Fallon and Michael Humble, Ph.D., for their successful Discovery Channel show on mold and the environment. (Photo courtesy of Steve McCaw)*

## **Unsung Heroes**

Bonnie Allen, Leona Maghan and Denise Lasko

## **PEER Awards**

Ronnie L. Dunn, Leesa Deterding, Ph.D.,  
Christine Alston and Lars C. Pedersen, Ph.D.

## **DHHS Secretary's Award for Distinguished Service**

Samuel Arbes, Ph.D., Gwen Collman, Ph.D., Diane Forsythe, D.V.M., Mary Grant, D.V.M., Angie Sanders, William Stokes, D.V.M., Claudia Thompson, Ph.D., Samuel Wilson, M.D., Beth Anderson, Allen Dearry, Ph.D., Richard Freed, Joseph Hughes, Stella Sieber, William Suk, Ph.D., Brenda Weis, Ph.D., and Mary Wolfe, Ph.D.

## FARE Awards

Sayura Aoyagi, Ph.D., Mercedes E. Arana, Ph.D., Jeffrey W. Card, Ph.D., Miguel Garcia-Diaz, Ph.D., Yu-Ying He, Ph.D., Kellen L. Meadows, Ph.D., Anita J. Reddy, Ph.D., Kathleen A. Smoak, Ph.D., Yuan Wang, Ph.D., Sufen Yang, Ph.D., Bryan L. Betz, Ph.D., Michelle L. Block, Ph.D., Shannon L. Dallas, Ph.D., Deborah A. Greer, Ph.D., Shannon F. Holmes, Ph.D., Zachary F. Pursell, Ph.D., Tina M. Saldana, Ph.D., Krisztian Stadler, Ph.D., Zongli Xu, Ph.D., and Eda Yildirim, Ph.D.



*Schwartz presented 13 post-doctoral fellows with cash awards and recognition for research excellence. (Photo courtesy of Steve McCaw)*

## NIH Director's Award

Connie Riley – Administrative  
Thomas Kunkel, Ph.D. - Scientific/Medical  
William Copeland, Ph.D. – Mentoring

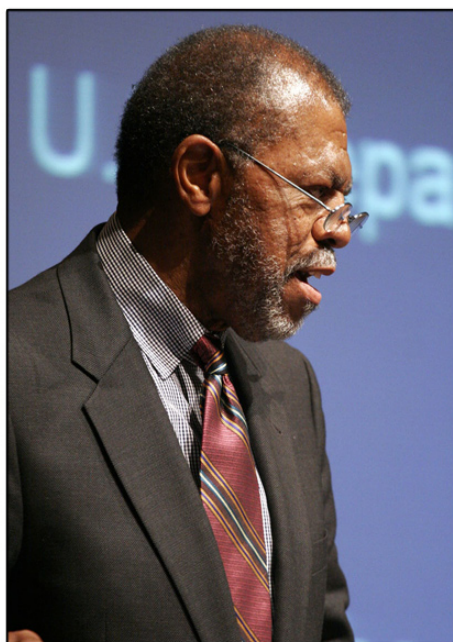
## 30 years of Service Recognition

Mary Alexander, Barbara Burkhart, Ph.D., James Dix, Donald Gula, Susan Johnson, Charle League, Leroy Long, Denise Orzech, John Pritchard, Ph.D., Colleen Anna, William Caspary, Ph.D., Beth Gladen, Ph.D., Laurie Johnson, Kenneth Korach, Ph.D., Edward Lebetkin, Scott Merkle, John Peterson, Jr.

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## NCT Pioneers Pay Tribute to Ray Tennant

*By Eddy Ball*



*Olden was the keynote speaker at the symposium. (Photo courtesy of Steve McCaw)*

On December 4, NIEHS opened the three-day Empowering Environmental Health Sciences Conference with a tribute to the accomplishments the former director of the [National Center for Toxicogenomics](#) (NCT), Ray Tennant, Ph.D. Moderated by Senior Scientist Richard Paules, Ph.D., the half-day symposium featured an introduction by NIEHS Deputy Director Sam Wilson, M.D., and concluded with a presentation by former NIEHS Director and current Senior Investigator Ken Olden, Ph.D.

As the NCT was being conceived in 2000, Wilson and Olden asked Tennant to serve as director. It was “a time when the conceptualization of how to operate the National Center of Toxicogenomics had not yet occurred,” Wilson explained. Unlike existing programs at the Institute, “the new center was envisioned as a blend of the Intramural and Extramural community at NIEHS.”

The Institute needed to deal with deeply ingrained conceptions about the responsibilities and management structures of the two well-differentiated divisions. What Wilson described as Tennant’s “huge challenge” involved

getting the divisions to collaborate effectively in launching the new science that became known as toxicogenomics — blending Intramural research/development and the Extramural community into a combined effort to move environmental science beyond classical toxicology.

One of the first major hurdles Tennant and NCT faced was setting program goals and creating a new series of definitions for a new lexicon, including the essential definition for the word “toxicogenomics.” In conjunction with program goals, the definition of this central term tied together the new laboratory technologies with the research agenda, the computational and database products, and the translational outcomes envisioned for the research.

An essential component of this research agenda was the creation of the Toxicogenomics Research Consortium (TRC) and the establishment of the collaborative partnership between the NCT and TRC. The consortium centers included Duke University, the University of North Carolina at Chapel Hill, the Fred Hutchinson Cancer Research Center at the University of Washington, Oregon Health and Science University (OHSU), and the Massachusetts Institute of Technology. Researchers at these centers would perform toxicogenomic research using microarray and “omics” or global applications as well as standardize platforms and develop best practices for laboratory investigations and study design. As a result of their aggressive research agenda, TRC investigators have published 142 articles in peer-reviewed journals with an average impact rating of 6.7 — a rating higher than many of the most widely read scientific journals.

Olden concluded the symposium with a presentation titled “The Promise of Genomics for Environmental Health: The Integration of Genetic Data into Toxicology.” Olden framed his talk as a rebuttal to a 2005 *Harvard Environmental Law Review* article, [“The False Promise of the Genomics Revolution for Environmental Law”](#) by University of Arizona law professor David E. Adelman. In his talk, Olden underscored the importance of the interaction of genetics and environment in disease pathogenesis and expressed his faith that researchers will overcome the technological difficulties in toxicogenomic research more easily than Adelman contends.



*Symposium Moderator Paules (Photo courtesy of Steve McCaw)*



*Symposium presenters and organizers gathered following the tribute to Tennant. From left, Olden, Weida Tong, Ph.D., Wilson, Tennant, Cindy Afshari, Ph.D., Peter Spencer, Ph.D., Bill Suk, Ph.D., Paules and David Balshaw, Ph.D. (Photo courtesy of Steve McCaw)*

Despite his strong misgivings about Adelman’s argument, Olden pointed to a key statement in the article’s conclusion about the influence of toxicogenomics. It is a statement, Olden observed, that would never have been possible without Tennant’s leadership at NCT. “The Environmental Genome Project is the first high-profile scientific initiative in environmental toxicology to receive broad stakeholder and government backing since the transformation of environmental law in 1970s,” Adelman wrote. “Federal support for toxicogenomics research represents a unique opportunity for environmental toxicology to benefit from a major infusion of resources.”

Following Olden’s presentation, Tennant addressed the symposium for the first time. He thanked the speakers and added a characteristically modest assessment of his own

role in NCT accomplishments. “I just want to say that I am touched and moved by all of the kind comments that all the speakers have made,” Tennant said. “But I do need to set the record straight. The accomplishments of the NCT were in fact because of the work of so many fine people, many of whom are represented here in the audience. They’re the ones who really accomplished what you’ve given me credit for.”

## Defining “Toxicogenomics”

Environmental toxicogenomics allows researchers to identify and characterize genomic signatures of environmental toxicants as gene and protein expression profiles. A major application of gene expression profiling is to understand human genetic variability and susceptibility to disease.

### Program Goals

- To facilitate the application of gene and protein expression technology
- To understand the relationship between environmental exposures and human disease susceptibility
- To identify useful biomarkers of disease and exposure to toxic substances
- To improve computational methods for understanding the biological consequences of exposure and responses to exposure
- To create a public database of environmental effects of toxic substances in biological systems

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## Portier Honored by World Innovation Foundation

*By Eddy Ball*

The [World Innovation Foundation](#) (WIF) has announced the appointment of NIEHS Associate Director Christopher Portier, Ph.D., to its prestigious group of members and fellows. According to the organization, “Membership in the World Innovation Foundation is now becoming considered in many parts of the world...[as] recognition of being a major global innovator of the highest order.”

