Fostering Communication and Collaboration

The NIH Catalyst

A Publication for NIH Intramural Scientists

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Copyrighting Right

How to avoid common copyright violations in scientific presentations and on the Web

by Stephanie Cooperstein & Christopher Wanjek

This summer a massive international meeting brought together the best minds in biomedical research, a high-profile gathering for high-profile science, perhaps not unlike the dozens of scientific meetings that NIH researchers attend.

The speakers used various materials to communicate their results and were sure to mention "all those who made this hard work possible," that is, the multitude of PIs and research staff.

Notably missing from many of the most creative presentations, however, was credit for the various literary and artistic endeavors that made the science-heavy talks all the more palatable—the classic artwork, photographs and even comic strips, for example.

See page 8 for punchline... and explanation.

The artistic work might be included to help the merely human viewing audience better relate to their complex scientific theories, or perhaps it was there to entertain, a splash of life mixed in with endless slides of cold and sterile scientific data.

Regardless of the intent, such works need to be not only properly credited but also legally obtained. Most modern literary and artistic works regardless of national origin are protected by U.S. copyright law. Works created after 1978 are protected for the lifetime of the creator plus 70 years.

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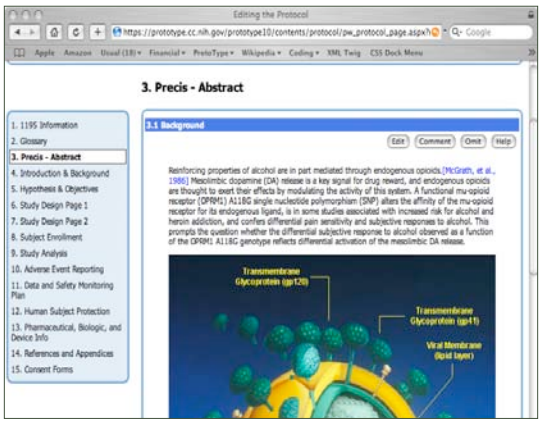
ProtoType ready for PrimeTime

by Christopher Wanjek

ProtoType, the Web-based clinical protocol writing system nearly eight years in the making, entered a new phase in September, greatly expanding its features to integrate a seamless submission process with NINDS's Protocol Tracking Management System.



ProtoType screen capture, courtesy P. Lightfoot.

The combined features of the two systems make ProtoType the most comprehensive tool available to clinical researchers confronted with the daunting task of writing a successful protocol.

Yet to call ProtoType an authoring tool sells the system short, says Clinical Center Director John Gallin, who had championed the concept since its incarnation circa 2000. ProtoType attempts to ease every step in the clinical protocol process, from crafting the protocol language, onward through the checklist of policy regulations specific to your research objectives, through reviews and revisions, and to adverse-event reporting and data sharing.

ProtoType, available to all NIH scientists, was created by protocol-writing pros who understand the pitfalls inherent in the process. They themselves have stumbled into them. Their goal was to create a user-friendly interface that would minimize guesswork and standardize the process, yet maximize flexibility. The system, updated continually, tracks institute-specific protocol requirements but never confines the principal investigator to narrow descriptions of their research.

"ProtoType was homespun by NIH investigators who envisioned a system that would handle all aspects of the protocol life cycle," said Philip Lightfoot, a systems analyst in the Department of Clinical Research Informatics and a primary contact on the ProtoType development team.

The ProtoType concept evolved from casual discussions between Gallin and institute clinical investigators. In 2002 Robert Nussenblatt, chief of the NEI Laboratory of Immunology, became very interested and assumed a leadership role in the development of a working "prototype" of ProtoType by 2002, used by NEI.

Word spread, and constructive input poured in. The most significant input came over the past year, as a major beta-testing effort by Barbara Karp, chair of

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From the Deputy Director for Intramural Research

Improving the Intramural Environment for Women Scientists


Michael Gottesman

In January 2007, Dr. Elias Zerhouni charged a committee of senior NIH scientists and science-administrators to formulate recommendations to facilitate careers for women in biomedical research. This was partially in response to a National Academy of Sciences report from a committee chaired by former DHHS Secretary Donna Shalala that pointed out the clear underrepresentation of women in many branches of science, including medical research, and partially in response to growing concern within the NIH that not enough was being done to foster career development of women in science.

I was asked to co-chair with Joan Schwartz, Assistant Director for Intramural Research, a subcommittee of the "NIH Working Group on Women in Biomedical Careers," which focused on changing the NIH work culture and improving the recruitment, retention and advancement of women at the NIH.

We have had an outstanding group of intramural scientists and NIH leadership to help us identify areas of concern and develop workable solutions. The impediments we identified to successful careers for women at the NIH included:

- a need for mentoring,
- a need for role models,
- a need to provide necessary training for professional development,
- a need to change the NIH work culture to enhance flexibilities,
- a need to enhance availability of child/family care options,
- a need to develop better recruitment strategies, and,
- a need to enhance the diversity of the NIH workforce.

Many of these problems reflect a necessity to change the culture at NIH to respect the needs of not only women but also all staff with personal responsibilities outside of the workplace. Dr. Zerhouni initiated this call for a culture change when he issued a statement entitled "Enhancing the Work Culture at NIH," which you should have received via e-mail on July 23, 2008, about the importance of respecting family and personal responsibilities and making the NIH a model family-friendly workplace.

