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CHANGES COMING

... to the Way We Compute

By Christopher Wanjek

There are days when Dan Sands wishes he were an immunologist. Sometimes even the frightening Ebolavirus seems tame compared to myriad computer viruses, worms, Trojan horses, rootkits, botnets, spyware, and other malware that Sands deals with daily as chief information security officer for NIH.

Combine these threats with the other major headache for Sands' colleagues in the NIH Office of the Chief Information Officer (OCIO) and the Center for Information Technology (CIT)—namely, the theft or loss of computers, particularly those with sensitive information—and you have no choice but to establish a computer network system that restricts how you can get on and where you can go.

And thus there are days when you wish you didn't work for the federal government.

Truth be told, all research organizations need to face the reality that they are under constant attack by experienced criminal enterprises and even state-sponsored groups intent on commandeering their computers—if not to gain access to locally stored data, then to hide in the ether of the 'net to infiltrate some bigger prize beyond the firewall.

These days you don't need to be so foolish as to click on the link in a Nigerian e-mail scam to have your computer compromised, Sands said. You are at risk merely by visiting a popular website, such as the *New York Times*. To expand on the biology analogy, infection is a result of risky behavior (clicking where you know you shouldn't) as well as the everyday threat of living in a crowded society (routine web browsing). Hackers are sophisticated, and several NIH computers have been compromised through no fault

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VITAL CULTURAL ELEMENT AT NIH: FAES 50 Years Onward

By Laura Stephenson Carter

What images does a theme song from an action movie conjure up? James Bond? Jaws? How about FAES?

Yes, strike up the strings. FAES, the Foundation for Advanced Education in the Sciences, the very element of NIH that imbues this federal facility with the feel of a college campus, now has its own theme music, a gift from the Manchester String Quartet, one of the many offerings FAES supports.

The jazzy musical motto was in honor of FAES's 50th anniversary celebration that has been ongoing since July 2009, and points to the major new projects to come: the Student Faculty Academic Center (SFAC), planned for the core of old Building 10, with more classroom space, a coffee bar and student and faculty lounges; and scholar housing near NIH.

FAES also sponsors graduate courses, a health insurance program, bookstore, reception facilities, and cultural escapes such as the Manchester String Quartet, which plays once a month on Mondays at lunchtime in the Masur Auditorium. FAES in fact has kept classical music vibrant at NIH, sponsoring the Chamber Music Series for nearly 40 years, until 2008, and then swooping in like an action hero to save the Manchester String Quartet this season when the Merck Foundation could no longer continue to support it.



David Hardy

One of the many features brought to you by FAES is the Manchester String Quartet's monthly concerts. Left to right: Glenn Garlick, cellist; Marissa Regni, violinist; Abigail Evans, violist; Hyun-Woo Kim, violinist.

So the FAES theme music was the Quartet's way of saying thank you.

"Composers often use musical motifs that have some extramusical significance," explained Glenn Garlick, who heads the Manchester String Quartet. "One day as we rehearsed the Brahms A Minor Quartet

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THINK GLOBALLY, ACT INTRAMURALLY



Michael Gottesman

One of the five major themes defining Francis Collins' goals as NIH director is to use NIH's talent and resources to improve global health. Recently the intramural research program (IRP) compiled an inventory of its many programs and projects that address global health problems and provided the list to participants at a summit of global-health experts convened by Collins. I am enormously proud of the contributions that NIH's intramural scientists have made to global health and wanted to share with you some highlights of our work.

Global health initiatives can be categorized based on impact (the number of individuals affected and the severity of the disease), the feasibility of the effort, the portability of the interventions, the sustainability of the programs, and meeting the need for trained biomedical scientists throughout the world. NIH intramural activities in global health illustrate the importance of each of these factors, and I will use them to outline some of our global-health efforts. A complete summary of what the intramural program is doing to improve global health can be found in the Intramural Research Sourcebook (visit http://www1.od.nih.gov/oir/sourcebook/oir/IRP_transition.pdf).

Impact

The three infectious diseases that produce the most morbidity and mortality in the world—prematurely ending the lives of millions of children and adults and severely affecting the welfare and productivity of millions more—are tuberculosis, malaria, and HIV. Intramural NIH, especially NIAID, has strong programs in basic pathogenic and epidemiology research, vaccine development, and treatment for these diseases.

In addition, it is clear that chronic diseases—such as major mental disorders, cancer, and heart disease—that now are prominent in the developed world are becoming more prevalent in developing countries. Thus, most of the translational studies in the intramural program targeted at these diseases will also have increasing global significance in the coming years.

Feasibility

For a global-health intervention to be practical, it must be relatively inexpensive and easy to deliver to distant sites. Preventing disease through vaccines is one of the best strategies. The IRP—especially the intramural researchers in NCI, NICHD, and NIAID—continues to develop vaccines to prevent diseases with global impact such as cervical cancer (human papillomavirus vaccine), malaria, anthrax, rotavirus, West Nile fever, leishmaniasis, Ebola and Marburg fevers, influenza, SARS (severe acute respiratory syndrome), Chikungunya virus, shigellosis, and salmonellosis. In addition, extensive epidemiology programs in several institutes—

including NCI, NIAID, NHLBI, NHGRI, NIAID, NEI, NIA, NIDCR, and NIEHS—define patterns of disease and suggest effective interventions for environmentally associated cancers, aplastic anemia, and genetically related diseases such as hypertension, obesity, prostate cancer, cleft palate, vision loss, and the aging process.

Portability

Much of the world, especially parts of sub-Saharan Africa, suffers from poor distribution of health services. Thus, it is essential that diagnostic tools, vaccines, and disease treatments be portable and robust enough to be useful in small villages that may be most affected by infectious diseases. Several institutes, such as NIAID and NIDCR, have collaborations aimed at improving the portability of diagnostics including methods of testing for infectious agents in saliva and sputum. And the NIBIB is collaborating with the Gates Foundation to improve imaging technology for diseases of the developing world.

Sustainability

Any prolonged positive effect on global health will require the development of an infrastructure that can continue to monitor disease and train future physicians and scientists in their home countries to do the research needed to support public-health efforts. One dramatic example of intramural NIH's building research capacity in other countries is NIAID's development of international centers for excellence in research (ICERs). ICERs in Mali, Uganda, India, Cambodia, Peru, Thailand, South Korea, and Tanzania build local research capacity and focus on diseases endemic in those countries. NIH intramural staff also oversees and provide training for the ICERs. In addition, several other institutes have established long-term collaborations to study the epidemiology of disease in many countries.

Training

NIH not only provides important training abroad, but is also perhaps the largest training site in the world for international scientists who will build research capacity in their home countries. At NIH, there are more than 1,800 visiting fellows as well as more than 400 visiting scientists, most of whom will return home to occupy scientific and medical leadership positions. Many of NIH's international alumni have already built biomedical research establishments around the world.

What more should we be doing? There are ongoing discussions about creating a graduate partnership program at NIH that focuses on health disparities in the United States as well as globally. How else can the NIH intramural program continue to be a leader in global health initiatives? As always, I welcome your suggestions. ■

—Michael Gottesman, DDIR

PHARMACEUTICAL DEVELOPMENT SECTION GETS NEW SPACE

By Maggie McGuire, CC

A vital contributor to intramural clinical research, the Pharmaceutical Development Section (PDS) of the NIH Clinical Center (CC) Pharmacy Department, is getting an environment and equipment upgrade.

The new space between the pediatric clinic and phlebotomy was created specifically for the PDS and debuted at a ribbon cutting on January 8, 2010. The various tasks of the section—preparing and making investigational drugs, testing their quality, and characterizing drug metabolism, using procedures that are consistent with evolving guidelines for Good Manufacturing Practices (GMP) set by the Food and Drug Administration—are all given devoted areas.

In short, the PDS serves the NIH intramural community by supplying drugs for clinical trials that take place at the CC. If the investigational drug is available from a commercial manufacturer, the PDS will register, randomize, package, and, if necessary, distribute and track it for the research team.

“In the double-blind studies in particular, all the drugs look alike, so we have to be really good about record-keeping and procedures,” said PDS chief George Grimes, Jr.

The PDS can also supply drugs that may not be commercially available in the desired form. There may be no commercial sponsor or if there is one, it may be too small and not have the resources to contract drug formulation, said Pharmacy Chief Robert DeChristoforo. “In many instances, the manufacturer of a commercially available drug may not be interested in pursuing a new indication [use] for their drug.”

The PDS helps an investigator file an Investigational New Drug application with the Food and Drug Administration and, once it's approved, formulates the desired medication or vaccine.

“To the best of our knowledge there is no other hospital pharmacy in the country that has a facility with the capability of PDS,” said DeChristoforo. “We can produce a product more quickly and at less labor costs by doing the operation ourselves. Investigators and visitors are amazed at what we can do for them.”

Such tailored products account for about a third of the 1,000 separate drugs (including placebos and varying strengths of medications) that the CC uses in its research protocols, said Grimes. For example, PDS's product-development unit is developing a topical, sterile gel of resinferatoxin to be used in research to treat pain.

“We wouldn't be as successful without your help and the help of your team, George,” Steven Rosenberg, chief of surgery for NCI, told Grimes at the PDS ribbon-cutting. “We deeply appreciate it.”