With his appointment, Portier joins a distinguished international group of intellectuals who are leaders in their respective fields. The members include a number of Nobel laureates, heads of international organizations and inventors. WIF invites into its membership individuals who have profoundly influenced the development of research and made innovative applications in their fields. The foundation honored Portier for his contributions to environmental medicine and the development of cutting-edge toxicological risk assessment.



*World Initiative Foundation Member Chris Portier  
(Photo courtesy of Steve McCaw)*

Portier has been with NIEHS since 1979, when he came to the Institute as a doctoral student. He is currently the director of the Office of Risk Assessment Research and the principal investigator with the Environmental Systems Biology Group. He also is serving temporarily as scientific advisor to the director, Public Health and the Environment, World Health Organization. From 2001 to 2005, Portier was associate director of the interagency National Toxicology Program (NTP), and he was the moving force behind the development of the NTP “Roadmap,” which was released in 2005 as part of the NTP 25th Anniversary Celebration in Washington, D.C.

When the Institute appointed him as director of the Office of Risk Assessment Research, NIEHS Director David A. Schwartz, M.D., praised Portier’s accomplishments as the leader of the NTP. “Dr. Portier has done an extraordinary job in overseeing the activities of the National Toxicology Program, and has developed strong relationships with scientists all over the world,” Schwartz observed. “This new NIEHS leadership role will allow him an opportunity to merge the fields of toxicology and environmental health sciences and prepare the world for tomorrow’s health challenges.”

WIF describes itself as “the only fully ‘independent’ scientific, technological, engineering and applied economic ‘think-tank’ in the world today. The WIF has no direct financial ties to any governments or corporate entities. It is therefore a free-thinking group of the world’s foremost creative minds.” WIF honorary members and fellows collaborate in consultations for the benefit and enlightenment of peace-abiding governments and nations throughout the world. The foundation aims to foster peace on the planet by promoting health, economic development and scientific progress for all.

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## OEO’s Kathy Odenwald Retires to a “Life without Musts”

*By Eddy Ball*

On December 15, Kathy Odenwald’s many friends and colleagues celebrated her 23-year career in federal service and her retirement from her position as liaison of the Office of Equal Opportunity and Diversity Management. After 11 years of being someone her NIEHS colleagues and clients could always depend on and compiling an impressive list of career accomplishments, Odenwald looks forward to January 2007 when she will start a completely new phase in her life.

Odenwald has plans to travel to see her family in her native Taiwan and her children on the east and west coasts, but otherwise life after retirement will be truly open-ended. “I’ve loved my job, but now I just want a chance to do whatever I feel like doing,” she explained. “I want my new life to be a ‘life without musts.’” After a seamless transition/reorganization over the past two years, the program has found its direction under Odenwald, and she feels “that now is the time for me to go and play.”

After completing her master’s degree in human relations from the University of Northern Colorado, Odenwald entered federal service in 1983 as a GS-9 Equal Employment Opportunity Manager for a small military community in Germany. As an immigrant who had struggled herself with new languages and cultural



*Odenwald has been practicing for her new life without obligations. (Photo courtesy of Kathy Odenwald)*



*Odenwald welcomed guests to the OEO office for her retirement reception. (Photo courtesy of Steve McCaw)*

conventions, she knew how it felt to be outside of the mainstream, often misunderstood and unsure about what people in different cultures expected of her.

Her experiences helped her empathize with the needs of people in similar situations. In this spirit, Odenwald and her colleagues developed a distinctly NIEHS kind of program that has been consistently successful in meeting the needs of the Institute’s employees with educational opportunities, such as the recent seminar on “Impressionism,” specialized training, cultural awareness for post doctoral fellows, scientific seminars and cultural activities.

When Odenwald oversaw the establishment of the NIEHS Diversity Council in 1998, she was committed to having the council reflect the same ratio of ethnicity, pay grades, occupational fields and gender as the workforce as a whole. Rather than making the council an insulated group with special interest agendas, Odenwald wanted the members to experience the spirit of inclusiveness every time they met and in every event they organized.

Odenwald’s strengths as a leader included her abiding respect for employees and her emphasis on working for change by emphasizing the positive over the adversarial. As an OEO professional, she is highly trained and competent in helping clients understand the complaint and grievance processes when necessary to get fair treatment. But her greater love is educating people, helping them to understand their similarities and differences, as well as learn to value the unique experiences and qualities of their colleagues.

Characteristically modest and admittedly low-key, Odenwald attributes the success and quality of the OEO/ Diversity program at NIEHS to the institute’s geographical distance from Bethesda and the level of support she has enjoyed from upper management. “Our events are probably the best attended of all the ones at NIH,” she noted, “and they also attract a healthy mix of people — not just ones from the group the event is celebrating.”

People who have worked with Odenwald know that geography and management support alone cannot fully explain the program’s successes. “Kathy has a golden touch and a special concern for the cultural diversity of our post docs, who represent some 30 countries,” said colleague EEO Specialist Ginny Ivanoff. “I consider myself very lucky to have had her as a mentor, a colleague and a friend. She has taught all of us a lot about diversity, and we’ll all miss having her there to turn to for support.”

Former Director Ken Olden, Ph.D., shares Ivanoff’s regard for her supervisor. “Kathy was one of the best appointments that I made during my tenure as director,” he said. “Kathy possessed the right combination of professional knowledge, human skills and compassion to emerge as one of the most effective OEO officials in the NIH. I wish Kathy the best of everything and hope to see her often in the years ahead.”

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*Ivanoff watched as Odenwald opened a gift from friends and associates. (Photo courtesy of Steve McCaw)*



# NCT Assistant Director Retires to Work in Private Sector

*By Eddy Ball*

National Center for Toxicogenomics Assistant Director for Database Development Mike Waters, Ph.D., retires from NIEHS on January 1 with 37½ years of service. However, rather than spending his time with hobbies or other interests, Waters will begin another career in private enterprise in research and development with Integrated Laboratory Systems, Inc. Like most of the moves he has made previously in his scientific career, this latest will keep him in Research Triangle Park.

Waters' six-year tenure at NIEHS ended as the Institute prepares for the official release into the public domain of the Chemical Effects in Biological Systems (CEBS) knowledge base. He was instrumental in developing CEBS and released it in collaboration with CEBS Scientific Administrator Jennifer Fostel, Ph.D., and through the combined efforts of contractor staff at Science Applications International Corporation (SAIC), Lockheed-Martin Information Technologies and Alpha-Gamma Technologies, Inc. In 2000, Waters came to NIEHS specifically to lead the development of CEBS. He worked closely with NCT Director Raymond Tennant, Ph.D., Deputy Director James Selkirk, Ph.D., and biologist Stan Stasiewicz, Ph.D., who was the first project officer on the SAIC contract. With Waters' departure, Fostel will work with Laboratory of Respiratory Biology Chief Steve Kleeberger, Ph.D., to manage the anticipated growth of CEBS.

Waters is a native North Carolinian born in Charlotte and educated at nearby Davidson College, where he received his B.S. in pre-medicine. He attended the University of North Carolina at Chapel Hill, where he earned his doctorate in biochemistry in 1969. "I had originally intended to go to med school," Waters said, "but I decided that I really wanted to do research. After a couple of years in zoology, I decided to go into biochemistry, and that's where I got into human cell culture and studies on enzyme regulation and collagen biosynthesis."

After completing his doctorate, Waters served for two years as a captain in the Army Chemical Corps conducting research on accelerating collagen synthesis to improve the rate of wound healing. Once he got back to North Carolina in 1971, he stayed, working 29 years for the newly established Environmental Protection Agency (EPA) before joining NIEHS. He worked at the temporary EPA clinical facility in Chapel Hill in the tissue culture laboratory researching pulmonary toxicology before moving to the new headquarters in RTP. The young biochemist with training and interests in toxicology soon convinced his employer of the need to establish a genetic toxicology division, which EPA then assigned Waters to build from the ground up.

As the genetic toxicology division grew, Waters got in on yet another ground floor opportunity at EPA. He conceived the EPA Gene-Tox Program and the resulting database, now hosted by the National Library of Medicine. He also developed the EPA/International Agency for Research on Cancer (IARC) Genetic Activity Profile Database, which forms the basis for the use of short-term tests in the evaluation of presumptive human carcinogens by the IARC.

With his experience in developing databases and his interest in genetic toxicology, the move to NIEHS in 2000 was another natural step in his career. CEBS is the most challenging database Waters has developed, and the progression from genetic toxicology to toxicogenomics was relatively straightforward. In his new career with



*NCT Assistant Director Mike Waters  
(Photo courtesy of Steve McCaw)*

Integrated Laboratory Systems, Inc., he will be using his planning and management skills in a multidisciplinary research organization to provide comprehensive support to federal and commercial clients.