In addition, several tangible steps were taken to address the issues listed above, which I think are an excellent start. These include:

- extending parental leave policy for NIH intramural trainees from 6 to 8 weeks in line with the extension for NRSA trainees;
- encouraging the use of the Voluntary Leave Transfer Program (VLTP) for maternity leave and development of a pilot leave bank that would make more leave available for maternity and chronic illness;
- extending the tenure-track clock by one year (with an option to opt out) to seven years (nine for clinical or population-based research) to allow a candidate extended family or sick leave;
- developing a mechanism to employ a temporary lab manager to continue lab/branch operations when a Principal Investigator is on extended medical or family leave;
- implementing a policy to review salaries on an annual basis to ensure that pay discrepancies are corrected;
- creating a subcommittee to work specifically on recruitment and retention of underrepresented groups;
- founding with several other local institutions the Mid-Atlantic Higher Education Recruitment Consortium (HERC), which will maintain a regional (Baltimore to Richmond) web-based search engine of all job listings at member institutions to enhance dual-career job searches, available as of October 2008;
- creating the trans-NIH mentoring committee; and
- working with the Foundation for Advanced Education in the Sciences (FAES) to develop a program for priority daycare spaces in a local daycare facility to facilitate tenure-track recruitments.

Obviously, this is a work in progress and additional steps will be taken to improve the situation for daycare on and off campus, including the construction of a new daycare facility as soon as funding is available. Additional steps to enable spousal recruitments, to disseminate information about workplace flexibilities, and to provide back-up childcare are in progress.

I describe some of these initiatives in the May 2008 edition of the DDIR web board, archived at <http://www.nih.gov/ddir/DDIRchive.html>. Joan Schwartz describes them in even greater detail at a forum at Lipsett Amphitheater on June 2 called "Initiatives to Promote Scientific Success in the NIH Intramural Program" with Drs. Raynard Kington and Vivian Pinn, archived at <http://videocast.nih.gov/launch.asp?14531>.

Please send me additional ideas so that we can make more progress in ensuring successful careers for women scientists at the NIH.

—Michael Gottesman, DDIR

Editor's note: See also the March-April 2008 *Catalyst* article, "Bias Against Women in Science: It's Still There, and It's Got to Go." The 2006 NAS Report, "Beyond Bias and Barriers: Fulfilling the Potential of Women in Academic Science and Engineering," is available at <http://www.nap.edu/catalog.php?record_id=11741>.

ProtoType Ready for PrimeTime

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the new neurosciences IRB, greatly improved ProtoType, making it more user-friendly with import features such as a robust reference manager, the ability to cut and paste figures, and the ability to send the protocol to the IRB and the Scientific Review Committee.

September marked the transition from beta-testing to the upgraded ProtoType's public debut.

Other features in ProtoType include an Investigational New Drug application "wizard" built with input from the FDA, automated filling of the Clinical Research Protocol Initial Review Application form (form 1195), a standard-language repository, rapid integration of NIH and other federal policies, an image library, an informed consent manager, ability to draft letters to referring physicians, ease of accommodating collaborations among intramural and extramural researchers, feedback and comment systems for coauthors and reviewers, the ability to view the full history of the protocol, the ability to compare protocols at different dates, and, of course, the possibility of keeping the protocol paperless.

Best of all, the program alerts the PI to any information gaps and guides the user on how to include the missing piece before proceeding.

ProtoType eventually will be used for adverse-event reporting, mapping research and projecting resources and will be linked to the Biomedical Translational Research Information System (BTRIS), making BTRIS a system that not only organizes data that has been collected but also data planned to be collected. ProtoType and BTRIS will assist investigators in registering protocols and reporting required outcome measures into ClinicalTrials.gov.

Other promising possibilities are the capacity to produce toxicity reports and alert PIs of trends in experimental treatments. Gallin spoke of interest in ProtoType outside of NIH, because there are no other systems like this.

ProtoType is not mandatory, but Gallin said there are so many positive aspects of the system that it would be counterproductive not to use it, even for veteran clinical researchers. In the past month 25 investigators have been trained in using ProtoType and 14 protocols are using it, in NEI, NIAAA, NIAID and NINDS. The large team behind ProtoType includes Kimberley Jarema, director of the Office of Protocol Services, who has been part of its development since the beginning.

Lightfoot briefed the NIH scientific directors on October 1, explaining how ProtoType will not show all of its value upon first use. "This is a tool built to grow with the investigator and their protocols," he said.

When you first start using it, ProtoType presents all of the data that the NIH and your IRB would like you to know regarding how to write a protocol. As you write the first protocol, you start to build your own language for procedures, your own image library and your own references. These data are then at your fingertips for the second protocol. By the third and fourth protocols, a snowball effect takes place. And when you perform yearly continuing reviews and amendments, all the information that has changed is right there for your IRB and for your collaborators.

Does ProtoType really live up to the hype? The only way to know is to try, and then provide Lightfoot and Jarema with feedback to make the system better. Prototype resides at <http://prototype.cc.nih.gov>. ■

—Eric Schaffer contributed to this article

"This is a tool built to grow with the investigator and their protocols," said Lightfoot. As you write the first protocol, you start to build your own language for procedures, your own image library and your own references... By the third and fourth protocols, a snowball effect takes place.

The ProtoType concept evolved from casual discussions between NIH Clinical Center Director Gallin and institute clinical investigators, circa 2000.

Three key members of the extensive, multi-institute ProtoType development team: Kimberley Jarema, Philip Lightfoot and Ryan Kennedy.

The Training Page

From the Fellows Committee: NIH Fellows Job Fair, S.T.E.M. Talent 2008

by Lori Keating (FDA CBER)

Fall has arrived, which means beyond a much needed respite from summer heat, it is time for the Research Festival. This year, the 21st NIH Research Festival will be held October 14–17. The entire NIH community is invited to enjoy a full program of talks and posters from the NIH intramural program's best.