The PDS Analytical and Quality Control Unit performs drug analysis and stability studies on all medications used in NIH's clinical trials, both ones developed by PDS and those from the outside. Ensuring that what should be, is—right dosage, pure grade—the analytical unit continues monitoring medications for continued safety and efficacy after they are dispensed to patients.

The drugs are studied not only for whether they work, but also for how they work. PDS's Clinical Pharmacokinetic Research Laboratory staff characterizes how new drugs are excreted and metabolized and what that may mean for the patient, DeChristoforo explained. Years ago, the lab published on the unexpected interaction between St. John's wort and the protease inhibitor indinavir, an antiretroviral used in HIV/AIDS treatment. St. John's wort speeds up the body's elimination of indinavir and some other drugs; the resulting low blood levels of indinavir can allow the virus to develop resistance.

“This was really a wake-up call for the public and physicians, so we have done more and more studies with natural products,” said DeChristoforo.

The varied but interrelated work of the PDS takes precision and expedience, which the section's former home was not originally built for. Established in 1956, the section of 20 pharmacists, chemists, and technicians was in a converted space near the NIH Blood Bank in the CC's Magnuson Building.

The new area complies with GMP recommendations, such as a separate space for almost every step of the drug-processing system to ensure better air and overall quality



Michael Spencer

George Grimes, chief of the PDS, does the honors at a ribbon-cutting celebrating the newly designed space for this section in the NIH Clinical Center. He got support from CC Director John Gallin (left) and Pharmacy Chief Robert DeChristoforo.

control, Grimes said. For example, in the Clinical Pharmacokinetics Research Laboratory, where staffers work with HIV-infected blood, negative air flow (pulling more air in than is pumped out) and the use of a biological safety cabinet decreases the risk of contamination outside the laboratory.

Each week, PDS produces three to four sterile product batches and three to four tablets and capsule batches, though the batch sizes vary, Grimes said. A vaccine will likely be made 1,000 vials at a time, whereas the number of capsules produced can run from 50 to 100,000 per batch. New equipment in the PDS is making that process run more smoothly—a new tablet-making machine has more safety measures than the old one from the 1950s, and the new equipment to make capsules runs at a much faster pace, Grimes said.

The sterile production machine is now connected to the Internet, allowing staff to monitor its output from a remote location and document its status, a GMP advisement. “There will be a huge improvement” in the ease and accuracy of production, said research pharmacist Haksong Jin.

With such improvements, the PDS is poised to be a model for similar facilities around the country and may potentially support research outside NIH. “My hope is this facility will have the capacity not only to meet the needs of all of our intramural investigators but also [to] help some of our extramural colleagues,” said NIH CC Director John Gallin. He hopes “that they will also find this a valuable service.” ■

THE TRAINING PAGE

FROM THE OFFICE OF INTRAMURAL TRAINING AND EDUCATION: Reaching Out to Community College Students

By Jennifer Crawford, NCI

The OITE has discovered a pool of untapped talent: community college students. According to the American Association of Community Colleges, 44 percent of all U.S. undergraduates are community college students; of these, 58 percent are women and 36 percent are minorities. OITE has launched a program to train community college students in the biomedical sciences.

NIH has already been involved with community colleges. For several years, NHGRI's training program coordinator Michelle Hamlet arranged for NIH scientists to speak in science, technology, engineering, and math classes at Prince George's Community College (Largo, Md.). Recently she organized a committee of OITE staff and training directors from several institutes and centers to discuss ways to expose the students to NIH's resources, and she helped launch NIH's first Community College Day, held

on September 25, 2009, and attended by 85 students. The event—led by OITE and the NHGRI and NIAMS training offices—included campus tours, workshops, and panel discussions with NIH scientists from more than 10 institutes and centers.

"The level of excitement of the students attending this event was phenomenal," said NIAMS training director Mario Cerritelli. "They were eager to learn about what we do at the NIH and the various career options available to them in science and health care."

"Community College Day was about breaking down barriers," said Christine Barrows, acting director of the Biological Sciences Department at Prince George's Community College. "Before, the students [saw] NIH as this great place that's inaccessible. After, they say . . . 'I can really do this.'"

OITE then created the Community College Summer Enrichment Program (CCSEP). CCSEP students will be matched with NIH principal investigators, perform

full-time research in an NIH laboratory, and participate in workshops and courses to help prepare them for careers in health care and in social, behavioral, and biomedical research. Enrollment will be 18 to 20 students this year and more in future years.

"A successful program will provide an opportunity a student otherwise wouldn't have, pique interest in research or other health careers, allow the students to make contacts and network, and hopefully, increase the rate of transfer to four-year colleges," said Hamlet.

Student inquiries should be directed to <http://www.training.nih.gov/student/sip/ccsep>. Investigators interested in hosting a community college summer student should contact OITE director Sharon Milgram (milgrams@od.nih.gov) as soon as possible.

Funding for the CCSEP is provided by the Office of Research on Women's Health, the Office of AIDS Research, and the OD. ■

FROM THE FELLOWS COMMITTEE: FelCom—A Voice for the Fellows

By Krista A. Zanetti, NCI

Feeling overwhelmed by all that NIH has to offer? Never fear, FelCom is here. The NIH Fellows Committee (FelCom), which was founded in 1991 by Michael J. Fordis, the first OITE director, works to enhance the training experience for all fellows and gives them a strong voice across all NIH campuses.

Some FelCom representatives are appointed or endorsed by their scientific, clinical, or training director. Others are volunteer, or ad hoc, members. Appointed representatives and ad hoc members help run FelCom's many standing subcommittees: Career Development, Clinical Fellows, Distinguished Clinical Teacher Award, Fellows Award for Research Excellence (FARE), Job Networking, Mentoring, Publications and Publicity, Social Activities, Visiting Fellows, Web Page, and the Wednesday Afternoon Lecture Series.

The FARE subcommittee is one of FelCom's major activities. FARE selects the top-scoring 25 percent of abstracts in each study section; winners each receive a

\$1,000 travel award to attend a scientific meeting to present their abstracts. (See the announcement on page 15 for details.)

The Career Development subcommittee offers a monthly seminar series, and the Job Networking subcommittee works with OITE to invite companies—such as Novartis Institutes for Biomedical Research, Illumina, McKinsey and Company, and others—to NIH to network with fellows.

In another exciting initiative, the Mentoring subcommittee is working with Joan Schwartz, assistant director in the OIR, on an NIH-wide mentoring survey that will be administered in spring 2010. The survey will assess whether mentors and supervisors are providing adequate scientific guidance to NIH fellows.

The Visiting Fellows subcommittee organizes Science Voices from Home, informal meetings that promote networking between international scientists and visiting fellows, and the International Opportunities Expo, which highlights international career opportunities.

The Clinical Fellows subcommittee holds quarterly meetings with the Clinical Center director to address issues such as clinical fellowships, patient care, and clinical research.

FelCom members also serve as liaisons to NIH-wide committees—including Animal Research Advisory, Child Care Board, Foundation for Advanced Education in the Sciences, Graduate Medical Education, Human Subjects Research Advisory, Medical Executive, NIH Training Directors, Scientific Conduct and Ethics, and Women Scientist Advisors—as well as to the National Postdoctoral Association.

These are only a few of the important efforts FelCom coordinates to improve the fellows' community life at NIH. If you would like to join a committee or learn more about FelCom's activities, please come to an upcoming meeting. FelCom is open to all fellows and meets the first Thursday of the month from 4:00 to 5:30 p.m. in Wilson Hall, Building 1. For more information visit <http://felcom.od.nih.gov>. ■

LETTERS

Confess to Loving Confessions

Thanks for proving, once again, that science really can have a sense of humor. I love the “confessions” article on the final page of the December issue. I think every person can relate to “Name Withheld” once they find their true passion in life. Whether it’s a fruit fly (icky in my book, but exceedingly cool if you ask my nephew), 19th-century French art (clean and safe, but painfully boring if you ask my nephew), scuba diving (dangerous, but cool if you ask me or my nephew), or whatever, when it comes to science, it’s a good thing we find the sheer diversity of life so fascinating. There is something for everybody.

—Judith Gustafson, NIBIB

Distracted by Vermilion Eyes

I’m writing to express my utter dismay with your shocking and bizarre article, “Laboratory Confessions: My Love Affair with *Drosophila*” in the December issue of *The NIH Catalyst* (see http://www.nih.gov/catalyst/2009/09.12.01/catalyst_v17i6.pdf). I realize that scientists have their share of idiosyncratic and eccentric behaviors, but this “confession” was too much to ignore.

I seriously question the author’s grasp of reality and sense of perspective, embodied by the admission that the writer “was distracted by the brilliant vermilion eyes on a fruit fly dining on an overripe banana. No doubt a wild type.” Everyone who is sensible knows that vermilion *Drosophila* eyes are mutant, resulting from an X-linked recessive mutation, and that the more distracting and noteworthy eye-color mutants are white and rosy!

Bah, the author was probably one of those high-throughput gene-sequencer types who has never spent any real quality time with flies, just a developmental geneticist wannabe. Besides, eye color mutants are passé. Call me when you see a really exciting *Antennapedia* fly, which has legs sticking out where the antennae should be—now that’s a mutant!