Although Waters is leaving NIEHS, he plans to continue serving on a number of database and toxicogenomics workgroups and advisory committees. He also intends to continue his work as an adjunct professor at the University of North Carolina at Chapel Hill and at Duke University Medical Center, where he now teaches toxicogenomics. He will continue to be the editor of the journal *Reviews in Mutation Research* and maintain his association with professional groups in his areas of interest.

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## Retired Researcher Refuses to Quit

*By Eddy Ball*

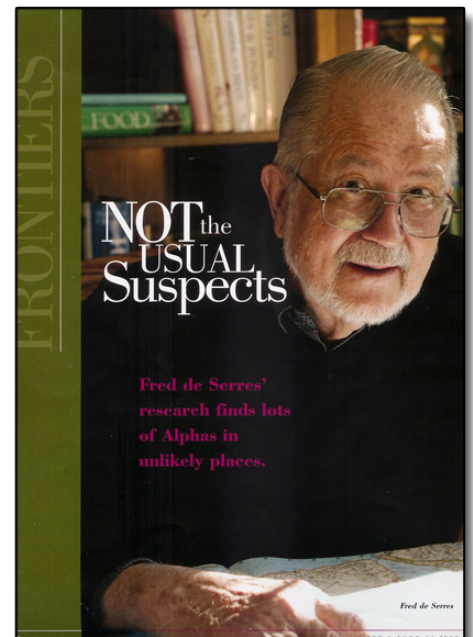
At age 77, long-time NIEHS scientist Fred de Serres, Ph.D., should, as he puts it, “sit and watch movies.” However, the semi-retired researcher has remained inspired by the kind of work he did as associate director of genetics in the Office of the Director at NIEHS from 1979 to 1986 and by his interest in Russian fairy tales and other children’s literature. He is also passionate about setting the medical community straight on a health condition that has had an enormous impact on his life.

In 1997, doctors diagnosed de Serres with a genetic mutation that causes a deficiency in the protease inhibitor alpha-1 antitrypsin (AAT) and makes him more susceptible to respiratory diseases. That diagnosis sparked his crusade to raise awareness of the importance of targeted screening for a condition that was once considered rare. His own diagnosis after so many consultations with some of the region’s most prominent specialists made him wonder, “How many others did they miss?”

For the past nine years, his research has been a quest to answer that question and help physicians learn to ask the right questions about AAT (see the report on de Serres’ AAT Deficiency studies in Science Notebook). “I feel a very strong commitment to the patient community,” de Serres explains, “to make sure others don’t go through what I’ve gone through.”

de Serres is currently a guest researcher at the Center for Evaluation of Risks to Human Reproduction at NIEHS. He began his career in biology at Oak Ridge National Laboratory after completing his doctorate at Yale, where he developed his career-long interest in the interaction between genetics and environment. In the course of his career, he has served on the editorial boards of 11 journals and been the guest editor of several special issues.

de Serres traveled extensively in Asia and Europe in his work with the US-Japan Cooperative Medical Sciences Program, the US-Soviet Environmental Protection Agreement and several international collaborative studies. A prolific author with a long career that predates PubMed, he has over 490 publications in science literature, including articles, book chapters, reviews and conference proceedings.



*de Serres was featured in the Spring 2004 issue of Frontiers, a publication of the Alpha 1 Foundation. (Image courtesy of Frederick de Serres)*

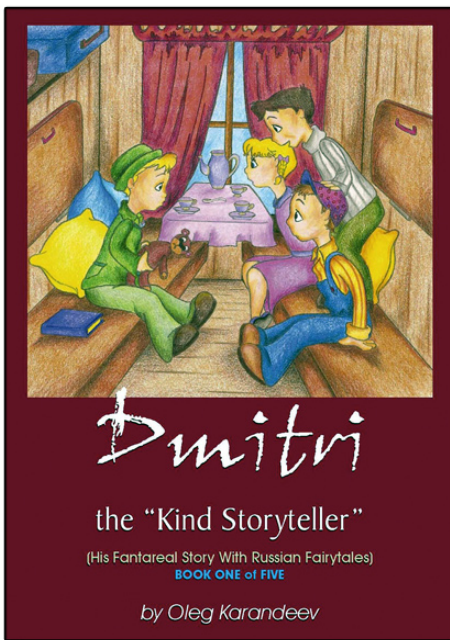
While working in several capacities at NIEHS and elsewhere in the Research Triangle scientific community, de Serres taught in the Department of Pathology at the University of North Carolina at Chapel Hill. He has received many awards in recognition of his accomplishments and has been a member of several professional societies and collaborative study groups, panels and foundations. One of de Serres' recent honors was the Alpha-1 Explorers Award presented by the Alpha-1 Association in 2002 in recognition of his research. He also serves on the Board of Directors of the Alpha-1 Foundation.



*This file photo shows de Serres at work at NIEHS in 1979. (Photo courtesy of NIEHS Photo Archive)*

Unlike many of his colleagues in environmental science, de Serres is also interested in children's literature.

In 2005 and 2006, he served as co-editor of *Dimitri, the "Kind Storyteller"* by Oleg Karandeev. A native of Nizhi Novgorod, Russia, Karandeev writes in both Russian and English, but Entry Way Marketing and Publishing, who issued the book in an American edition, realized that his English was too formal and stilted to appeal to native speakers. That's where de Serres came in.



*de Serres was co-editor of this fairy tale collection. (Graphic courtesy of Frederick de Serres)*

The scientist combined his love of folk lore and fairy tales with his practiced ear for conversational English to produce a far more readable version of the fairy tales.

More recently, de Serres has collaborated with an American writer of children's stories, Christopher Forte, who is a prolific writer of children's stories. His first book, titled *Cookie Island*, is already at the printers, and he has a backlog of over 250 stories that he has written "just for the fun of it."

de Serres would love to retire after he completes the two new AAT studies presently in the works at NIEHS (see related story in Science Notebook) and leave his work to others. He also wants to pursue his lifelong love of photography. In the course of his travels, he has taken over 6000 slides that he hopes to catalogue and digitize.

However, de Serres is a man called to a mission. Even as he talks about the lure of retirement, he suggests it may be that "God [just] doesn't want me to retire."

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# NIEHS Enhances Outreach Efforts to Advocacy Groups

*By Eddy Ball*

In a reorganization of what was previously known as the Public Interest Liaison Group, the Office of Science Policy (OSP) has changed the group's name and expanded communication efforts between NIEHS and a group of advocates for disease, at-risk and environmental organizations. The group is now called the Public Interest Partners Group (Partners) and chaired by [Nsedu Obot-Witherspoon](#), executive director for the Children's Environmental Health Network (CEHN).

In addition to CEHN, partners include representatives from the American Lung Association, Alzheimer's Association, World Wildlife Fund, Parkinson's Action Network, National Breast Cancer Coalition, Environmental Defense, Autism Society of America, West Harlem Environmental Action and other groups concerned with environmental health.

The organizations, together representing thousands of concerned individuals, are truly "partners," according to OSP Director Joyce Martin, J.D. "It's a two-way street," Martin explained. "NIEHS research funding has a direct impact on these groups and their members. We need to learn more about the priorities of these organizations, and they, in turn, need to know what we are doing to address their needs and concerns."

OSP has adopted a "plain English" nomenclature by renaming the organization "Partners," a term that better suggests the two-way communication involved. In addition, NIEHS has expanded the frequency of communication with its Partners. Between annual meetings, the group now meets with NIEHS senior staff about new initiatives via conference calls every four to six weeks.

These initiatives have included the Strategic Plan, the Gene-Environment Initiative and the Children's Environmental Health Research Review. OSP has scheduled the next conference-call meeting for January 25, when senior staff plan to present information about the collaborative Head-off Environmental Asthma in Louisiana (HEAL) study.

Other changes initiated under the leadership of Director David Schwartz, M.D., and implemented by Martin and her OSP staff include adding a Partner representative as a voting member of the National Advisory Environmental Health Sciences Council. Also, Schwartz attends annual meetings, giving him an opportunity to get information and input from the Partners in person.

The most recent meeting took place on November 28 in Washington, D.C., at the American Public Health Association headquarters. Having Schwartz at the meeting helped the Partners feel an even more integral part of the process. As one participant remarked afterwards, "How often do you get to sit ten feet from director of an NIH institute and question him and get his candid thoughts?"

According to OSP Special Assistant John Schelp, another important development is the introduction of regular e-mail distribution to Partners. "We send thorough presentation information prior to conference call meetings," he said. E-mailings also include information about new research and programs.