In addition to learning about your colleagues' latest research developments, postdoctoral fellows reaching the end of their tenure at the NIH can explore career opportunities at a special event all day on October 16 at the Natcher Conference Center (Bethesda, NIH Building 45) called S.T.E.M. Talent 2008: A Symposium and Career Fair for Postdocs in the Capital Region. S.T.E.M. stands for science, technology, engineering and mathematics.

This offering is part of the Festival's Symposium and Career Fair for Postdocs. This year OITE and FelCom have teamed with Rockville Economic Development, Inc. (REDI), and other local organizations to provide a career fair with a goal of keeping scientific talent in the D.C. metropolitan area, working for local companies or perhaps launching new business ventures. The career fair "is designed to help local companies find the talent they need for their continued success," said Sally Sternbach of REDI.

Although local companies and organizations will be a focus, several national biotechnology and pharmaceutical companies including Regeneron Pharmaceuticals and Illumina also will be at S.T.E.M. Talent 2008. Over 40 companies and organizations are expected to attend. In addition to the companies and organizations with employment vacancies to fill, numerous workshops focused on training topics and employment opportunities will be offered.

Panel discussions include Opportunities for Career Training; Interviewing Skills; Working in Established Companies; Governments and Other Opportunities; Working in Non-Profits; Making the Move to a New Position; and Entrepreneurial Opportunities. Dr. Chad Womack, co-founder, president and chief scientific officer of NanoVec, LLC, will give a keynote address at 9:00 a.m. More information, including a list of the employers who are coming to S.T.E.M. Talent 2008, is available at <http://www.postdocconference.org>.

Whether or not you are planning to continue your career in the D.C. area, this event will be a great opportunity to see what local companies and organizations have to offer or to explore national employment options.

Job seekers, if you do attend, be prepared to impress your future employer by dressing professionally and bringing several copies of your CV and résumé. ■

From the Fellows Committee: FelCom Seminar Series, Career Development for Fellows

by Sudha Chennasamudram (FDA CBER), FelCom Publicity Subcommittee

Finding the right career path can be a challenge. To help postdoctoral fellows at the NIH, FelCom's career development subcommittee offers a series of seminars and workshops illuminating various career options and all their nuances.

These seminars and workshops, organized with support from OITE, are offered throughout the year (except during summer) as a part of an on-going series. Most of the seminars feature individuals who work in a particular field and who can tell you what it is like to do that job and the path they took to get there.

Starting a career as an independent researcher and finding funding can be a difficult task. One seminar explains how to apply for the K99/R00 research grant, a funding mechanism to support early career researchers in the transition to their own laboratory. Similarly, a seminar offered in December will help fellows interested in teaching at small colleges and primarily undergraduate institutions.

For fellows considering careers beyond the laboratory or academia, we are developing seminars on opportunities available in the field of science policy and within the federal government. The seminar series also offers information about résumé writing and interviewing.

A complete list of the seminars and events organized by FelCom's career development subcommittee for the 2008–2009 series follows. For information about upcoming career development offerings, refer to <http://felcom.od.nih.gov/subCommittee/careerDev.aspx>. For other career development seminars, see the OITE website at <http://www.training.nih.gov/trainees>. Note that many past seminars are archived at <http://videocast.nih.gov/PastEvents.asp>. We hope the series will help you find your dream job. ■

FelCom Career Development Subcommittee 2008–2009 Career Development Seminar Series

Tuesday, September 16, at 10 a.m.: CV/résumé workshop
Thursday, October 16, 11 a.m.–3 p.m.: Job Fair
Thursday, Novemer 13, 1–3 p.m.: Science Policy
Thursday, December 11, 1–3 p.m.: Small Colleges/Primarily Undergraduate Institutes
Thursday, January 15, 1–3 p.m.: Getting a Job with the Federal Government (KSAs, etc)
Thursday, February 12, 1–3 p.m.: Industry or Project Management
Thursday, March 19, 1–3 p.m.: Publishing in High-Impact Journals
Tuesday, April 7, 1–3 p.m.: K99/R00 Grants
Tuesday, May 19, all day: NIH Career Symposium

Making the Rounds at the FDA

Demystifying the FDA with two- to six-week on-site rotations

by Christopher Wanjek

To many an outsider, the Food and Drug Administration comes across as a regulatory octopus responsible for the safety of billions of dollars worth of consumer goods, from most food items, to drugs and medical devices, to cosmetics and even animal feed. The FDA estimates that it oversees items accounting for 25 cents of every dollar spent by consumers.

And somewhere within this fantastic machinery—amongst green onion recalls and approval of the latest LASIK technique—lies your future, an Investigational New Drug (IND) application, the culmination of years of basic research you want to take to the bedside. Understanding the FDA could substantially increase your odds of trouble-free application process.

The FDA, of course, is our partner in a common mission to improve the health of all Americans. To this end, the NIH and FDA have teamed up to offer short-term rotations at the Center for Drug Evaluation and Research (CDER) that include tutorials on how to prepare for an IND and on therapeutic area-specific drug-development guidelines. The rotation spins both ways, with FDA scientists spending time at the NIH to understand how we work.

The new program, over two years in the making, was spearheaded by Juan Lertora, director of the Clinical Pharmacology Program at the NIH Clinical Center.

The program is open to all scientists and is perfect for trainees and junior investigators, Lertora said. NIH participants would benefit from access to various closed-door meetings and the chance to see and participate in reviews of preclinical and clinical data on investigational drugs. Participants would make valuable contacts at the FDA, as well. The program is flexible but advanced planning is required; the rotation can start anytime and last for about two to six weeks.