—Chuck Dearolf, Assistant Director, OIR
Former *Drosophila* developmental geneticist
Writing (mostly) tongue-in-cheek

Ames Replies

I would like to correct a few errors of fact and interpretation in the article about me in the October 2009 *NIH Catalyst* (“The Ames Assay: Of Salmonella, Rodents, and Humans”).

The original article suggested that I expected and showed that all carcinogens would be detected as mutagens. It reported that I showed 90% of carcinogens were mutagens and then implied that I later improved the test by adding liver extract. However the 90% figure did include tests using liver extract.

I haven’t thought and don’t think “our test was too sensitive” or showed “almost everything to be mutagenic” as the original article said. It is a widely used test that contributes to understanding a complicated area of toxicology.

The article suggests that I showed that synthetic chemicals were likely to be mutagens and I was in favor of constraining their use, but it omits that my main emphasis has been on comparing synthetic chemicals to the huge natural background. Instead, the article should read: “He and other labs also showed that a variety of naturally occurring chemicals in our diet are mutagenic, e.g. products of cooking and natural pesticides that plants make to kill predators.”

—Bruce N. Ames
University of California, Berkeley

We thank Dr. Ames for correcting what he perceived to be errors in our historical article about his important contribution to science. We drew from various sources: the NIH Office of History, information on the web, and general and scientific publications, including an article that Ames wrote about his career (Journal of Biological Chemistry 278:4369–4380, 2003). Another source was an interview with Ames that appeared in the book Myths, Lies, and Downright Stupidity (2006) by John Stossel, former co-anchor of the ABC News show “20/20.” The book extols the virtues of the Ames test, explains how it “was hailed as a major scientific breakthrough,” and that today, it “is one of the standards used to discover if a substance is carcinogenic.” But after the hair dye and flame retardants were banned “people started using our test,” [Ames told Stossel], ‘and finding mutagens everywhere—in cups of coffee, on the outside of bread, and when you fry your hamburger!’ This made him wonder if his tests were too sensitive, and led him to question the very bans he’d advocated” (<http://abcnews.go.com/2020/Stossel/story?id=1898820&page=1>).

A revised version of the article with Ames’s edits is available at http://www.nih.gov/catalyst/2009/09.10.01/catalyst_v17i5.pdf. ■

NIH ABBREVIATIONS

CC: NIH Clinical Center
CIT: Center for Information Technology
FAES: Foundation for Advanced Education in the Sciences
FelCom: Fellows Committee
HHS: Health and Human Services Department
NCCAM: National Center for Complementary and Alternative Medicine
NCI: National Cancer Institute
NCMHD: National Center on Minority Health and Health Disparities
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OD: Office of the Director
OTTE: Office of Intramural Training and Education
OIR: Office of Intramural Research

BTRIS: A HOT NEW BIOMEDICAL TOOL

By Mark Budd (Clinical Center) and Eric Schaffer

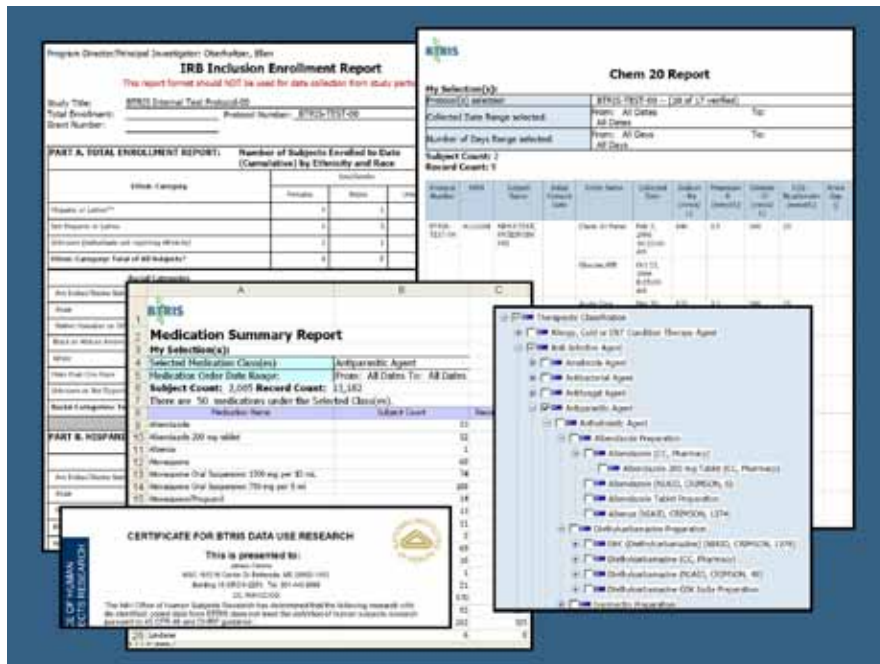
To hear NIH researchers talk about BTRIS, you'd think you were listening to a late-night infomercial. "Everything is at my fingertips," enthused Amy Chi (NHLBI). "It's all-in-one shopping," Theresa Ferrara (NCI) attested. "It is better than sliced bread," declared Rick Davey (NIAID). BTRIS—which stands for Biomedical Translational Research Information System—is all that and more. The new technology is opening up new frontiers for translational research and is changing the way NIH investigators work with clinical research data. More important, there's no gimmick. You don't have to "act now" and pay four easy installments for a questionable product. BTRIS has been field-tested and is ready for action.

BTRIS gives investigators easy access to vast amounts of data, including demographics, vital signs, lab tests, and medication history. Currently, data are pooled from the Clinical Center, NIAID, and NIAAA. NCI is slated to add its data sometime in 2010, and soon other institutes will be participating, too.

BTRIS's strength lies in its ability to quickly and easily generate reports from clinical research data pulled from multiple active protocols as well as from institute archives. With a few clicks of a computer mouse, an investigator interested in, say, blood pressure in Asian-American men over 50 can generate a data set and put it into a spreadsheet for analysis. Previously, a task like that would require downloading information patient by patient from multiple databases and painstakingly figuring out which data fields are comparable.

To standardize these disparate data sets, the *Research Entities Dictionary (RED)* has been created to allow users to more easily ask BTRIS for the data they want. The RED groups data into conceptual classes so that a researcher can ask for all data at some desired level of specificity—say, blood pressure—without having to worry about the variety of ways data may be labeled in different systems or protocols.

The developers of BTRIS hope that



Sample BTRIS reports using artificial data (clockwise from upper left): IRB Inclusion Enrollment Report, required each year by Institutional Review Boards; Chem 20 Report, a summary of clinical chemistry laboratory results for all subjects in a protocol; a hierarchy of medication concepts from the RED; automatically generated certificate that authorizes the use of de-identified data; and a Medication Summary Report (in this case, for antiparasitic agents) for subjects in the BTRIS database (Courtesy: James Cimino)

making clinical research data easier to access and analyze will open the door for large-scale studies that were previously unimaginable. "It makes population studies practical," said James Cimino, creator and director of the BTRIS program. BTRIS can empower translational research by making it easier to ask questions about large numbers of patients.

"You just need to know what makes sense to ask," said Cimino. "Then you need to understand how to map your concepts to the concepts in the database." Once BTRIS is used effectively for large-scale statistical analyses, it could provide clues for new lines of research.

Since its NIH-wide inauguration in July 2009, BTRIS has not yet yielded any results from population-wide studies. But it has generated a lot of traffic for another of its important features: report compiling.

BTRIS users have access not only to data from various institutes and centers but also to patient information within their own protocols. Users can generate

Institutional Review Board (IRB) patient enrollment reports and other reports automatically. "In the past, I would have to pull up individual patients' data in CRIS [Clinical Research Information System] or pull shadow charts or medical records to find the information," said Amy Chi. Using BTRIS, investigators can generate these reports in minutes, rather than hours or days.

The accolades go on. "My research team was thrilled when we learned about the capabilities of BTRIS," said Joan Han (NICHD). "BTRIS is a powerful and efficient tool."

Melanie Schwandt (NIAAA) loves BTRIS's "ability to perform focused searches using a specific patient list to get information on just those patients you are interested in."

"The system is user friendly," said Chi. "I can't wait for more ungrades."

To get set up and schedule a training session on BTRIS, call 301-827-8270. For more information, visit the BTRIS website at <http://btris.nih.gov>. ■

WHEN SCIENCE AND SOCIETY INTERSECT

By Stephanie Guzik, NCI

The 2009 H1N1 flu virus strain is still a hot topic being debated around the world. As the media-fueled discussions have intensified—often at the unfortunate cost of losing hard facts and correct interpretation of data—a group of NIH trainees has begun its own deliberations. The trainees have engaged in some scientific discussion of H1N1, but mostly they have focused on the effect misinformation has on the general public.

These fellows are members of the Science Policy Discussion Group, which was started last summer—by Sandra Chapman, a graduate student in NIAID, and Kristofor Langlais, a postdoctoral fellow in NICHD—as a journal club for summer interns. It has since become a permanent fixture on the NIH campus.

“We recognized a strong interest within the NIH fellows’ community in science policy matters, and more generally in how science and society intersect,” said Langlais. “There was a complete lack of an appropriate venue for trainees to explore and discuss these topics at NIH, so we decided to continue the group to fill this gap.”

“We recognized a strong interest within the NIH fellows’ community in science policy matters, and more generally in how science and society intersect.”