*OSP Director Joyce Martin  
(Photo courtesy of Steve McCaw)*

Coordinating the Partners is just one of the important responsibilities of OSP. Martin's workgroup provides broad support to the director and other senior NIEHS staff in defining and interpreting the programs and research of the Institute to the Congress, the public, and the scientific and public health communities. OSP further serves as a liaison between Congressional staff, other government agencies and health and science organizations, and various stake holder groups to ensure that NIEHS is accessible and responsive.

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## Science Notebook

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### NIEHS Conference Explores Omics Technologies

*By Eddy Ball*

NIEHS held its Empowering Environmental Health Sciences Research with New Technologies conference December 4-6 at the Friday Center in Chapel Hill. Attendees included NIEHS DIR and DERT scientists associated with the former National Center for Toxicogenomics (NCT) along with grantees working at the five centers that make up the Toxicogenomics Research Consortium and in other research initiatives nationwide.

NIEHS described the event as “A Conference on Omics Applications in the Environmental Health Sciences.” Along with a half-day Symposium in Recognition of the Contributions of Ramond Tennant and the National Center for Toxicogenomics (see related Spotlight story), sessions included reports from participants in the Toxicogenomics Research Consortium (TRC), Functional Proteomics Initiative, and Metabolomics Application Initiative. In addition to 34 presentations, the conference also featured a poster session on the second day that included 27 abstracts.

Several of the presenters focused on the technical aspects of omics approaches. For example, NIEHS Laboratory of Respiratory Biology Staff Scientists Scott Alper, Ph.D., and Ivana Yang reported on the “Genetics of Innate Immunity” in a study utilizing two high-throughput RNA-interference assays developed in their laboratory. UNC Environmental Health Physician-Scientist Ivan Rusyn, M.D., Ph.D., presented the “TRC Standardization Experiment #3 Report,” which focused on the application of microarray analysis to study hepatotoxicity induced by acetaminophen using the power of a prospective multi-laboratory investigation.

Two presenters, Cynthia Afshari, Ph.D., who had helped to develop toxicogenomic assessments for NIEHS before joining the biomedical company Amgen, and Weida Tong, Ph.D., of the Food and Drug Administration



*In his presentation on day two of the conference, Paules reported on research into a genetic screen for toxicity.  
(Photo courtesy of Steve McCaw)*



*Fostel took her audience through sample searches using the CEBS Knowledgebase. (Photo courtesy of Steve McCaw)*

(FDA), spoke on the translational applications of toxicogenomic research in drug development and regulation. Of primary concern to Afshari is the pharmaceutical industry's ability to predict toxicological response early in the clinical trial process in order to expedite drug development and minimize expense. Tong's regulation efforts are often hampered by data variability between FDA and other testing sites, and he has worked to achieve platform standardization.

A number of speakers explored mechanisms of disease and the body's response to toxicity. UNC Lineberger Cancer Center Fellow Katherine A. Hoadley, Ph.D., for example, reported on her findings in "EGFR Signaling Pathways in Breast Cancer." Peter Spencer, Ph.D., of Oregon Health and Science University, explored the actions of organic solvent neurotoxicity employing proteomic and genomic applications. University of California at Davis Entomologist Bruce Hammock, Ph.D., spoke on "Metabolomic Approach to Pulmonary Inflammation Resulting from Air Pollution" and the insights gained from metabolomic analysis of effects on the arachidonic cascade in exposed subjects.

A smaller number of presenters spoke on translational aspects of their research in the clinical setting. One of these was NIEHS Laboratory of Molecular Toxicology Senior Scientist Rick Paules, Ph.D., who reported on his work "Linking Phenotype Endpoints with Genomics to Identify Signatures Predictive of Adverse Health Effects." His work addressed the poor performance of clinical chemistry in predicting outcomes of acetaminophen (APAP) overdose and the need of health care providers for accurate indicators of exposure in surrogate tissue to discriminate between mild, moderate and severe injury.

Paules compared blood gene expression data from rats exposed to APAP with blood expression levels of orthologs of the rat discriminatory genes in human blood samples. He was able to use analysis of a small group of human samples to separate APAP-intoxicated patients from controls, demonstrating a potentially useful clinical tool for traumatic injury health care providers. Improving predictive ability will help providers reduce the number of deaths and serious injuries among the more than 50,000 patients who seek emergency room treatment for APAP overdose each year.

## Omics Applications in Toxicogenomics

Omics applications are distinguished by their unbiased and global analyses of specimens for specific categories of analytes. They include proteomics (proteins), metabolomics (products of metabolism), and genomics (transcription of individual genes), performed with a high throughput technology. The most common technologies for proteomics and metabolomics are Gas-Liquid Chromatography and Liquid Chromatography-Mass Spectrometry, which produce peaks from analytes identified in an extract. Genomics studies utilize DNA Microarray, which measures the transcription of thousands of genes simultaneously and produces a color-coded printout of results.

Theoretically, the number of analytes measured in an omics approach is limited only by the sophistication of available technology. In the words of presenter Bruce Hammock, Ph.D., "This approach allows one to both test and generate hypotheses regarding mechanism of action of toxins or therapies in a high throughput fashion." Thus, the approach is global and largely discovery-oriented, rather than strictly hypothesis-driven. "The most valuable approach," Hammock maintains, "is one using an integrated database of results from the genomic, transcriptomic, proteomic and metabolomic levels."

CEBS Scientific Administrator Jennifer Fostel, Ph.D., reported on her collaboration with NCT Assistant Director for Database Development Mike Waters, Ph.D., to create an integrated toxicogenomic database. The two recently completed version 2.0.8 of the Chemical Effects in Biological Systems (CEBS) Knowledgebase. CEBS contains enormous amounts of both private and public data, including toxicity findings, microarray data and proteomics images and spectra that can be downloaded from CEBS.

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## Expert Panel Debates Health Risks of BPA

*By John Peterson*

Fifty of the country's leading environmental health experts gathered at the Chapel Hill Sheraton November 28-29 to debate the potential health risks of bisphenol A (BPA), an environmental contaminant that has come under increasing scientific scrutiny. Sponsored by NIEHS, the National Institute of Dental and Craniofacial Research, the U.S. Environmental Protection Agency and Commonweal, the expert panel was convened to examine the recent literature on BPA and come to some conclusions regarding its effects on wildlife, laboratory animals and human populations.

BPA is a man-made chemical used in the production of polycarbonate plastics, epoxy resins for dental sealants and container linings, and many consumer products such as toys, baby bottles, eyeglass lenses and medical tubing. Each year manufacturers worldwide produce more than 6 billion pounds of the chemical.

The exposure of wildlife and humans to BPA is a concern, say the expert panel members. The compound is an endocrine-disrupting chemical that mimics the effects of estrogen and other naturally occurring hormones in the body, potentially leading to changes in growth, development and reproduction.

Lou Guillette, Ph.D., professor of zoology at the University of Florida and head of the wildlife panel, presented data from studies on fish showing that BPA exposure can result in feminization of male sex organs, reduction in sperm motility and a delay in the timing of ovulation and spawning. Researchers have also observed BPA-induced gonadal changes in birds and reptiles.

To illustrate the extent of BPA in the environment, Guillette produced a sample of ocean water, collected a thousand miles off the California coast, which contained hundreds of small and mid-sized pieces of floating debris. "As BPA enters the marine environment through biodegradation, there is the potential for bioaccumulation of the compound in fish and other wildlife," said Guillette.

Data collected by Frederick vom Saal, Ph.D., an endocrinologist with the University of Missouri, and other researchers shows that low-dose administration of BPA produces a wide spectrum of developmental and reproductive effects in mammals. These effects include an increase in aggressive behavior in male rats,



*Conference participants gathered for a group photo during a break in the meeting. (Photo courtesy of Jerry Heindel)*

early onset of sexual maturation in female mice, changes in mammary gland development in the offspring of treated dams, and a decrease in testosterone levels and sperm production in male rats.

Gail Prins, Ph.D., professor of physiology at the University of Illinois at Chicago, presented some recent evidence suggesting that BPA exposure early in life may increase cancer susceptibility years later. According to Prins, laboratory rats given BPA during the first five days of life were much more sensitive during adulthood to the carcinogenic activity of estradiol. “This study suggests that an environmental reprogramming of a normal response, combined with subsequent exposure to a cancer-causing agent, can work together to promote cancer,” said Prins.

Concerning the potential health consequences of BPA exposure, panel experts debated such issues as the degree to which the results of in vitro studies can be used to predict effects in laboratory animals and whether data collected on animals relates to the question of human health effects. “The fact that the effects seen in wildlife are very similar to those observed in laboratory animals suggests that these kinds of changes might be occurring in humans,” said Wade Welshons, Ph.D., associate professor at the College of Veterinary Medicine, University of Missouri-Columbia.