Four FDA scientists have completed a rotation with clinical research teams at NCI and NIAID, but so far only one NIH scientist has gone to the FDA. Although the program officially started in 2007, it was not until this year that the FDA could work through its own administrative roadblocks to allow outsiders such unprecedented access. NIH scientists need to sign a confidentiality agreement, for example.

"We finally got the green light this year," said Lertora, who hopes the program will take off as more scientists learn about it.

Juan Lertora, director of the Clinical Pharmacology Program at the NIH Clinical Center, spearheaded the FDA rotation program.

"Now there is a mechanism."

Lertora is the point of contact for NIH scientists interested in the program, and he can be reached at lertoraj@cc.nih.gov. The rotations take place in CDER's Office of Clinical Pharmacology, led by Larry Lesko. Lertora requests that those interested should obtain approval from their fellowship Program Director at the Clinical Center and contemplate a therapeutic area of interest and proposed timeframe for the FDA rotation. Lertora would then help identify mentors at the FDA. ■

Demystifying Medicine, 2009 Schedule

The Demystifying Medicine course comprises presentations about patients, pathology, diagnosis and therapy in the context of major disease problems and current research. Primarily directed toward Ph.D. students, fellows, and staff, the course is also of interest to medical students and clinicians. The course is designed to help bridge the gap between advances in biology and their application to major human diseases. Each session includes clinical and basic science components, which are presented by NIH staff and outside invitees.

Those seeking academic credit may register with FAES. Those not seeking academic credit should register through the course e-mail list. Refer to <http://www1.od.nih.gov/oir/DemystifyingMed/> for details, or contact Win Arias at ariasi@mail.nih.gov. The course is held 4:00–6:00 p.m. in the ground floor auditorium of Building 50 on the NIH Bethesda campus. Registrants who attend more than 60 percent of the sessions and pass a computerized final exam will receive a certificate. Lectures are presented live via online streaming video, and recorded videos are available for viewing online within a few days after the live event. ■

Jan 13 Bacterial sepsis: a new epidemic and an old receptor; Tara Palmore, MD (NIAID), Gilbert Ashwell, MD (NIDDK), John Hanover, PhD (NIDDK)

Jan 20 Viral hepatitis: a global problem and the role of interferon; Jay Hoofnagle, MD (NIDDK), Katherine Zoon (NIAID)

Jan 27 HIV: the epidemic persists globally and locally; Anthony Fauci, MD (NIAID), Henry Masur, MD (CC)

Feb 3 Intestinal bacterial infections and the food chain; Stephen Savarino, MD (NMRC), John Robbins, MD (NICHD)

Feb 10 Melanoma and the sun; Thomas Hornyak, MD, Margaret Tucker, PhD, John Yang, MD (NCI)

Feb 17 Spinal cord injury and stem cells; Ron McKay, PhD (NINDS), Suzanne Groah, MD (National Rehabilitation Hospital)

Feb 24 Diabetes, Type 2: the epidemic continues; Judith Fradkin, MD (NIDDK), Lori Bonnycastle, PhD (HGRI)

March 3 Arteriosclerotic cardiovascular disease:, number one killer and the Framingham experience; Daniel Levy, MD (NHLBI), Richard Cannon, MD (NHLBI), Leslie Beisecker, PhD (NHGRI)

March 10 Fibrous dysplasia of bone and stem cells; Pamela Robey, PhD (NIDCR), Michael Collins, MD (NIDCR)

March 17 Blindness; Joram Piatigorsky, PhD (NEI), Robert Nussenblatt, MD (NEI)

March 24 Hepatocellular cancer: a global epidemic; Snorri Thorgeirsson, MD, PhD (NCI), Win Arias, MD (NICHD)

March 31 Fragile X: most common inheritable retardation defect; Walter Kaufman, MD (JHH), Karen Usdin, PhD (NIDDK)

April 7 Drug resistance and cancer; Michael Gottesman, MD (NCI), Susan Bates, MD (NCI)

April 14 Aging, progeria and heart disease; Elizabeth Nabel, MD (NHLBI), Tom Mistelli, PhD (NCI)

April 21 Excema and the skin microbiome; Julie Segre, PhD (NHGRI) , Hirsch Komarow, MD (NIAID)

April 28 Human Papilloma Virus and cancer: prevention by vaccination; Maura Gillison, MD PhD (JHH), Douglas Lowy, MD (NCI)

May 5 Multiple myeloma: diagnosis and treatment in the genomic era; Geraldine Schechter, MD, (VA), Luis Staudt, MD (NCI)

May 12 Finale: Career opportunities in biomedical science for PhDs; TBA

The Wednesday Afternoon Lecture Series (WALS)

The 2008-2009 WALS season features another full schedule of lectures by some of the world's top researchers in the biomedical sciences, to help keep NIH intramural researchers abreast of cutting edge research. Lectures are in Masur Auditorium, Bldg. 10, from 3–4:00 p.m. Updated schedule at www1.od.nih.gov/wals/schedule.htm.