“We feel it is very important to encourage communication among the training scientists here at the NIH about the current issues in science policy so that we will have a better understanding of the critical issues facing science and our community,” said Chapman.

Of the group’s 30 passionate and dedicated fellows, some have already begun to transition into careers in science policy. A few are science policy fellows at NIH and the American Association for the Advancement of Science (AAAS). Other participants have not left the bench, but are eager

to learn how to better communicate their own science to the general public.

“The variety of perspectives within the group brings new ideas to the conversation,” said the group’s secretary, David Cabrera, a fellow in the NIH Management Intern Program.

Members of the group have joined because they want an “interesting forum to discuss relevant policy issues,” acknowledged Jodi Gilman, an AAAS Science Policy Fellow who recently finished her Ph.D. training with NIAAA and Brown University (Providence, R.I.). “I think that often scientists become extremely focused on their own research, without considering the various issues surrounding research that truly affect people.”

The group “has given me an awareness of various fields that I’ve never previously had the chance to learn about,” noted Emma Kurnat-Thoma, an NINR Ph.D. candidate in nursing from the University of Utah (Salt Lake City). She appreciates learning “how to assist colleagues, family members, and community leaders to better understand the science that informs their health information.” And, thanks to the group, she has become very “well-informed for future interviews, networking opportunities, mentoring, and community-outreach teaching.”

The group meets twice a month, with the first meeting used to explore, discuss, and debate a current hot topic in science policy and the second to discuss issues with an invited expert.

For the H1N1 pandemic discussion, the invited guest was David Morens, senior scientific advisor to the NIAID director. Morens was impressed by the group’s professional discussion. “The group was extremely well prepared and had obviously thought a lot about the subject, particularly about how media interactions and communications work both as a process and as a mechanism for informing the public about science and what it means,” he said. “We talked a lot about . . . how in the digital age . . . misleading and flat-out false information

“We talked a lot about how in the digital age misleading and flat-out false information floods the info universe, and it is difficult for the public to figure out the truth.”

floods the info universe, and it is difficult for the public to figure out the truth.”

Genomics and health disparities were addressed by guest speaker Edward Ramos, a science-policy analyst and research fellow at NHGRI’s Center for Research on Genomics and Global Health. “I found the participants to be engaged and forward-thinking in their analysis of topic areas I presented that ranged from race and genetics to health disparities to personalized medicine,” he said. He also acknowledged the need for this type of discussion group on campus, citing that it “provides a much-needed forum to discuss and debate current and relevant issues that intersect public policy and basic science.”

Other topics have stimulated similarly successful and insightful discussions with the invited experts. At the group’s initial meeting, Dan Poux, AAAS’s associate director of outreach, operations, and leadership development, gave an overview of science policy. A later session on science graduate education featured George Walker, a senior vice president at Florida International University (Miami).

Future discussion topics may include the human papillomavirus vaccine and cervical cancer screening, the new mammography guidelines, alternative sources of energy, the future of the NASA space program, biodefense, the health-care debate, and laws surrounding treatment of mental illness.

Membership in the group is limited, but a call for new members will be announced this summer. For more information, contact Kristofor Langlais (langlais@mail.nih.gov) or Sandra Chapman (dsandra@niaid.nih.gov). ■

THE SIG BEAT:

News from and about the NIH Scientific Interest Groups

New SIG: Engineering and Physical Science Interest Group

The Engineering and Physical Science Interest Group (EPSIG) promotes applications of engineering and the physical sciences within biomedical research. A main goal is to facilitate interactions among researchers trained in biomedicine and the physical sciences. Areas of interest encompass the physical principles underlying biological systems, tools used to study those systems, and bioengineering approaches to medical diagnostics, therapeutics, and disease prevention.

EPSIG's activities include a lecture series by extramural and intramural scientists, as well as sponsorship of symposia and poster sessions at which NIH postdoctoral fellows can present their own research. An additional aim is to educate postdoctoral scientists who have engineering and physical science backgrounds about the techniques, concepts, and scientific issues that will enable them to pursue biomedical careers. The group will facilitate communication among biologists, mathematicians, and physical scientists.

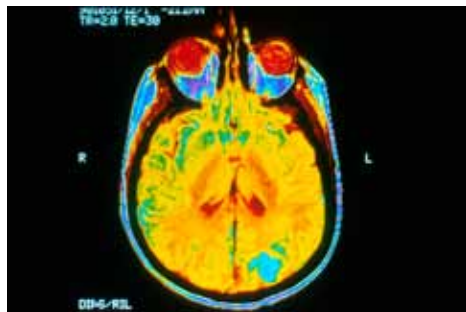
Moderators Richard Leapman (NIBIB), Antonina Roll-Mecak (NINDS), and Rob Tycko (NIDDK) invite anyone who is interested in fostering increased communication among scientists to join the EPSIG. For more information visit <http://sigs.nih.gov/epsig>.

New SIG: Pediatric Imaging Scientific Interest Group

The Pediatric Imaging Scientific Interest Group promotes the development and use of translational imaging methods to monitor milestones in normal and abnormal development, help diagnose childhood diseases, and assess the effects of trauma in the pediatric population. Attention will be given to promoting the development of quantitative imaging methods and disseminating their use in pilot studies and clinical trials.

This interest group aims to bring together basic science investigators who develop new imaging methods and techniques (positron-emission tomography, magnetic resonance imaging, computerized axial tomography, optical imaging, image processing); statisticians working

on image analysis, design of clinical trials, and group analysis; clinical researchers working on neuropsychiatric disorders including epilepsy, autism, schizophrenia, and other developmental disorders; pediatric oncologists and surgeons; and researchers on metabolic diseases that affect organs other than the brain.



MRI brain scan. Courtesy: Dr. Leon Kaufman, University Of California, San Francisco.

The group moderator is Carlo Pierpaoli of NICHD's Program on Pediatric Imaging and Tissue Sciences in the Section on Tissue Biophysics and Biomimetics. For more information, visit <http://sigs.nih.gov/pedimaging>.

New SIG: Microbiome Working Group

A Microbiome Working Group has been formed by investigators at NCI-Frederick to bring together NIH staff interested in the analysis of the microbiome and/or modification of the host microbiome through the use of probiotics or other microorganisms. The group will meet monthly to hear presentations on current research, problems, day-to-day frustrations, new technologies, new ideas, and other aspects of research projects that the presenters would like to discuss.

The group is open to all NIH staff. Videolinks from Frederick to Executive Boulevard and the NIH Bethesda campus will be established for the meetings. NIH labs outside of these areas are also encouraged to participate through videolinkage. Meetings are held the first Thursday of the month from 11:30 a.m. to 1:00 p.m. For more information or to join the e-mail list, contact Howard Young (NCI-Frederick) at 301-846-5700 or younghow@mail.nih.gov. ■

Remembering History . . . While We Continue to Make It

The Office of NIH History has undertaken several initiatives to not only educate the public (and by the way, that includes you) about the NIH intramural program's remarkable contributions to biomedical and behavioral research but also to better enable scientific investigators to use history as a research tool for improving health.

The new website at <http://history.nih.gov> reflects these changes. Among recent additions, under the direction of archivist Barbara Faye Harkins, the History Office has redesigned and expanded the archives website. This is the main portal for inquiries on NIH history.

The effort succeeded in reaching several goals: The site is more user-friendly, allowing users to more easily search texts, images and objects related to NIH developments, scientists, and administrators. The site also now directs users to other NIH websites that may have historical material, notably the NLM History of Medicine Division and the NIH Library. Most important, new software facilitates cataloguing of both archival materials (texts and images) and Stetten Museum objects in the same database. Warning: You can spend considerable time clicking and re-clicking the "Random Images" button to marvel at fascinating tools and questionable fashion choices.

As part of the archival process, the History Office met with the NLM and NIH Library to coordinate our collection of historical materials going forward. This is crucial and exciting as we continue to make history and as a wave of "historical" NIH senior personnel inch their way to retirement.

Please note that the archive is extensive and the History Office continues to perfect the site. ■

—Michael Gottesman

For a complete list of Scientific Interest Groups, go to <http://www.nih.gov/sigs/>. To create a SIG, contact the OIR Communications Director Christopher Wanjek (wanjekc@od.nih.gov).

COLLEAGUES

RECENTLY TENURED

Having the “ability to engage in high-risk, innovative research” is one of the things that Susan Mackem enjoys about working at NIH. The Omaha, Neb., native received a Ph.D. in virology from the University of Chicago in 1982 as a Medical Scientist Training Program trainee. She completed her M.D. at the Johns Hopkins University School of Medicine (Baltimore) in 1984 and then came to NIH to do a residency in anatomic pathology at NCI. After completing her training, she joined NCI’s Laboratory of Pathology, first as an expert and later—in 1995—as a senior clinical investigator. Today she is a senior investigator in NCI’s Cancer and Developmental Biology Laboratory in the Regulation of Vertebrate Morphogenesis section. Mackem’s research focuses on understanding how skeletal morphogenesis is regulated at the molecular level.



Susan Mackem, NCI

Normal development requires coordinated cell proliferation, apoptosis, and differentiation, but these processes often go awry in cancer and other diseases. An integrative systems approach may explain how subtle perturbations in regulatory cascades governing developmental processes ramify into overt phenotypes during development and in disease. The vertebrate limb is an excellent model to elucidate the control and mechanics of morphogenesis because it is amenable to embryonic manipulation, rich in genetics, and driven by evolutionary adaptation.