Retha Newbold, a biologist with the Developmental Endocrinology Studies Group at NIEHS and a conference participant, argued that carefully designed epidemiology studies must be conducted and evaluated. Only then can researchers make definitive conclusions about the effects of BPA in humans. “The current data we have from wildlife and laboratory animal studies is not sufficient evidence that BPA increases cancer risk in humans,” Newbold concluded.

“This was a very stimulating meeting,” says Jerry Heindel, program administrator at NIEHS and one of the meeting organizers. “This is the first time a group of experts has examined all of the published literature on a particular environmental agent and developed a consensus statement based on the strength of the data. This information will be valuable not only to scientists, but also to risk assessors and the general public, who want to know if what they are exposed to can cause harm.”

## **Expert Panel’s Consensus Statements On Bisphenol A**

The unique conference format included expert panel presentations based on white paper reports prepared by the participants in advance of the meeting. The presentations were divided into five subject areas -- effects on wildlife, in vitro studies, laboratory animal experiments, data on human exposures and cancer. Following morning breakout sessions in which the groups finalized their reports, each group presented a brief overview of the published literature in its assigned area of expertise. Presenters were also asked to rank each observation as either confident, likely but requiring confirmation, or needing additional research, based on the strength of the available data, and create consensus statements on the compound:

- BPA interacts with and modulates estrogen receptors
- Prenatal and neonatal BPA exposure in animals results in organizational changes in the prostate, breast, testis and brain
- Sensitivity to BPA varies extensively with life stage
- Adult exposures cannot be presumed to predict the results of developmental exposure
- Circulating levels of BPA in humans exceed the BPA levels extrapolated from acute exposure studies in laboratory animals
- There are compelling data to support the low-dose effects of BPA in wildlife and animal studies



# Distinguished Lecturer Aaron Hsueh

*By Eddy Ball*

Aaron J. W. Hsueh, Ph.D., presented the most recent talk in the 2006-2007 NIEHS Distinguished Lectures series at 11:00 AM on December 12 in Rodbell Conference Center. Hsueh is a professor and head of the Division of Reproductive Biology, Department of Obstetrics and Gynecology, Stanford University. His topic was “Coevolution and Bioinformatic Discovery of Polypeptide Ligands and Receptors.”

Laboratory of Signal Transduction Supervisory Biologist John Cidlowski, Ph.D., was the sponsor of Hsueh’s lecture. Cidlowski described the guest lecturer as a leader in a number of fields related to reproductive physiology, with a specific emphasis on the ovary. “His lab was the first to describe the role of apoptosis in the ovary,” Cidlowski said. “He is simply a world authority in ovarian function... and continues to lead the way in understanding ovarian function.”

Hsueh’s lecture focused on his recent work using a bioinformatics approach to discover a new family of G-protein coupled receptors and new polypeptide ligands. Although many in the field had thought that all of the receptors and ligands had already been discovered, Hsueh took an evolutionary genomic analysis approach to match ligands and receptors based on the co-evolution of genes.



*Lecturer Aaron Hsueh (Photo courtesy of Steve McCaw)*



*Sponsor John Cidlowski introduced the distinguished lecturer. (Photo courtesy of Steve McCaw)*

The lecture began with a discussion of integrating Darwin’s theory of evolution from a common ancestor with data from the Human Genome Project. This orientation led Hsueh and his colleagues to look at all of the genomes and take a comparative genome approach to hormone analysis. They used genomic sequences for human and multiple model organisms to elucidate the evolutionary origins of human genes.

Working with the hypothesis that the basic signaling pathways were probably already fixed in lower life forms, the researchers analyzed gene sequences to see how they changed from lower to higher forms, a process Hsueh compared to reading through the Library of Life. Tracing the evolution of the genes, Hsueh’s lab examined orthologs, which are highly conserved in function and sequence through evolution, and paralogs, which show evolutionary adaptation through species.

“Based on the lower species’ receptors,” Hsueh explained, “we searched the human genome.” The researchers found orthologs in life forms as ancient as the sea anemone. “Then we went the other way,” Hsueh continued, identifying fixed sequence elements in novel paralogs and discovering new ligands that had not been described

before. Because the human genome is completely sequenced, Hseuh was also able to determine whether known paralogs were also playing some roles that were not completely understood.

“I hope this concept is not just for the receptor, but for any of the genes you are dealing with,” Hseuh told his audience. His lab’s work focused on hormones because that was its primary research interest. Theory of evolution-driven genome searches, he concluded, should be applicable to any physiological process being studied. “I hope this concept will help in other fields also, in terms of what is going on.”

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## DIR Researchers Target Colorectal Cancer Prevention

*By Eddy Ball*

In an NIEHS-funded study published in the November issue of *Gastroenterology*, DIR investigators working in the NIEHS Laboratory of Molecular Carcinogenesis (LMC) and Laboratory of Reproductive and Developmental Toxicology report on the anti-tumorigenic effects of over-expression of nonsteroidal anti-inflammatory drug-activated gene (NAG-1) in transgenic mice. By elucidating the specific role of NAG-1 gene over-expression, the study’s findings may have important consequences in the clinical setting. Colorectal cancer is one of the most common cancers and is responsible for the deaths of over 50,000 Americans each year.

The study’s lead author, LMC Senior Investigator Thomas Eling, Ph.D., explained that investigators developed a transgenic mouse (NAG-Tg<sup>+</sup>) expressing the human form of a protein called NAG-1 to analyze the effect of the gene’s expression in preventing intestinal tumor development *in vivo*. Researchers evaluated two colorectal carcinogenesis models in NAG-Tg<sup>+</sup> mice to determine the efficacy of NAG-1 over-expression. They used a known intestinal carcinogen, azoxymethane, to induce tumors chemically and an intestinal tumor-specific genetic mutation (*Apc*<sup>Min+</sup>) to induce cancer genetically in NAG-Tg<sup>+</sup> mice and controls. Both groups of NAG-Tg<sup>+</sup> mice showed a greater than 50% reduction in intestinal cancer, confirming the tumor suppression activity of NAG-1.

The research team’s result “demonstrates that expression of NAG-1 *in vivo* can suppress chemically induced carcinogenesis in the colon.” Crossing the NAG-Tg<sup>+</sup> mice with *Apc*<sup>Min+</sup> mice resulted in a 60% reduction in polyp load compared to controls with genetic induction. The animals showed no apparent physical side effects other than a reduction in weight, especially in males.

The study built on previous *in vitro* findings. Results constitute the first confirmation of NAG-1 anti-tumorigenic effects *in vivo* and may lead to development of preventive agents that will not have the damaging cardiovascular and gastric side effects of cyclooxygenase (COX) inhibitors. Despite the efficacy of COX-1/-2 inhibitors in reducing risk of colorectal cancer, the side effects preclude their routine use.

This research adds to earlier work by Eling and several members of this research team demonstrating *in vivo* that a new experimental anticancer drug, Phortress, induces NAG-1 and significantly inhibits tumor growth. The study was supported by NIH grants and the NIEHS Intramural Research Program.

For Eling’s research team, this publication in *Gastroenterology* marks the recognition by the mainstream gastroenterological community of the clinical potential of stimulating NAG-1 expression by means other than COX-1/-2 inhibitors. The journal *Gastroenterology* is the official journal of the American Gastroenterology Association Institute and is widely considered to be the most prominent journal in the field of gastrointestinal

disease. In 2005, Institute for Scientific Information Journal Citation Reports ranked the journal first out of 47 gastroenterology and hepatology titles and calculated its Impact Factor at 12.386.

*Citation:* [Baek SJ, Okazaki R, Lee SH, Martinez J, Kim JS, Yamaguchi K, Mishina Y, Martin DW, Shoieb A, McEntee MF, Eling TE.](#) 2006. Nonsteroidal anti-inflammatory drug activated gene-1 over expression in transgenic mice suppresses intestinal neoplasia, *Gastroenterology* 131(5):1553-60.

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## Guest Researcher Explores Epidemiology of AAT Deficiency

*By Eddy Ball*

Since his own diagnosis with the genetic disease alpha-1 antitrypsin (AAT) deficiency in 1997, NIEHS Guest Researcher Frederick de Serres, Ph.D., has published a series of studies examining the prevalence of the disease and its link to respiratory and other conditions. His studies have developed a central theme articulated in the title of his 2003 commentary in *Environmental Health Perspectives*: “Alpha-1 antitrypsin (AAT) deficiency is not a rare disease but a disease that is rarely diagnosed.”

de Serres’ work has challenged the medical community to revise its notions about how widespread AAT deficiency is and how much of the world’s population is actually affected. Once considered a rare disease of white Europeans, where it is the most prevalent, AAT, according to de Serres’ research, “may actually be one of the most common single-locus genetic diseases in the world.”