September 3, 2008
Alejandro Sánchez, HHMI Investigator, University of Utah School of Medicine
"Dying Young as Late as Possible: Planarians Regeneration and Stem Cells"

September 10, 2008
Joseph Schlessinger, Professor and Chair of Pharmacology, Yale School of Medicine
"Cell Signaling By Receptor Tyrosine Kinases: From Basic Principles To Cancer Therapy"

September 24, 2008 (Dyer Lecture)
Nathan Wolfe, UCLA Professor of Epidemiology, NIH Pioneer Award Winner
"Viral Forecasting"

October 1, 2008
Ana Maria Cuervo, Albert Einstein College of Medicine, Department of Developmental & Molecular Biology
"Chaperone-Mediated Autophagy: Tales from an Old 'Picky' Broom"

October 8, 2008
Warner Greene, Director and Senior Investigator, Gladstone Institute of Virology and Immunology, UCSF
"The APOBECs: A Biodefense Against 'Retro-threats' Foreign and Domestic"

October 22, 2008 (Mider Lecture)
Elaine Ostrander, Chief of NHGRI's Cancer Genetics Branch
"Genetics and the Shapes of Dogs"

October 29, 2008 (Stetten Lecture)
Roger Kornberg, Stanford University Medical School, 2006 Nobel Prize in Chemistry
"The Molecular Basis of Eukaryotic Transcription"

November 5, 2008
Virginia Lee, Director, Center for Neurodegenerative Disease Research, UPenn Medical School
"TDP-43: A New Class of Proteinopathies in Neurodgenerative Diseases"

November 12, 2008
Judy Cameron, Professor, Oregon Regional Primate Research Center, Oregon Health & Science University
"Exercise is Good for the Brain as well as the Body: Effects on Gene Expression, Neural Functioning and Neuroprotection"

November 19, 2008
Leonard Guarente, Novartis Professor of Biology, Massachusetts Institute of Technology
"Sirtuins, Aging and Disease"

December 2, 2008
John Collier, Professor, Harvard Medical School
"Structure and Function of the Anthrax Toxin Pore"

December 3, 2008
Jon Beckwith, Professor, Harvard Medical School
"Evolution and Diversity of Pathways for Disulfide Bond Formation and Reduction"

December 10, 2008
Tobias Meyer, Professor, Stanford University Medical School
lecture title TBA; expert on systems biology

December 17, 2008 (Director's Lecture)
D. Holmes Morton, "country doctor," founder and director of the Clinic For Special Children
"A Pediatrician's Perspective on the Human Genome Project and Genomic Pediatrics"

January 7, 2009
Victor Ambros, Professor, University of Massachusetts Medical School
"MicroRNA Pathways in Animal Development"

January 14, 2009 (Astute Clinician Lecture)
Harry Dietz, HHMI Investigator, Johns Hopkins University School of Medicine
"Marfan Syndrome and Related Disorders: From Molecules to Medicines"

January 21, 2009
Martha Gray, Director, Harvard-MIT Division of Health Sciences and Technology
"Towards Imaging Biomarkers for Osteoarthritis: Surprises, Challenge, and Opportunities"

January 28, 2009
Aravinda Chakravarti, Professor, JHU School of Medicine and School of Public Health
"Human Genome Analysis, Disease Pathophysiology and Genetic Medicine"

January 29, 2009
Thomas Südhof, HHMI Investigator, Director, Center for Basic Neuroscience at Southwestern Medical Center
"Molecular Physiology of Neurotransmitter Release"

February 4, 2009
James Ntambi, Professor, University of Wisconsin, Madison
"Role of Stearoyl-CoA Desaturase-1 in Metabolism: Implication in Human Diseases"

February 11, 2009 (Cultural Lecture)
Atul Gawande, *New Yorker* columnist and Associate Professor of Surgery at Harvard Medical School
"Ignorance vs. Ineptitude: Science and the Causes of Failure in Medicine"

February 18, 2009
Steve Kay, Dean of Biological Sciences, University of California, San Diego
lecture title TBA; expert on circadian clocks

February 25, 2009
David Relman, Professor, Stanford University Medical School, NIH Pioneer Award Winner
lecture title TBA; expert on host-pathogen interactions

March 4, 2009
Janet Rossant, Chief of Research at the Hospital for Sick Children, Toronto
lecture title TBA; expert on early lineage development in the mouse embryo

March 11, 2009
Jeffrey Peters, Prof. of Env't Toxicology, Penn State Dept. of Veterinary and Biomedical Sciences
"Peroxisome Proliferator-Activated Receptors As Molecular Targets for the Treatment and Prevention of Diseases"

March 18, 2009
Christine Jacobs-Wagner, Associate Professor of Molecular, Cellular, and Developmental Biology, Yale
"Exploring the Bacterial Internal Organization: Cell Polarization and Cytoskeleton-Dependent Cell Morphogenesis"

March 25, 2009
Alfred Wittinghofer, Professor of Biochemistry, Max Planck Institute of Molecular Physiology
lecture title TBA; structural biology expert

April 1, 2009
A. James Hudspeth, HHMI Investigator, Rockefeller University Laboratory of Sensory Neuroscience
"Making an Effort to Listen: Mechanical Amplification by Myosin Molecules and Ion Channels in Hair Cells of the Inner Ear"

April 8, 2009
S. Ananth Karumanchi, HHMI Investigator, Beth Israel Deaconess Medical Center
"Pathogenesis of Preeclampsia"

April 15, 2009
Lois Smith, Professor, Children's Hospital Boston
lecture title TBA; expert on retinopathy of prematurity

April 22, 2009
Ruslan Medzhitov, HHMI Investigator, Yale School of Medicine
"Innate Host Defense: Mechanisms and Pathways

April 29, 2009
Erkki Ruoslahti, Burnham Institute for Medical Research (former President and CEO)
"Vascular Zip Codes in Targeted Delivery of Multifunctional Nanodevices"

May 6, 2009 (Director's Lecture)
Eric Nestler, University of Texas Southwestern Medical Center
"Transcriptional Mechanisms of Drug Addiction"

May 13, 2009
James Collins, HHMI Investigator, Boston University, NIH Pioneer Award Winner
lecture title TBA; expert on systems biology and reverse engineering

May 20, 2009
Tom Rapoport, HHMI Investigator, Harvard Medical School
"Mechanisms of Protein Translocation Across Membranes"

May 27, 2009
Hidde Ploegh, Professor of Biology, MIT Whitehead Institute
lecture title TBA; immunologist expert