My lab focuses on the Sonic Hedgehog gene (*Shh*) and its signaling targets in the vertebrate limb. This signaling pathway plays critical roles from embryogenesis through maturity and is deregulated in several diseases including cancer. The Shh protein prevents the full-length activating transcription factor Gli3A from being cleaved to the repressor Gli3R. Stabilized Gli3A activates Shh targets, which in the limb, launches digit patterning. It’s still unclear how *Shh* specifies different digits. Current models propose spatial or temporal integration of Shh activity to specify progressively anterior digit 2 (index finger) to posterior digit 5 (pinkie).

Recently, we showed that *Shh* plays dual roles: a transient, early role that controls

digit pattern and an extended growth-promoting role that determines the number of digits. Our results challenge the current paradigm that the Shh protein acts as a temporally integrated morphogen to specify digit identity. To act later, Shh signals must be relayed, since digit identity is not fixed early, but is still regulated by interdigital mesenchyme (IDM) signals even as digit condensations form.

Downstream of *Shh*, the roles of *5'HoxD* genes extend from early to late limb development, when they may control the effectors of morphogenesis. Several *5'HoxD* (and related *5'HoxA*) genes, with similar *AbdB*-type DNA-binding domains, additively regulate digit pattern and are thought to be key Shh targets. But despite the efforts of many labs, it has been difficult to determine how *5'Hox* genes guide digit morphogenesis and what their downstream targets are. Using *HoxD12* as a prototype, we were the first to show that *Shh* is induced by *5'HoxD* genes. A large body of work now indicates that *5'HoxD* and *HoxA* genes initiate Shh expression and set limb anteroposterior (AP) polarity.

Subsequently, Shh maintains *5'HoxD* expression. We discovered genetic and physical interactions between *5'HoxD* and Gli3 proteins that modify Gli3R func-

tion (and hence Shh output), converting Gli3R into an activator. We are currently investigating Gli3-HoxD interaction roles in the developing limb. Gli3-Hox interactions may activate targets in other Shh-dependent contexts, such as normal (or neoplastic) renewal of skin and gut epithelia.

We are also analyzing how *5'HoxD* genes regulate late digit morphogenesis. We have found that they may locally reverse the cartilage differentiation program to form and position joints, thereby affecting features of digit identity. This late role also appears to involve the modulation of Gli3R function by HoxD interaction.

Our long-term goal is to unravel the regulatory interplay between *Shh* and *5'HoxD* genes. We hope to understand how digits are specified and assembled as a paradigm for how signaling networks orchestrate the formation of a complex tissue. We are developing combined genetic, genomic, and proteomic tools to study transcription factors and signaling cascades in the developing limb and elucidate the regulatory hierarchy between early patterning and digit morphogenesis. Toward this goal, we are using genetic tools coupled with an unbiased screen of signaling pathways active in IDMs, as well as genome-wide chromatin immunoprecipitation analyses (ChIP-Chip, ChIP-Seq) to understand how digit pattern and limb outgrowth are regulated at the molecular level. ■

Calling All Recently Tenured

If you are an NIH intramural scientist or clinician and have been tenured within the past year or so, we invite you to write about your work for *The NIH Catalyst*. Being featured in the *Catalyst* may increase campus-wide interest in your research.

All you have to do is respond to our invitation. We'll ask you to provide your CV and a photo, answer a few basic questions, and then write a brief description of your work.

To find out more, please contact Laura Carter, managing editor of the *Catalyst*, at carterls@od.nih.gov or 301-402-1449. Or just say “Yes” when you get that invitation in your e-mail.

RESEARCH FESTIVAL HIGHLIGHTS: SELECTED SYMPOSIA (A CONTINUED STROLL THROUGH THE FESTIVAL)

For those of you who couldn't get enough of the 2009 NIH Research Festival, here are the reports we didn't have room for in the December 2009 issue of *The NIH Catalyst*.

Gene Regulation

When gene regulation goes awry, cancer, AIDS, heart disease, or other diseases and disorders may follow. Scientists across NIH are determined to gain a comprehensive understanding of the mechanisms regulating gene expression and are studying sequence variations and structural differences in DNA, structural organization of the nucleus, and transcription factor binding sites.

NCI's **David Levens** and **Ofir Hakim** are investigating how the structure of DNA and organization of the nucleus control gene expression. Levens has identified regions of non-B-DNA (the B-DNA form is the type commonly found in cells) throughout the genome because non-B-DNA has been shown to regulate the *c-myc* oncogene. Hakim is finding locations of glucocorticoid receptor (GR) binding sites within the genome to characterize how GR genes are organized in nuclear space.

Leila Taher (NLM) and **Laura Elnitski** (NHGRI) are studying how

sequence variations within genomic DNA regulate gene expression. Taher identified hundreds of functional orthologs (genetic sequences that share a common ancestor) between humans and zebrafish. Elnitski used computational approaches to discover unknown regulatory regions; she analyzed four million genetic variants in the genomes of more than 200 individuals.

Alan Michelson (NHLBI) and **John O'Shea** (NIAMS) are unlocking the mysteries of transcription factor binding sites. Michelson is determining how cells acquire genetic programs and identities during embryonic development. O'Shea is investigating the role of signal transducers and activator of transcription (STAT) proteins in the differentiation of helper T cells. He has identified STAT4- and STAT6-specific binding regions.

When gene regulation goes awry, cancer, AIDS, heart disease, or other diseases and disorders may follow.

The knowledge gained from different research perspectives is helping NIH researchers develop a better understanding of how the deregulation of gene expression triggers and promotes disease. Their findings may one day lead to better methods to fight genetic diseases.

—*Natalie Goldberger, NCI*

At the Root of It: Stem Cells

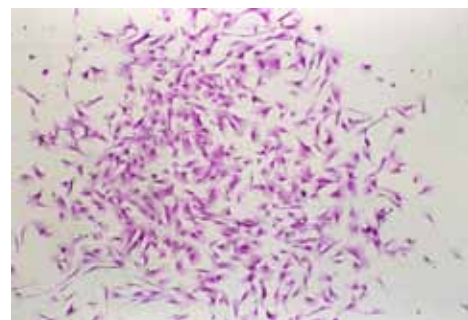
Research Festival attendees crammed into the Natcher Center auditorium to hear the latest news on NIH stem cell research. Scientists from several institutes enthralled them with tales of human embryonic stem cells (hESC) and induced pluripotent stem cells—cells that have been genetically reprogrammed to an embryonic stem-cell-like state.

Stem cells are undifferentiated cells that can be induced to become organ- or tissue-specific cells with specialized functions and can self-renew indefinitely, explained session co-chair **Pamela Robey** (NIDCR). These properties make stem cells exciting prospects for use in tissue engineering and regenerative medicine.

But the work is far from easy. **Minoru Ko** (NIA-Baltimore), whose laboratory is profiling and manipulating the potency and differentiation of stem cells, described inducing pluripotent stem cells as an “uphill battle.”

A key goal is “to develop good in vitro models,” said postdoctoral fellow **Josh Chenoweth** (NINDS), who is working on pluripotent hESCs. “We are making good progress in model systems for schizophrenia and Parkinson's disease.”

Blood-forming, or hematopoietic, stem cells from bone marrow have been used in bone-marrow transplants for over 40 years. These cells can form all types of blood cells and make ideal therapeutic vehicles for gene delivery. **John Tisdale's** (NHLBI) team has conducted clinical trials to perform allogeneic (cells from different but matched individuals) stem cell transplants to treat sickle cell anemia (a genetic blood disorder in which the body makes an abnormal



Colony of bone marrow stromal cells

form of hemoglobin). Patients tolerated the regimen, and their hemoglobin levels normalized. Tisdale's group has been long at work developing an autologous (from the same individual) stem cell gene-transfer system.

Eva Mezey (NIDCR) described her research using bone-marrow stromal cells (BMSC). BMSCs can regenerate bone and associated tissue and exhibit immunomodulatory effects. She found that 40 percent to 50 percent of sepsis-infected mice survived with a single injection of BMSC, which reprogrammed their lung macrophages. Based on this and other work showing the immunomodulatory effects of BMSCs, the NIH BMSC Transplantation Center was established about a year ago to harvest and grow clinical-grade BMSCs and develop protocols to treat patients who have acute and chronic graft-versus-host disease, inflammatory bowel disease, cardiovascular disease, and osteonecrosis of the jaw. Postdoctoral fellow **Rachel De Kluyver** (NCI-Fredrick) is using a mouse model to work on cancer stem-cell-directed therapies.

Much work remains to be done before stem cells can be routinely used as therapeutic agents. For more information about stem cells, visit <http://stemcells.nih.gov/info/basics/>.

—*Erika Ginsburg, NCI*

Bacterial Pathogenesis

NIH researchers can't resist tackling bacterial diseases that are becoming frighteningly resistant to antibiotics. **Anders Omsland** from NIAID's Rocky Mountain Laboratories (Hamilton, Mont.) is studying *Coxiella burnetii*, which causes

NHLBI BEHIND 3RD-HOTTEST PAPER OF 2009

the debilitating flu-like illness Q fever and is considered a biological threat. Until recently scientists have been unable to grow the pathogen axenically (outside of a eukaryotic host). After evaluating *C. burnetii*'s metabolic requirements, Omsland—who's in **Robert Heinzen's** group—created a nutrient medium that the pathogen can feed on. The axenic cultivation of *C. burnetii* will facilitate studies of the organism's pathogenesis and genetics and aid in the development of a Q fever vaccine and other preventatives.