Based on meta-analyses of genetic epidemiological data from around the world, de Serres has estimated incidence of the deficiency among 4.7 billion people in the 69 countries he has studied. He concludes that there are at least 286 million carriers of the two most prevalent phenotypes (PI MS and PI MZ) and an additional 3.8 million with deficiency allele combinations (PI SS, PI SZ and PI ZZ), indicating that approximately one person in every 25 is either a carrier or a homozygote/heterozygote for these two deficiency alleles. de Serres estimates that in the United States there may be as many as one carrier or deficiency allele combination phenotype for every 11.3 individuals. The rate varies from country to country and is as high as one in 4.5 among people from the Iberian peninsula.

AAT is produced mainly in the liver by hepatocytes and, under normal conditions, is continuously released into the blood stream. There it acts as a serine protease inhibitor to give the lungs lifelong protection from the proteolytic damage of neutrophil elastase (NE), which causes inflammation in tissues. In people who have AAT deficiency, the protease inhibitor is not readily released into the blood stream. The resulting deficiency can reduce the lungs’ defense against NE and lead to early onset of panlobular pulmonary emphysema, especially in smokers.

In addition, AAT can aggregate in the liver, leading to liver disease. AAT deficiency has been linked to neonatal cholestasis that may progress to infant and juvenile cirrhosis. In adults, AAT accumulation in hepatocytes can result in slowly progressing liver disease. In a recent study of the causes of death in persons with AAT deficiency, researchers concluded that severe airflow obstruction and liver disease account for excess mortality in affected individuals.

In his collaborative research with Spanish physicians, de Serres has explored the association between AAT deficiency and patients with chronic obstructive pulmonary disease and estimated the distribution of the genetic mutation worldwide. He and his colleagues have examined Caucasian populations in Europe, North America, Australia and New Zealand, where AAT deficiency is most common. In earlier studies, the researchers estimated rates in Africa and the Middle East. Their most recent meta-analysis, published in the December 2006 issue of *European Respiratory Journal*, evaluated data from 20 Asian countries and found a significant incidence of AAT deficiency among people there.

## AAT/World Trade Center Link?

Recent research suggests that the AAT mutation may help explain World Trade Center cough and the chronic diseases that a number of 9/11 first responders developed after the attack. Historically, a significant portion of members of the New York Police and Fire Departments have been members of ethnic groups, such as Irish and Italians, who have a high incidence of AAT deficiency.

In a presentation at Chest 2006, the annual meeting of the American College of Chest Physicians, David Prezant, M.D., of New York's Montefiore Medical Center reported preliminary findings that firefighters with an AAT deficiency had significantly faster declines in lung function than those with normal AAT levels. Prezant and his colleagues have been studying 12,000 of the New York firefighters who were at Ground Zero in the aftermath of the attack and for whom lung function tests both before and after are available.

### *Citations:*

[de Serres FJ, Blanco I, Fernández-Bustillo E.](#) 2006. Estimated numbers and prevalence of PI\*S and PI\*Z deficiency alleles of {alpha} 1-antitrypsin deficiency in Asia. *Eur Respir J* 28(6):1091-1099.

de Serres FJ, Blanco I, Fernández-Bustillo E. 2006. Estimating the risk for alpha-1 antitrypsin deficiency among COPD patients: evidence supporting targeted screening. *COPD: Journal of Chronic Obstructive Pulmonary Disease* 3:133-139. (Not PubMed indexed; contact the author at [deserres@bellsouth.net](mailto:deserres@bellsouth.net))

[Blanco I, de Serres FJ, Fernández-Bustillo E, Lara B, Miravittles M.](#) 2006. Estimated numbers and prevalence of PI\*S and PI\*Z alleles of alpha1-antitrypsin deficiency in European countries. *Eur Respir J* 27(1):77-84.

[de Serres FJ.](#) 2003. Alpha-1 antitrypsin deficiency is not a rare disease but a disease that is rarely diagnosed. *Environ Health Perspect* 111(16):1851-1854.

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## DETR Papers of the Month

By Jerry Phelps

### Tissue-Specific Functions of the Mammalian Clock Protein BMAL1

NIEHS grantee Christopher Bradfield has shown that expression of a clock gene known as *BMAL1* in specific tissues is necessary for proper physiological function. Using mutant mice, Bradfield and colleagues determined that circadian rhythm was normalized only when the protein was produced in the brain, but normal activity and body weight also required expression in muscle tissue. These findings are consistent with the tissue-specific variation in circadian gene expression and suggest that central circadian clock components act differently in a variety of tissues in mammals at the molecular, cellular and systems levels.

Research into dioxin toxicology and the Ah receptor-ARNT signal transduction pathway led to the discovery of the family of proteins that *BMAL1* is a part of – the PAS proteins. They act as both sensors of environmental cues and transmitters of these signals to the nuclei of cells. The recent explosion in the number of known members of the PAS family led to the discovery of sensors that are involved in responses to low atmospheric oxygen, tissue hypoxia, exposure to polycyclic aromatic pollutants and body rhythms.

Bradfield has been instrumental in the discovery of PAS proteins and the Ah receptor signaling pathway. Through his high productivity and exceptional grant writing skills, the grant that supports this work was converted to a prestigious Method to Extend Research In Time (MERIT) award.

*Citation:* [McDearmon EL, Patel KN, Ko CH, Walisser JA, Schook AC, Chong JL, Wilsbacher LD, Song EJ, Hong HK, Bradfield CA, Takahashi JS.](#) 2006. Dissecting the functions of the mammalian clock protein BMAL1 by tissue-specific rescue in mice. *Science*. 2006 Nov 24;314(5803):1304-8.

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### Sea Urchin Genome Sequenced

An international team of 240 scientists from 11 countries has successfully sequenced the genome of the sea urchin, adding to the list of organisms whose complete genomes have been unraveled. The effort took two years and included researchers supported by NIEHS. The importance of the effort is demonstrated in the remarkable genetic connections between the spiny echinoderm and humans. The team predicts that the complete DNA sequence will contribute valuable insight into human development processes.

The complete sequence is 814 million DNA bases, which is roughly one-quarter the size of the human genome, although it contains roughly the same number of genes (greater than 23,000). More than seven thousand of the genes are shared with humans, making sea urchins closer genetically to humans than other widely studied organisms. Genetically, sea urchins have the most complex innate immune system of any animal studied to date. Surprisingly, they carry genes related to many human diseases such as muscular dystrophy and Huntington's disease as well as genes associated with taste, smell, hearing and balance. Another surprising finding is that the eyeless creatures actually have genes associated with vision that are expressed in tissues in their feet.

*Citation:* [Sea Urchin Genome Sequencing Consortium.](#) 2006. The genome of the sea urchin *Strongylocentrotus purpuratus*. *Science* 314(5801):941-952.

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# Caution Advised in Genetics Research on Smoking

In a commentary in *JAMA*, NIEHS-supported scientist Chris Carlsten, along with a colleague at the University of Washington, warns that genetic testing and subsequent risk identification might not be good public health practice regarding cigarette smoking.

Carlsten cites two approaches where genetic testing might improve rates of getting smokers to successfully kick their habits. Genetic testing could be used to warn individuals at higher risk of lung cancer and subsequently increase their motivation to stop smoking. Also, genetic testing might identify candidates for more intensive cessation programs based on increased cancer risk or conceivably help determine more effective cessation approaches, such as drug therapy based on the genotypes of individual smokers. However, Carlsten points out that data currently available on genotype and risk are not necessarily highly motivating in modifying behavior. The data suggest that knowledge of small increases in risk of disease is insufficient in motivating smokers to quit. In addition, there is little evidence that nicotine therapy tailored to individual genotypes is effective.

For these reasons, as well as to reduce the risks of bystanders from second hand smoke inhalation, Carlsten recommends the more standard, societal approaches for getting smokers to quit, including smoking bans in public areas, high taxes on tobacco products and government-sponsored anti-smoking campaigns.

*Citation:* [Carlsten C, Burke W.](#) 2006. Potential for genetics to promote public health: genetics research on smoking suggests caution about expectations. *JAMA* 296(20):2480-2482.

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# Neurodevelopmental Effects of Prenatal Pesticide Exposure

Inner-city children in New York City exposed *in utero* to high levels of the pesticide Dursban (chlorpyrifos) experienced delays in mental and psychomotor development compared to children with low prenatal exposure, according to a study funded by NIEHS and conducted by the Columbia Center for Children's Environmental Health. Highly exposed children with chlorpyrifos levels >6.17 picograms/gram of plasma scored on average 6.5 points lower on the Bayley Psychomotor Development Index and 3.3 points lower on the Bayley Mental Development Index at 3 years of age than children with lower exposures. These two tests are widely used developmental indicators used to diagnose developmental delay in young children.