June 3, 2009 (Gordin Lecture)
Leon Gordis, Johns Hopkins School of Public Health
lecture title TBA; expert on epidemiology of childhood and chronic diseases

June 10, 2009 (Pittman Lecture)
Susan Lindquist, Professor of Biology, MIT Whitehead Institute
lecture title TBA; expert on protein folding

June 17, 2009 (Director's Lecture)
Huda Zoghbi, HHMI Investigator, Baylor College of Medicine
lecture title TBA; expert on neurodegenerative and neurodevelopmental disorders

June 24, 2009
Karen Hsiao Ashe, Professor of Neurology and Neuroscience, University of Minnesota
"Molecular Mechanisms of Memory Loss in Alzheimer's Disease"

Spring 2009
Stefan Hell, Director, Department of NanoBiophotonics, Max Planck Institute for Biophysical Chemistry
lecture title TBA; expert on sub-diffraction-resolution microscopy

Spring 2009
John Rich, Professor, Drexel University, MacArthur Fellow
lecture title TBA; expert on public health management; men's health; violence; urban health issues

Copyrighting Right

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Automatic renewals applied to many works created prior to 1978 ensure that most works from the 20th century still have copyright protection today.

Twenty years ago, when making your scientific presentation, often you could "get away" with a minor copyright infringement—or as the lawyers say, your liability was less—because your audience was limited to the room in which you were presenting. That is, you were technically breaking the law when you used a "Peanuts" comic strip without permission from the owner, but Charles Schultz likely wasn't attending that annual meeting of your specialized professional society and was none the wiser.

Not so in 2008, when presentations not only are archived on the Web but often are videocast to a broad audience. "Take a document created for a local presentation and put it on a public Web site, and you have changed the playing field," said Dennis Rodrigues, chief of the On-Line Information Branch in the NIH Office of Communications and Public Liaison.

The ease of dissemination means that NIH researchers need to be more careful today than ever before in upholding copyright law. You could place your institute at risk for fines and yourself at risk of embarrassment.

This article addresses some common misconceptions about copyright and provides resources to help you understand the law. Obtaining permission to use protected material or purchasing rights is not difficult, as this article demonstrates with the inclusion of the "Non Sequitur" comic strip.

Copyright Defined

U.S. Copyright Law is documented in a 13-chapter, 326-page thriller, which you can download at <http://www.copyright.gov/title17/>. The 2008 *Associated Press Stylebook* captures the essence of the law, "the right of an author to control the reproduction and use of any creative expression that has been fixed in tangible form, such as on paper or computer... The types of creative expression eligible for copyright protection include literary, graphic, photographic, audiovisual, electronic and musical works."

Misconception #1: As a researcher, and thus an educator, everything I do is "Fair Use."

Fair Use is a doctrine within U.S. Copyright Law that allows for a limited use of copyrighted material without the need for the copyright holder's permission. The four factors that should be considered to determine a fair use (as stated in the Copyright Act of 1976, 17 U.S.C. § 107) are:

1. the purpose and character of the use, including whether such use is of a commercial nature or is for nonprofit educational purposes;
2. the nature of the copyrighted work;
3. the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and
4. the effect of the use upon the potential market for or value of the copyrighted work.

There's plenty of gray area here, but concerning the first element, you might have a difficult time arguing in court that your inclusion of that "Far Side" comic strip of dinosaurs smoking cigarettes (the real reason for their extinction) in your presentation at the American Lung Association meeting was for educational purposes. The comic strip was there to entertain.

The fourth element above comes into play when your inclusion of a copyrighted work infringes on the owner's potential profits. One famous case from the 1980s involved

A thin moustache demonstrates the thin line of copyright violation. There is no copyright on Leonardo da Vinci's "Mona Lisa;" there is a copyright on Marcel Duchamp's "L.H.O.O.Q.," a Mona Lisa parody made by painting a moustache and goatee on a cheap reproduction. Yet we can print the latter without permission because of its educational value in demonstrating "fair use."

The Nation magazine printing a mere 300 words from Gerald Ford's 200,000-plus-word autobiography. The case reached the U.S. Supreme Court, which ruled this was a copyright violation in part because these were arguably the most important 300 words—the reason why Ford pardoned Richard Nixon. Readers had less incentive to buy the book, unless they wanted to know about Ford's golf game.

Astronomer Phil Plait, author of *Bad Astronomy* and the forthcoming *Death from the Skies!*, uses a 30-second clip from the television program "The Simpsons" in his presentations to show how the character Bart, and indeed you, could pick up a meteorite that has just reached earth; it surprisingly is not that hot. While the clip is entertaining, it does not impinge on "The Simpsons" copyright owners' profit, convincingly has educational value, and is a stepping-stone to Plait's lecture on meteorite physics.

As you can see, sometimes there is a fine line of distinction.

Misconception #2: Few people will see it.

U.S. copyright law does consider the level of infringement on the copyright holder's rights. Playing a movie clip or displaying copyrighted work without permission to a small roomful of people does not significantly violate those rights. As the audience grows larger, however, so too does the level of infringement and your liability.

You would be prudent to remove copyright-protected material from your presentation if that presentation is to be videocast or archived, thus expanding the potential audience. Often researchers do not realize their presentations are indeed archived. Once you create your presentation and make that available to others in an electronic form, you yourself, like Gary Larson, "have lost all control of that content," said Dennis Rodrigues. "It's out of your hands, gone."

Once online, "your" inadvertent posting of copyrighted material might contain tags that notify the copyright owner about the contents. So even if the presentation is on an obscure Web site, the copyright owner might find it.