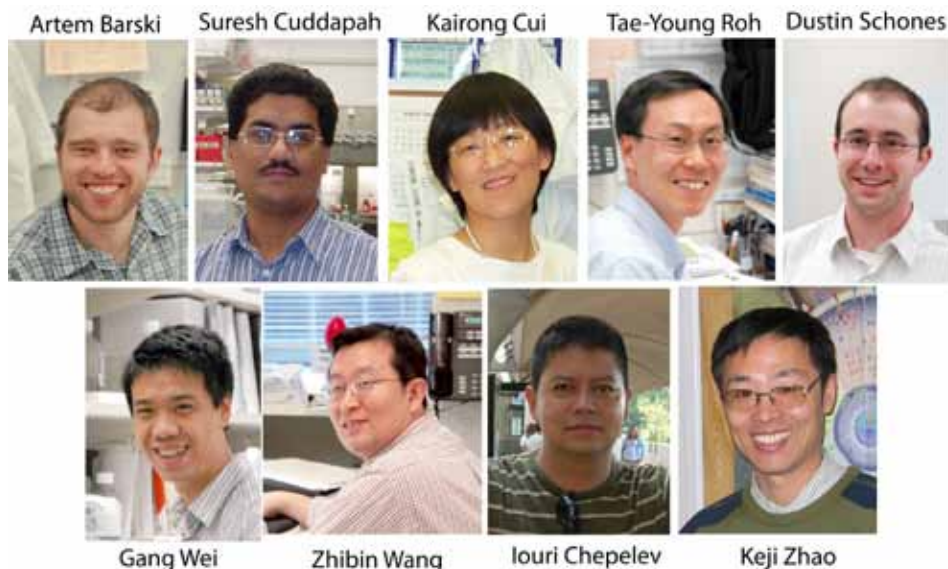
Scott Stibitz and other researchers at the FDA division on the NIH campus are concerned about whooping cough because of its increasing incidence since 1975 despite the widespread use of vaccines against it. Stibitz has undertaken a genetic and biochemical approach to identify biomarkers of virulence and attenuation of *Bordetella pertussis*, which causes the disease.

Mattias Machner (NICHD) has taken on Legionnaires' disease and hopes his work may lead to effective treatments. He's analyzing the molecular processes used by *Legionella pneumophila* to infect human cells.

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is another scary pathogen that can cause a multitude of serious infections, including toxic shock, scalded skin syndrome, endocarditis, and pneumonia. **Michael Otto** (NIAID) described how CA-MRSA secretes amphipathic peptides called phenol-soluble modulins (PSM) that lyse human neutrophils and play a key role in virulence. The PSM-mec peptide represents the first known example of a staphylococcal toxin gene that is transferred together with antibiotic resistance. PSMs may represent promising targets for anti-staphylococcal drug and vaccine development.

Finally **Anton Simeonov** (NCGC, NHGRI) alerted the audience to new resources at NHGRI's Chemical Genomics Center (NCGC) that will help NIH scientists in their quest to conquer bacterial pathogens. The NCGC is using the tools of small molecule discovery to develop chemical probes for the study of protein and cell functions.

—Laura Stephenson Carter



Members of the NHLBI lab team who worked on what became one of hottest papers in 2009.

Recently *The Scientist*, borrowing data from *ScienceWatch* (<http://sciencewatch.com/>), identified the top five hottest papers of 2009, with hotness measured by the number of citations they garnered. A paper in *Cell* from Keji Zhao's lab in NHLBI's Laboratory of Molecular Immunology, with lead author Artem Barski, came in at #3 with 560 citations and counting. Although the paper, "High-resolution profiling of histone methylations in the human genome," was published in *Cell* in May 2007, the paper had more than 299 citations in 2009 alone (*Cell* 129:823–837, 2007).

As relayed in *The Scientist*: "This study looked at how histone modifications influence gene expression in more detail than previous attempts. Using a powerful sequencing tool called Solexa 1G, the researchers mapped more than 20 million DNA sequences associated with specific forms of histones, finding there were differences in methylation patterns between stem cells and differentiated T cells." *The Scientist* had highlighted this work in a 2007 article, "Profiling human histones" (*The Scientist* 21:70, 2007).

Zhao's lab has also "provided the first genome-wide nucleosome positioning map

in the human genome [to] gain interesting insights into the relationship between epigenetic modifications and gene transcription as well as other genome functions," according to his research website (*Cell* 132:887–898, 2008). His long-term "goal is to understand how histone modification patterns are established during development and how the epigenetic signals contribute to normal development and disease states."

To learn more about Zhao's work, listen to his Director's Seminar Series lecture—"Dynamic Regulation of Mammalian Epigenomes during Development"—which was presented in April 2008 and is archived at <http://videocast.nih.gov/ram/dss042508.ram>. Zhao also presented at the Marshall Nirenberg tribute in November 2009, "Genes to Proteins: Decoding Genetic Information." His talk starts at about the 1:04-hour mark in the five-hour videocast at <http://videocast.nih.gov/ram/nirenberg111209.ram>.

Or visit his website at <http://public.nhlbi.nih.gov/Staff/Home/UserInputForPerson.aspx?OID=895&tab=AboutMe&LabID=LMI>. ■

—Christopher Wanjek

FAES

continued from page 1

we noted the use of a friend's motto in the opening phrase. Joseph Joachim used a musical motto FAE for the words 'Frei aber einsam,' or 'free, but lonely.' I commented that if we added an E flat to that theme, we could use the German spelling of E flat (*Es*) to come up with a musical motto for FAES. Marissa Regni played it once on her violin, then said for an organization as powerful and multifaceted as FAES, the theme should be more active than passive. She rearranged the notes, gave them a rhythm, and came up with something much more like a theme to an action movie."

Get it? Don't worry: The Quartet members aren't likely to get complicated explanations of biomedical research, either. Nevertheless FAES exists so that you have the opportunity to understand such musical references as well as deepen your scientific knowledge.

FAES was launched in 1959 with a mission "to foster and encourage scientific research and education . . . by whatever means may be practicable." FAES enrolls some 1,500 students a year in its graduate programs (it does not grant degrees, but credits may be transferable to students' home institutions). Classes include introductory courses in anatomy, biochemistry, immunology, and medical genetics; advanced courses in such areas as gene regulation, protein structure, and nanobiotechnology; and lots of other courses including neurobiology, technology transfer, and even several languages. NIH scientists and others who like to teach in their spare time make up the faculty. They are offered a modest stipend, but some turn it down.

Physical chemist Ted Becker, NIH scientist emeritus and president of FAES's 26-member board, taught various courses at the school for 30 years, including several in nuclear magnetic resonance. "I've written two books resulting from those courses," he said. He's taken FAES courses, too, even one in computers "back when computers were new."

"A lot of people have said they've learned much from him," said FAES Executive Director Krishna "Balki" Balakrishnan.

And thousands more have learned from countless other talented NIH scientists and administrators through the years.

"It helped me so much with the research I was doing," said Monica Gonzales (NCI), who has taken several FAES courses. "I was also impressed with the speakers that came and talked to the class. I can't imagine a university offering that."

"I was surprised and pleased that NIH offered the intensive hands-on BioTrac



Top: Social and Academic Center building

Middle: One of FAES's many classes

Bottom: FAES Bookstore

courses for more advanced researchers," said postdoctoral fellow Jodie Fleming (NCI). BioTrac is a series of daytime biotechnology training courses that include both laboratory and lecture sessions. "I also like the idea of continuing my education by taking graduate level classes at night here at NIH. The professors are experts in the field and keep you up to date on the newest theories and technologies."

FAES's other activities include providing health insurance to more than 4,000 visiting scientists, fellows, and other trainees who are not covered by the federal government's health-insurance program; running a bookstore (located near the B1 level cafeteria in Building 10), which supplies the

text books for the courses; and sponsoring chamber music concerts since 1968.

Even the music series is educational. At the Manchester String Quartet concerts, held monthly except in the summer, Garlick presents as a prelude a mini-seminar to help audiences better appreciate what they are about to hear. In January, audience members were delighted when just before the Brahms concert, the musicians presented FAES with its own musical motto. "Now all we need is someone like Johannes Brahms to weave it into a string quartet," joked Garlick.

In addition to being honored with its own musical motto, FAES has hosted open houses and ice cream socials and is planning a special event to coincide with its board meeting in April 2010. What's more, Becker and Balakrishnan hope to restore FAES to the prominence it enjoyed in the 1970s, when more than 1,800 people, both on campus and in chapters throughout the country, paid modest dues to be members. Membership benefits include receiving discounts at the bookstore and being able to rent FAES's Social and Academic Center (SAC), on Old Georgetown Road in Bethesda, for events. Membership used to be common among NIH scientists.

"Initially . . . the SAC was used as a social place for different groups after work," said Becker, who joined in the 1960s. "Then interest waned. And the system for dues renewal was not well organized."