Additionally, children born to mothers who had been exposed to high levels of the pesticide were five times more likely to have psychomotor delays and nearly 2.5 times more likely to have delayed mental development. Dursban was also marketed under the trade name Lorsban. It is a widely used insecticide, although indoor uses of the pesticide were banned in 2000. The chemical is still approved for many agricultural applications. Products used indoors that contained the pesticide included pet tick collars, termite sprays, and roach and ant control systems.

Dursban is an organophosphate insecticide. It works by disrupting acetylcholinesterase, the enzyme responsible for the breakdown of the neurotransmitter acetylcholine — a reaction necessary to allow a cholinergic neuron to return to its resting state after activation.

*Citation:* [Rauh VA, Garfinkel R, Perera FP, Andrews HF, Hoepner L, Barr DB, Whitehead R, Tang D, Whyatt RW.](#) 2006. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. *Pediatrics* 118(6):e1845-1859.

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## DIR Papers of the Month

By Eddy Ball

### Indoor Fungus Exposure Linked to Asthma

In a study funded by NIEHS and the U.S. Department of Housing and Urban Development, an interdisciplinary team of DIR and Constella Group researchers found a significant association between indoor exposure to allergens from the fungus *Alternaria alternata* and asthma symptoms in a nationally representative sample of U.S. homes.

The data are from the National Survey of Lead and Allergens in Housing (NSLAH), a cross-sectional survey of 831 housing units inhabited by 2,456 individuals, 26% of them children, in 75 different U.S. locations. It was the first population-based study to examine the health effects of allergenic components of *Alternaria* using a polyclonal anti-*Alternaria* antibody assay. The team of investigators showed that the prevalence of current asthma increased with higher *Alternaria* allergen levels, likely in an exposure-dependent manner. Residents in homes with high concentrations of *Alternaria* allergen were 1.84 times more likely to have current asthma than residents in homes with low concentrations of the allergen.

This study provides new information on *Alternaria* exposures in relation to asthma symptoms. Because the health impact of indoor fungal exposures has not been studied as extensively as outdoor exposures, the study also underscores the importance of preventing mold and moisture-related problems and having homes cleaned on a regular basis.

*Citation:* [Salo PM, Arbes SJ Jr, Sever M, Jaramillo R, Cohn RD, London SJ, Zeldin DC.](#) 2006. Exposure to *Alternaria alternata* in US homes is associated with asthma symptoms. *J Allergy Clin Immunol* 118(4):892-898.

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### Fidelity of DNA Synthesis by Yeast Polymerase Delta

In an NIEHS-funded study published in *Nucleic Acids Research*, a team of investigators reports on the effects of accessory proteins on the fidelity of DNA synthesis by yeast polymerase delta (pol  $\delta$ ) *in vitro*.

The investigators examined the error rates of DNA replication and repair by pol  $\delta$  alone and in combination with the single-stranded DNA-binding protein complex replication protein A (RPA) and/or the processivity clamp proliferating cell nuclear antigen (PCNA) and its loader replication factor C (RFC). The results indicate that fidelity for errors involving single base pairs is largely determined by pol  $\delta$  itself. However, investigators determined that the accessory proteins strongly modulated the ability of pol  $\delta$  to delete large numbers of nucleotides between directly repeated sequences. In the presence of either RPA or PCNA the error rate was reduced by approximately 10-fold and by a rate equal to or more than 90-fold in the presence of both.

This research points to the importance of PCNA and RPA in protecting the genomes of higher plants and animals against the biological consequences of large deletions, with possible implications in regard to instabilities associated with hereditary degenerative diseases.

*Citation:* [Fortune JM, Stith CM, Kissling GE, Burgers PM, Kunkel TA.](#) 2006. RPA and PCNA suppress formation of large deletion errors by yeast DNA polymerase delta. *Nucleic Acids Res* 34(16):4335-4341.

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# Genetic Modification Proposed to Combat “Phosphate Crisis”

NIEHS intramural researchers, collaborating with researchers from the University of Pittsburg and North Carolina State University, have demonstrated that an avian phytase may help poultry, pigs and other monogastric production animals release phosphate from the phytic acid (InsP<sub>6</sub>) in their feed.

Researchers determined that rat and human recombinant “phytase,” multiple inositol polyphosphate phosphatase (MINPP), hydrolyzed InsP<sub>6</sub> at the very slow rate of 6nmol/mg protein per minute. The recombinant avian MINPP, in contrast, was 100-fold more efficient as a phytase. The study’s results raise the possibility that a genetically-modified chicken that secreted MINPP into the digestive tract may digest InsP<sub>6</sub> effectively *in vivo*. The researchers also used an avian model cell line to demonstrate how MINPP could be modified to ensure it is secreted.

This research points to the potential of a strain of genetically-modified chickens for addressing the current “phosphate crisis.” Such production animals could help to conserve the planet’s diminishing phosphate reserves and reduce pollution by decreasing phosphate levels in manure. Avian MINPP is predicted to perform as well as microbial phytases, and its expression in animals is less expensive and potentially safer for farm workers than using phytase as a feed additive.

*Citation:* [Cho J, Choi K, Darden T, Reynolds PR, Petite JN, Shears SB.](#) 2006. Avian multiple inositol polyphosphate phosphatase is an active phytase that can be engineered to help ameliorate the planet’s “phosphate crisis.” *J Biotechnol* 126(2):248-259.

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# Depression and Pesticide Exposure in Female Farm Spouses

In a study funded by the NIH Intramural Research Program, National Cancer Institute and NIEHS, researchers used questionnaire data from the Agricultural Health Study (AHS) to evaluate the relationship of reported depression to pesticide exposure among ~29,000 female spouses of licensed pesticide applicators, mainly farmers.

The researchers used data from questionnaires completed at enrollment in the AHS (1993-1997). The researchers defined cases as respondents reporting a physician diagnosis of depression requiring medication (N=2,051). Controls were respondents who did not have doctor-diagnosed depression. Lifetime pesticide use was categorized as never used pesticides, low exposure as up to 225 lifetime days, and high exposure as more than 225 days and a history of diagnosed pesticide poisoning.

The team found that a history of pesticide poisoning was associated with a more than three-fold increase in risk of self-reported, physician-diagnosed depression among female spouses of licensed pesticide applicators. Pesticide use in the absence of poisoning had little effect. Non-pesticide risk factors for depression included age, health status, smoking, frequent alcohol use, and working a job off the farm. “This study highlights the importance of preventing pesticide poisoning because the chronic effects of those poisonings may contribute to high rates of depression,” the authors concluded.

*Citation:* [Beseler C, Stallones L, Hoppin JA, Alavanja MC, Blair A, Keefe T, Kamel F.](#) 2006. Depression and pesticide exposures in female spouses of licensed pesticide applicators in the agricultural health study cohort. *J Occup Environ Med* 48(10):1005-1013.

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# Did You Know?

## Holiday Craft Fair Bounty Lures Shoppers to Mall Area

*By Eddy Ball*

During the annual Holiday Craft Fair on December 7, vendor tables lined the mall area from the entrance to B Module all the way to nearly the end of F Module. NIEHS staff, contractors and visitors took advantage of the opportunity to shop during lunch or on break as vendors and crafts people from the Institute and the Triangle area sold a variety of items ranging from cookies, cakes and floral arrangements to jewelry, kitchenware, bags, quilts and art work.

The Holiday Craft Fair has been a part of NIEHS since it was started in 1992 by the local chapter of the Federal Women's Program. According to NIEHS Troubleshooter Sarah O'Donnell, who has organized the event since 2000, the 2006 Craft Fair was very well attended. "We also had a lot of new vendors this year," O'Donnell said.



*Area artist Barbara Dillard replenished her display paintings from under her table as the crowds cruise the mall looking for unusual gifts and great deals. (Photo by Eddy Ball).*



*Staff Scientist Elena Braithwaite, Ph.D., waited for the next customer hungry for her baked goods. (Photo by Eddy Ball)*



*Patsy King of the Laboratory of Signal Transduction was the woman to see about bags and casserole carriers. (Photo by Eddy Ball)*



*Juanita Bradley of Contracts was delighted by the chance to spend her lunch hour shopping. (Photo by Eddy Ball)*



Area vendor Kristy Shaefer was one of the many sellers who took advantage of any available space in the crowded mall. (Photo by Eddy Ball)



This display of handbags and drawings reached almost to the end of the mall in F Module. (Photo by Eddy Ball)

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## Nottingham Staff Welcome the Holidays

*By Eddy Ball*

Nottingham NIH, NIEHS and contract staff got the holiday season off to an early start on December 13 with a covered-dish/holiday party in their main conference room. The room was packed, and virtually everyone with offices on the second floor participated in the event, which featured musical entertainment, a comic skit and a lively White Elephant gift exchange. For a week afterwards, the break room refrigerators were still filled with cheeses, sweets, baked goods and other food items.