Then there's the creator's wishes to respect. Gary Larson, the creator of "The Far Side," has posted an open letter about the use of his work. "These cartoons are my 'children,' of sorts, and like a parent, I'm concerned about where they go at night without telling me," he wrote.

In general, the gratuitous use of privately-owned and copyrighted material in scientific presentations, regardless of audience size, is not prudent and would not be well-received by the government lawyers consulted for this column.

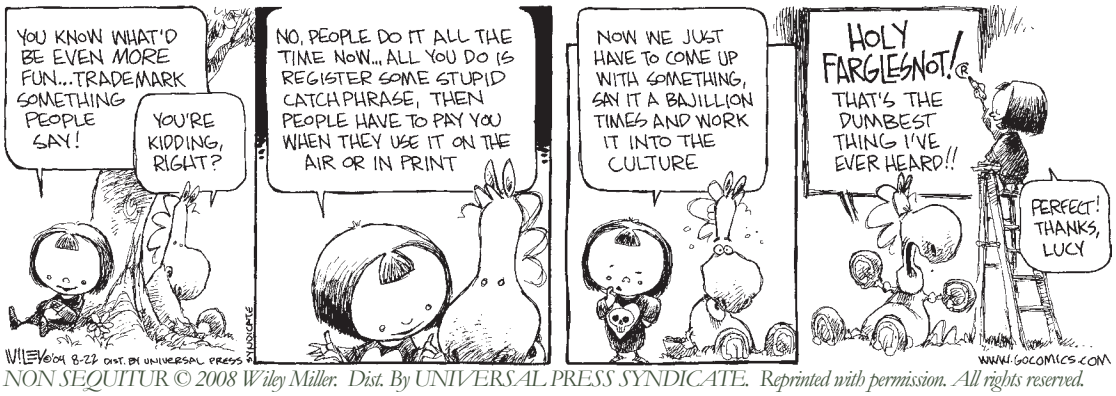
Misconception #3: I grabbed it from a government site, so it must be free to use.

This can get you into trouble for numerous reasons. For starters, it is only federal government work that cannot be copyrighted; state and local government works are copyrightable. Also, just because it is on, say, the NIH Web site, doesn't mean that no one owns the copyright.

NIH often licenses privately owned material for display on its website, but the scope of the licenses are rarely broad enough to allow the public to use the material for other than a fair use. NIH sites typically alert the public to this fact in their standard disclaimers.

Misconception #4: There was no copyright symbol, so I can use the work.

A work becomes copyright protected once it is "fixed in tangible form," that is, placed on paper or saved as an electronic file. Works without that little "circle c," ©, are still protected by copyright. The circle c may only be used to denote works that are registered in the Copyright Office. Registration of a work is



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wise because it creates a public record of the date of the work's creation, necessary before an infringement suit can be filed in the United States. If the work is registered before an act of infringement, statutory damages are available to the owner, where as only actual damages and lost profits would be otherwise available.

Misconception #5: Everyone has seen it; it must be in the public domain.

You should assume that most artistic works from the last 100 years are protected by copyright. All of Norman Rockwell's illustrations for the Saturday Evening Post, for example, are owned by Curtis Publishing. Even some folk and blues music that is labeled "public domain" do indeed have owners, a fact that has gotten many a rock musician in trouble.

Copyright protection does expire eventually. Shakespeare's works are no longer protected by copyright, but modern translations of his works are. "The Mona Lisa" ("La Gioconda") is not protected, but Marcel Duchamp's parody of the Mona Lisa with a mustache ("L.H.O.O.Q.") is protected under French copyright law until 2039—although one could place both side by side in a presentation about "what is copyright" without incurring significant liability because the educational value would render the use "fair."

For works created around the turn of the (last) century, you should research whether the copyright has been renewed. Much of John Singer Sargent's artwork remains protected, even though he produced his great works in the 19th century and died in 1925.

Suffice it to say that borrowing a Jackson Pollock piece from the midcentury for your Web site on systems biology would be a no-no.

Misconception #6: No one would go after the NIH, that bastion of good will and hard work.

Wishful thinking. The NIH is occasionally accused of copyright infringement, and this requires Department attorneys to negotiate an appropriate resolution and even defend the agency in court. A recent case involved one group not realizing that their time-limited rights to display a certain image had expired. The copyright owner apparently realized this innocent (but costly) lapse because of tags placed within the image.

As with potential acts of plagiarism, the NIH researcher is responsible for understanding the nature of ownership of works placed or referred to in a presentation or on a Web site. If you do pepper your creations with legally obtained artwork, proper credit is appropriate. Do not assume that your audience knows the name of that Italian Renaissance painting showing man and nature in symbiosis, however remotely familiar it is. And you should do your best to note the ownership status of the images and whether the images can be freely used by the public.

Getting Permission

The "Non Sequitur" comic strip by Wiley Miller included with this article is funny. But is it $75 worth of funny? That's how much *The NIH Catalyst* paid to secure the one-time rights to use the comic strip.

For *The Catalyst*, this comic strip seemed related to the topic at hand and provided some eye-candy, similar perhaps to multimedia in your presentation or on your Web site. There's little educational value. What justified the cost, in *The Catalyst* editor's opinion, is the instructional value it could provide to the readers of this article: That is, we obtained proper rights for a modest fee rather quickly; and you can, too, if you really need it.

To secure permission, *The Catalyst* identified the copyright owner, represented by Universal Press Syndicate, and submitted a request form through its website. The approval process took about a day.

Universal Press Syndicate has specific rules for use of its copyrighted material, depending on whether, for example, it is for profit or for education. The rules also vary by creator: "Calvin and Hobbes" creator Bill Watterson prohibits any online posting of his strip for educational use, but printed forms are fine; "For Better or For Worse" creator Lynn Johnston limits educational use to five strips; other times Universal Press Syndicate allows seven free uses of its comic strip for educational use per school year.