FAES hopes to resurrect interest in membership and will launch a membership campaign with yearly dues set at \$15.

In addition, FAES has undertaken a scholar housing project on four acres of land it acquired starting in the early 1960s opposite NIH on Cedar Lane. Most of the land is vacant and includes four houses, which are rented to families and grad students. FAES has requested a rezoning of the tract to permit 31 townhomes that would accommodate about 150 predoctoral and postdoctoral trainees. The construction projects are funded with income from FAES's ongoing operations as well as investments in mutual and money market funds and certificates of deposit.

For more information about FAES, go to <http://www.faes.org> or call 301-496-7976. Courses are open to members of the NIH community, other federal employees, and the general public. The Manchester String Quartet's free concerts are held in NIH's Masur Auditorium (Building 10) at 12:30 p.m. (upcoming concerts: February 8, March 8, April 5, May 10). ■

THE EARLY DAYS OF FAES

By Daniel Steinberg

Daniel Steinberg was the first President of FAES and is the sole surviving member of the original board of directors. The others who incorporated FAES and served on its initial Board were Nobel Laureate Christian B. Anfinsen, Jr., Robert W. Berliner, Murray C. Brown, Kenneth S. Cole, Roger M. Cole, Hewitt G. Fletcher, Seymour S. Kety, Robert B. Livingston, David Shakom, and Dewitt Stetten, Jr. The first meeting of the Board was September 9, 1959.

When I joined the newly established National Heart Institute in 1951 there were no formal teaching programs of any kind at NIH. Teaching was the province of the universities; research was the only recognized mission of NIH. There was concern within the NIH administration that formal teaching programs would be an undesirable distraction from the research mission.

With the opening of the Clinical Center in 1954 there was a huge expansion in the numbers of research scientists and postdoctoral research fellows on the NIH campus but there was still no formal framework within which the extensive and sophisticated expertise of the scientific staff could be made available to the predoctoral and postdoctoral trainees. Some of us—including myself; my thesis adviser, Christian B. Anfinsen; and Robert W. Berliner—felt strongly the absence of an academic setting. We all referred to the Bethesda site as the “NIH campus” but it was a campus without teaching. We sought to correct this by proposing a modest program of formal course work.

NIH Director James Shannon felt he could not use NIH funds to support such a program but would allow us to use NIH space. We became aware that the U.S. Department of Agriculture had a “license to teach” night-school classes at various federal sites in the D.C. area. We approached them and they agreed to fold our program into their already up-and-running operation. So the beginnings of education at NIH were under the auspices of the Department of Agriculture!

For several reasons this arrangement proved unsatisfactory. With Shannon’s approval we created a nonprofit corporation to take over the financing and administration of the NIH teaching program. The Foundation for Advanced Education in the Sciences, Inc., was incorporated on July 2, 1959.

The value of the foundation and its

educational program became most evident as the size of the NIH Research and Clinical Associate program grew. Because of the outstanding credentials of its scientific leadership and also in no small measure because of the Korean War doctor draft, the associate positions at NIH were highly prized. We got the cream of the crop.

They were eager to learn how to do research and they took advantage of the Graduate Program (no degree programs) run by FAES. The enrichment provided by the formal course work made their two- to three-year stay more rigorous and equipped them to undertake a broader array of research directions. I believe the availability of the teaching programs under FAES helped us to have a continuing flow of outstanding Research and Clinical Associates after the doctor draft ended and allowed us to continue competing with the universities on an even playing field.

Still, the Office of the Director was wary about expanding the role of NIH in formal teaching. In the mid-1960s I approached William D. McElroy, chair of biology at Johns Hopkins University in Baltimore, about the feasibility of a joint NIH-Hopkins graduate school in the biomedical sciences. The idea was that students would spend their first two years in Baltimore and then move to NIH to do their thesis work under an NIH researcher. The discussions were very positive and we put together a formal application to the NIH for grant support.

We were waiting to see how we fared in the review process when Shannon called me to his office and made it clear that he did not feel this would wash. If NIH were to get into the graduate school business, he said, any and all universities in the United States would have to have equal opportunity to participate. Besides, such a program might dilute the concentration on research, the real mission of NIH. Our arguments—that it might actually strengthen the research atmosphere by adding formal training opportunities and bringing young minds into the institute—failed to convince him. He told us he was pulling the Hopkins proposal out of the hopper. It never even got reviewed.

When we founded FAES we only had one thing in mind: creating a framework to encourage education within the walls of NIH. In a sense the FAES provided a sanctuary for education that the NIH, as a



Daniel Steinberg, the sole surviving founder of FAES, recounts the organization's early days.

government agency, felt was not allowable under its official mission. Once that “extra-NIH framework” was established, other good uses were found for it. For example, it was the umbrella under which a not-for-profit bookstore was started in the Clinical Center. Foreign visitors found it difficult and expensive to buy health insurance for a year or two. The foundation undertook negotiations on their behalf and was able to make solid coverage affordable. Today FAES provides insurance coverage to more than 4,000 domestic and foreign postdoctoral fellows.

As a final example, Giulio Cantoni, a passionate music lover, thought it would be nice to run a chamber music series in the Clinical Center auditorium. Well, believe me, that did not fit comfortably into any congressionally mandated missions of NIH. They just could not do it. But FAES could. With a nonprofit organization handling the funding, the NIH could—and did—make the space available to FAES as it could to any other private group. It worked beautifully! For more details, see the article by Henry Metzger in the March-April 2006 issue of *The NIH Catalyst* (<http://www.nih.gov/catalyst/2006/06.03.01/page7.html>).

I left the NIH in 1968 to head the Division of Metabolic Disease at the newly established School of Medicine here at the University of California at San Diego in La Jolla. I have followed with interest the growth and development of FAES. At my age (87!?) I find myself involved in a lot of 50th anniversaries, including the 50th anniversaries of the NHLBI and of the *Journal of Lipid Research*. This 50th of the FAES gives me especially warm feelings. I know that the NIH has been blessed with special status in some respects but it is still a government agency. I’m proud to have participated in the establishment of the FAES, which has helped and continues to help NIH and its outstanding people accomplish things “outside the box.” ■

COMPUTER SECURITY*continued from page 1*

of their users.

While many NIHers feel frustrated by the increasingly stringent rules for NIH computing, one should keep in mind that, as with biomedical and behavioral advances, the NIH intramural program hopes to lead the way for the U.S. research effort with computer security protocols that balance security with usability.



Changes are coming to NIH computing this year that, on the surface, may seem overly restrictive. But if implemented correctly, the changes may very well make computing a more enjoyable experience.

Smart Cards

By June 2010 all NIH staff will have new “smart-card” badges, called personal identity verification (PIV) cards. By year’s end, most NIH computers (excluding medical devices) must be equipped with devices and software to read the badges and to enable secure log-in.

Herein lies a major source of unnecessary anxiety, said Mark Silverman of OCIO, who is helping to lead the transition to smart-card login: Only those NIH employees who have access to sensitive data are required to log in with a smart card instead of a password. If you don’t have access to sensitive information, Silverman said, then using the smart card to access your computer will be optional unless your institute or center states otherwise.

There are many positive aspects of this new system that might make the smart-card login method useful for all NIH employees, Silverman said. Just like an ATM card, the smart card would have a static PIN—that is, a six- to eight-digit code that doesn’t need to be changed regularly. You insert the card into your computer, type in your PIN to prove you own the card, and remove it. Eventually, you will be able to use this single mechanism to log in not only to the NIH network but also to other government-wide applications, for example, myPay (for your payroll information) or myEOPF (for your Electronic Official Personnel Folder).

“We will all soon be able to use the card instead of remembering pesky user IDs and constantly changing passwords,” Silverman said. “Only a few of us who need to access sensitive systems will be required to use the smart card.”

For now, the government-wide aspect is not in place. In order to support the continued use of access by log-in and password, you will still be prompted to change your NIH password every 60 days whether you use it daily or not.

Another caveat is that the definition of what constitutes “sensitive data” is difficult to pinpoint. The same data in different contexts can be considered sensitive or nonsensitive. For example, pre-award grant and contract data are sensitive but post-award data are not. NIH is developing a guide to help the NIH community identify sensitive data. For now, the decision on when a smart card is required to access data or systems rests with the institutes and centers.

Undoubtedly there will be more to come in policies concerning smart cards and sensitive data over the next year, said Jack Jones, NIH chief information officer and acting director of CIT.

Problems, Solutions

Silverman said that the perceived limitations and worries about the smart cards are real but overstated. The card readers are quite robust, he said. Some are built into the computer; others will be retrofitted, likely via a USB port. There’s little risk of the reader not working, but if it fails, you can still log in the old way, albeit with no access to sensitive data until the reader is fixed.

You might forget to remove your card after you log in and then leave your ID at work or even lock yourself out of your office. Both Sands and Silverman confess to this happening to them. But once is enough, they said, to make you remember to remove your badge and check whenever you leave the office that you have it.

Rumors abound that the system will lock you out every 15 minutes and that you will have to constantly reinsert your smart card. Not so. The smart-card log-in merely mimics the existing username and password method—you would just have to re-enter your PIN when the computer times out. And if you lose your badge or forget it while working off-campus, you can still use the old username and password route to log in. You just won’t have access to any part of your computer that is a portal to

sensitive information.