Master of Ceremonies Rob Levine kept the entertainment in perspective: “We have plenty of entertainment,” he quipped, “just not a lot of talent.” Still, even if a few singers weren’t always on-key and if a rare joke bombed, everyone had a great time eating, laughing and applauding the performers.



April Parker and Ellen Moul in her Christmas sweater were already in the holiday spirit when the party began. (Photo courtesy of Dona McNeill)



*The chorus of HR and Ethics staff delivered a medley of Christmas tunes. (Photo by Eddy Ball)*



*The musicians from Administrative Services and Analysis were a little heavy on kazoos and percussion, but they made up with spirit what they lacked in instrumentation. (Photo courtesy of Dona McNeill)*



*From left going around the table, Cynthia Redford, Kathryn Woods, April Parker, Betty Wilkins and Mitsue Parrish enjoyed their holiday lunch. (Photo by Eddy Ball)*



*Whether it was “talent” or “entertainment,” the audience seemed to enjoy themselves thoroughly. (Photo by Eddy Ball)*

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## **NIEHS Celebrates Humor and Diversity at International Day**

*By Eddy Ball*

NIEHS employees and contractors enjoyed food from around the world, good (and not so good) jokes and holiday fellowship at the 2006 International Day Celebration following the Director’s Annual Honor Awards Ceremony on December 14. The theme of this year’s event was “A World of Laughter,” promoting the NIEHS mission to improve health by promoting laughter and all the healthful benefits of good humor.



*Jerry Phelps read jokes submitted by employees, as Don McNeill prompted the audience with her Laugh Meter. (Photo courtesy of Steve McCaw)*

The event featured Mistress of Ceremonies Eli Ney, Jokemeister Jerry Phelps and Silly Hat Specialist Dick Sloane, along with a Funny Holiday Hat Contest, video humor clips and holiday karaoke. The highlight of the celebration, however, had to be seeing kids from First Environments decorating the Christmas tree.

On stage and behind the scenes, International Holiday Awards Celebration Committee members made it all possible: Eli Ney, Ginny Ivanoff, Dona McNeill, John Maruca, Farida Sharief, Terry Blankenship-Paris and Diane Spencer.



*Rich Freed joined Eli Ney at the microphone.  
(Photo courtesy of Steve McCaw)*



*Dick Sloan joined McNeill on stage for a skit.  
(Photo courtesy of Steve McCaw)*



*The food was great and the entertainment was fun, but what really gave International Day the seasonal touch was the crowd of children decorating the tree. (Photo courtesy of Steve McCaw)*



*Ed Lebetkin and Diane Spencer added spanakopita to their plates. Thanks to Diane Crawford and the cafeteria staff, the food was delicious and abundant. (Photo courtesy of Steve McCaw)*

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# NIEHS Holiday Open House

*By Eddy Ball*

The NIEHS Holiday Open House sponsored by the Institute's leadership moved downstairs to the lobby this year, and there were two new hosts at the 2006 event, but the spirit of cheer and fellowship on December 20 remained the same. Joined by Deputy Director Sam Wilson, M.D., Associate Director William Martin, M.D., and Associate Director for Management Marc Hollander, Director David A. Schwartz, M.D., welcomed the NIEHS family to refreshments, personal appreciation for dedication and hard work, and best wishes for a peaceful new year.



*Bill Suk, Ph.D., and host David Schwartz enjoyed the refreshments as Steve Akiyama, Ph.D., and Diane Crawford talked in the background. (Photo by Eddy Ball)*



*From left to right, hosts Sam Wilson and Marc Hollander talked with Mary Hollander as Elliott Gilmer and Charletta Fowler sampled the punch. (Photo by Eddy Ball)*



*Charletta Fowler took a break to enjoy the fruits of her labor. (Photo by Eddy Ball)*



*Don Gula (left) and Bruce Wiggins (right) laughed with host Bill Martin. Kim Peterson stood behind Martin. (Photo by Eddy Ball)*



*Mary Wolfe, Ph.D., Allen Dearry, Ph.D., and Mitsue Parrish filled their plates with refreshments. Although healthier choices were readily available, the most popular items seemed to be from the sugar and salt food groups. (Photo by Eddy Ball)*



*Thanks to volunteers Kim Peterson (foreground) and Charletta Fowler, everyone had plenty to eat. (Photo by Eddy Ball)*

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## Upcoming Distinguished Lecture

*By Eddy Ball*

James E. Haber, Ph.D., will present the next talk in the 2006-2007 NIEHS Distinguished Lectures series at 11:00 AM January 9 in Rodbell Conference Center. Haber is a professor of Biology, Yeast Genetics and Molecular Biology at Brandeis University. His topic will be “Checkpoint Responses and Repair of a Broken Chromosome.”

Haber’s lab studies how potentially lethal breaks in the DNA double helix are repaired and what effects they have on the cell. “Recombination between homologous sequences is a fundamentally important process both in meiosis and in mitotic cells,” he explains. “We are interested in understanding at the molecular level how recombination occurs and what roles are played by the many proteins involved in DNA recombination, repair and replication.”

Laboratory of Molecular Genetics Staff Scientist Dmitry Gordenin, Ph.D., is the sponsor of Haber’s talk.

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*Distinguished Lecturer James Haber (Photo courtesy of James Haber and Brandeis University).*

# Upcoming Global Environmental Health Workshop

*By Eddy Ball*

NIEHS will host a Global Environmental Health (GEH) Workshop January 10-13, 2007 at the Stanford Court Hotel in San Francisco. Associate Director and Director, Office of Translational Research, William Martin, M.D., has invited environmental health experts worldwide to participate in the meeting to explore environmentally-associated disease in terms of the “life course” model.

The participants will break into three working groups - maternal, childhood, and adult. Each working group will be composed of two chairs and approximately 8-12 participants. The workshop structure will be broken down into three sessions, each designed to elicit recommendations for three outcomes:

- A list of key diseases/project ideas in GEH that align with the NIEHS mission and that NIEHS could successfully undertake
- Identification of the infrastructure barriers that NIEHS/NIH will need to address to conduct effective GEH research
- Recommendations on how to establish synergistic/strategic global partnerships to conduct this research

At the end of the workshop each working group will produce an 8-10 page background summary based on its work output for each of the sessions.

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*Workshop Organizer William Martin  
(Photo courtesy of William Martin)*

## Also Upcoming

- **January 3** in Rall D350, 12:00 – 1:00 PM — LMG Seminar Series with Shay Corvo, Ph.D., speaking on “Repair of Complex Double-strand Breaks in Mammalian Cells”
- **January 4** in Rall E193, 1:00 – 2:00 — LSB Seminar Series with Brandeis Professor Melissa Moore, Ph.D., Investigator, Howard Hughes Medical Institute, speaking on “An RNA play in two acts: (1) A novel function for the exon junction complex at neuronal synapses and (2) degradation of non-functional ribosomal RNAs in budding yeast”
- **January 9** in Rall Rodbell Auditorium, 11:00 – 12:30 — Distinguished Lecture by James Haber, Ph.D., speaking on “Checkpoint Responses and Repair of a Broken Chromosome”
- **January 10** in Rall D350, 12:00 – 1:00 — LMG Seminar Series with Sherine Chan, Ph.D., speaking on “Mitochondrial disorders involving pol gamma mutations”
- **January 17** in Rall D350, 12:00 – 1:00 — LMG Seminar Series with Krystal Finney, Ph.D., and Xuting Wang, Ph.D., speaking on “Smoking-induced gene expression and in silico discovery of SNPs in regulatory elements “
- **January 19** in Rall Rodbell C, 11:00 – 12:00 —LRDT Seminar Series with Scott Coonrod, Ph.D., speaking on “Epigenetic Reprogramming in the Murine Oocyte and Early Embryo”
- **January 22-23** in Rall Rodbell Auditorium, 8:00 – 6:00 — Children’s Environmental Health Workshop
- **January 24** in Rall Rodbell Auditorium, 8:00 – 12:00 — Children’s Centers Funding Panel Public Meeting
- **January 25** in Rall Rodbell Auditorium, 9:00 – 5:00 — Travel and Vacation Fair
- **January 31** in Rall D350, 12:00 – 1:00 — LMG Seminar Series with Ben Van Houten, Ph.D., speaking on “Idebenone effects in Friedreich’s Ataxia patients”

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