By June 2011, all NIH staff with an NIH laptop must use a smart card to log in to that machine. Why the necessity? First, hackers know how to intercept passwords. Also, not a day goes by at the NIH when someone doesn’t report a lost or stolen laptop, BlackBerry, or flash drive, Sands said.

The use of PIVs is part of a Homeland Security Presidential Directive from 2004 to provide greater confidence that the person logging in to your computer is indeed you. This is a federal requirement by which NIH must abide.

Yet CIT and OCIO, in implementing a federal mandate, are not trying to thwart productivity. “Keep in mind that the policy says ‘where practicable,’” said Silverman. “Where smart cards cannot be supported, or their use will ‘break’ the system, they are not required.”

Because many NIH employees may be using their NIH password less frequently once the smart-card system kicks in, they are more likely to forget it. Sands recommends that everyone sign up now for the Password Self Service, which allows you to reset your password or unlock your account yourself, without calling the NIH Help Desk. You need to first complete the one-time sign up with your current password, however. Go to <https://iforgotmypassword.nih.gov>.

Bigger Changes to Come

According to Health and Human Services Department policy, all new computer purchases must include a smart-card reader, either built in or as an attachment.

The battle between disease and treatment is ongoing. Sands envisions a day when you, and only you, would have seamless and reliable access to your computer and a network with minimal intrusion. The computer would somehow just know who its master is.

Similarly, your social security and credit card numbers won’t be in the hands of criminals, and patients’ genetic and other health information would remain accessible only to those who hope to heal, not harm.

We are inching our way in that direction, Sands said. Until then: Log on, tune in, but don’t drop out.

Further reading:

<http://smartcard.nih.gov>

<http://nitaac.nih.gov/SmartCardPurchaseInstructions.asp>

Web 2.0 and You

The Internet is a dangerous place. Some federal agencies, particularly those involved in defense and nuclear regulation, must maintain the strictest computer security protocols. Access to the network is more restrictive at NCI-Frederick than at the Bethesda campus, for example, because of its encampment within Fort Detrick, a U.S. Army base.

The Center for Information Technology (CIT) and the Office of the Chief Information Officer (OCIO) are striving for that sweet spot that allows NIH researchers to protect themselves from nasty surprises on the Internet by practicing safe information sharing. For now, OCIO bans the use of many social media and file-sharing tools, such as Facebook, MySpace, and Skype. The reason is not because management thinks the staff will goof off at work, said OCIO's Dan Sands. Rather, the risk of "catching a disease" from these sites is high. It's a security-protocol issue, not an acceptable-use issue along the lines of gambling and porn sites.

LinkedIn, a professional networking site popular among scientists, is accessible via the NIH network because it is perceived as a safer networking tool. LinkedIn is not inherently different from Facebook other than the narrower interests and volume of the clientele it attracts. Hackers, for efficiency, tend to target the most popular sites such as Facebook, much as they target PC instead of the Macs because the former constitutes over 92% of the market.

NIH Chief Information Officer Jack Jones doesn't see arbitrary banning as a solution to computer security, particularly at a research facility.

This year, said Sands, the CIT will test new "dynamic web filtering" tools that would permit more liberal use of social networking, blogging, and file sharing. CIT will test these tools on the approximately 300 NIH employees granted access to Facebook.

(Jones and Sands, both Mac users, also hope to squelch the rumor that Macs will be banned, to be replaced with a uniform operating machine or browsing tool. "Macs aren't going anywhere," Sands said.) ■ — CW

ANNOUNCEMENTS

**Public Meeting:
National Cancer Human Biobank
February 19, 2010
8:30 a.m. to noon
Natcher Auditorium (Building 45)**

NCI is announcing the development of a national biobank and will provide information about the planning process. Contact information: 301-594-2212 or biospecimens@mail.nih.gov. The session will be videocast. To register, visit <http://biospecimens.cancer.gov/cahub/meetings>.

**NCI's Translational Genomics:
Looking Back and Moving Forward
March 4-5, 2010
Natcher Auditorium (Building 45)
Deadline: February 12, 2010**

This symposium will provide a forum for the exchange of information on novel technologies, the development of clinical and bioinformatic infrastructure, and the best methods for translation into clinical practice. Seating is limited. To register and submit abstracts, go to <http://web.ncifcrf.gov/events/TranslationalGenomics/default.asp>. For more information, contact Julia Lam at lamj@mail.nih.gov.

**TAT 2010: 8th International Symposium
on Targeted Anticancer Therapies
March 4-6, 2010
Bethesda, Md.
Register Now**

NCI and the European Society for Medical Oncology are co-sponsoring the program, which will include keynotes, reviews of emerging targeted agents for cancer therapy, and updates on early-phase clinical studies. To register and submit abstracts, go to http://www.nddo.org/page_include_tat2010.shtml.

**"Current Topics in Genome Analysis"
Lipsett Amphitheatre (Building 10)
Tuesdays, 10:00-11:30 a.m.
January 12-March 23, 2010**

These NHGRI lectures are geared at the level of first-year graduate students, are practical in nature, and are intended for a diverse audience. For more information, visit <http://www.genome.gov/COURSE2010>.

Stadtman Seminars

The 10 finalists for first Earl Stadtman Investigators will be invited for public seminars on the NIH main campus in February and March. Check the NIH weekly calendar of events at <http://calendar.nih.gov/app/MCal-Welcome.aspx> for times and locations.

**NCI's 3rd Annual Biospecimen
Research Network Symposium:
"Advancing Cancer Research
Through Biospecimen Science"
March 24-25, 2010
Bethesda, Md.
Registration Closes: February 22**

Learn about the impact of pre-analytical biospecimen variables on cancer research and molecular medicine. Hear from leaders in biospecimen research, genomics, proteomics, oncology, pathology, biobanking, hospital administration, and pharmaceuticals as well as from patient advocates. For more information and to register, go to <http://brnsymposium.com/meeting/brnsymposium/2010>.

Oncology Fellowship Opportunities

Opportunities for Ph.D.'s, M.D.'s, and M.D./Ph.D.'s or their equivalents in cancer-related scientific research and research-related regulatory review. For more information, visit <http://iotftraining.nci.nih.gov>.

NIH Medical Arts Lowers Hourly Labor Rate More Than 25 Percent

Medical Arts has reduced its hourly rate from \$125 to \$91 for medical illustration, express services, design illustration, and Photomic and Photomac services. For details, visit <http://medarts.nih.gov>. Customer Service 301-496-3221; Medical Illustration 301-496-5566; Photomic/mac Photography 301-496-4971; Express Services 301-435-6128; Design 301-496-5566. Stop by for a tour and a review of its portfolio (Building 10, Room B2L103).

HHS Mentoring Program

Permanent federal employees interested in serving as mentors and mentees at NIH are invited to join the NIH April 2010 cohort! For more information, go to the NIH-HHS Mentoring Program website at http://trainingcenter.nih.gov/hhs_mentoring.html.

FARE Deadline: March 23, 2010

NIH intramural trainees are invited to submit applications for the annual Fellows Award for Research Excellence (FARE) competition. Winners will each receive a \$1,000 stipend to attend a scientific meeting, present their work at the 2010 NIH Research Festival, and serve as judges for the next FARE competition. Application and abstracts must be submitted online between February 23 and March 23. Winners will be notified by June 30. For more information, visit <http://felcom.od.nih.gov/subCommittee/fare.aspx>.

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CATALYTIC REACTIONS?

If you have a photo or other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation that scientists might appreciate that would be fit to print in the space to the right, why not send it to us via e-mail: catalyst@nih.gov; fax: 301-402-4303; or mail: *The NIH Catalyst*, Building 1, Room 333.

Also, we welcome "letters to the editor" for publication and your reactions to anything on the *Catalyst* pages.

In Future Issues...

- Stem Cells
- Prions
- Undiagnosed Diseases

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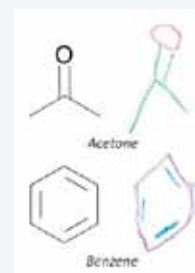
By Dan Appella, NIDDK

At ages 5 and 2, my daughter and son are very receptive to new languages. "Obayou gozaimasu," my daughter tells me she learned in pre-school. (It means "good morning" in Japanese.) "Shuey!" says my son. (It's the Chinese word for "water" that he picked up from watching "Ni Hao, Kai-Lan" on TV.) I like seeing them exposed to many languages, but in my opinion the most important one to learn is *chemistry*.

As a chemist, I speak the language of molecules every day, and teaching my kids this language feels natural. I started by teaching them the names of a few simple chemical structures, such as acetone and benzene (shown on the left side of the figure). On a nice day, we practice outside and I draw chemical structures on the asphalt driveway with sidewalk chalk.

In restaurants, I confiscate the complimentary crayons that come with the coloring place mats for kids and I start drilling them with chemical structures drawn on napkins. They are learning rapidly, as shown by their chemical artwork (on the right side of the figure). I am very proud of what they have learned, but I am sad that there are no other kids around who speak the same chemical language.

To create more friends for my kids to talk with, I now slip chemical terminology into casual conversation with other parents with the hope that they will pass the words onto their kids; so, "Please pass the sodium chloride and the piperine!"



Editor's note: Have a late-night laboratory confession? We might print it if it is indecent enough.