Universal Press Syndicate calculated the $75 fee by factoring several elements: For example, a one-time use of the comic strip for a nonprofit newsletter with a small audience, printed for educational purposes.

A simple Internet search can yield several companies selling rights to artistic works, which can be purchased and downloaded immediately. *New Yorker* cartoons, for example, cost about $20 for scientific presentations. Sometimes artists are willing to grant rights for free, depending on the nature of the use.

Bottom line, reprint permissions vary, and NIH researchers are responsible for understanding the extent of the permissions—and getting that agreement in writing.

What's Free... Usually

There are several government websites, such as the CDC's PHIL (http://phil.cdc.gov) and NIH's Photo Galleries (http://www.nih.gov/about/nihphotos.htm), that contain a mix of protected and copyright-free images and multimedia elements. "Items that are already free and accessible are easy to use, and relevant, with no copyright restraints," said Harrison Wein, editor of *NIH Research Matters* and *NIH News in Health*.

There are limitations, though. A search on PHIL for "lung cancer" returned only eight photographs, and the best one—one of those campy ads from the 1950s with Arthur Godfrey (who later died of lung cancer) saying how Chesterfields are healthy and mild—is protected by copyright. Sometimes you need to pay to get what you want.

Where To Go For Advice

The NIH has technical and legal experts that can help with your copyright questions, particularly about those gray areas. Most NIH institutes and centers have an Office of Communication, and they can refer your question to the Office of General Counsel if appropriate.

The Library of Congress maintains a thorough Web site on copyright at <http://www.copyright.gov>. Two keys links are to Fair Use, at <http://www.copyright.gov/fls/fl102.html>, and the FAQ at <http://www.copyright.gov/help/faq>.

The Office of Management Assessment provides information about the proper procedures for creating scientific and technical presentations, in the NIH Manual Chapters, at <http://www1.od.nih.gov/oma/manualchapters/management/1184>.

One other link of possible interest is to a list of FAQs on copyright specifically for federal employees, at <http://www.cendi.gov/publications/04-8copyright.html>, maintained by CENDI, an interagency group of senior Scientific and Technical Information managers. See especially Point 5.1.1 in the FAQs at the CENDI site. ■

Learning from Sharks: Identifying natural anticancer products found in the body

by Vanessa C. McMains (NIDDK), Special to The Catalyst

Back in the early 1990s, the shark cartilage craze was in full bloom. Inspired by a best-selling 1992 book "*Sharks Don't Get Cancer*," both healthy people and those stricken with cancer were popping pills of pulverized shark cartilage with hopes of staying healthy or even completely curing themselves of malignant tumors.

The logic, according to author William Lane, was that sharks rarely get cancer compared with most other animals, and the defining feature of their biology, aside from a healthy diet of fish, was a skeletal system made of cartilage rather than bone.

Mass hysteria ensued as holistic enthusiasts sought over-the-counter quick preventatives at the expense of the shark population. Unfortunately, shark cartilage did not live up to its reputation. Contrary to the book's bold title, sharks do sometimes get cancer. Up to 42 different types of cancer have been documented so far, including cartilage cancer.

Yet all animal cartilage does have anticancer properties. While the use of cartilage as medicine has not yet proven fruitful, NIH intramural scientists have identified unique characteristics in cartilage that someday could be exploited to slow or stop cancer growth. The research hopes to bring out the shark in all of us.

From the Ashes of Clinical Trials

Researchers have known for decades that cartilage has therapeutic properties. Studies from the late 1960s revealed that bovine cartilage reduced inflammation. Building on this, research from the 1970s found that bovine cartilage contains a substance that blocks angiogenesis and thus could check tumor growth.

The 1980s brought laboratory and animal studies and the first clinical trials testing bovine cartilage as a treatment for cancer. Gradually the research turned to shark cartilage, because pound for pound, sharks have more cartilage than cows. Also, researchers thought that shark cartilage might be more active than bovine cartilage in preventing new blood vessels from being formed.

To date over a dozen clinical trials have been conducted on shark cartilage as a cancer treatment. Seven of these studies have been published. Even though preliminary experiments in cell culture showed reduced cancer cell growth, none of the trials have yielded positive results.

The most recent clinical trials, sponsored by the NCI and the Mayo Clinic, involved a liquid extract of shark cartilage called Neovastat, administered orally. These, too, failed to produce positive results in cancer patients and have since been halted.

But the research isn't dead. Research at NIH demonstrates how following up on the anticancer properties found in cartilage or other tissues has led to new types of therapeutics. Labs are focusing on identifying specific candidates in tissues, rather than using whole slurries of dead animals, and they are showing much more promising results.

Enter the Matrix

Cartilage is composed of sparsely distributed chondrocytes and an extracellular matrix (ECM). The ECM is a web of structural proteins—such as fibronectins, collagens, laminins and proteoglycans—that provides a scaffold that holds the tissue together. Because this tissue needs to be mechanically strong, there are fewer cells and blood vessels than in other tissues.

Cartilage's unique and imposing structure makes it nearly immune to cancer growth. It is difficult for cells to penetrate through the network of ECM, thus thwarting metastasis.

"Sharks may be less likely to get cancer than humans because of their abundance of ECM, which just so happens to be a major component of cartilage," said David Hall, group leader of the NIAMS Cartilage Biology and Orthopaedics Branch, who had studied the cartilage-anticancer connection for several years before turning more of his attention to osteoporosis and arthritis.

For cancerous cells to thrive and spread, they need an abundance of nutri-

Sharks reportedly are not pleased with the use of their cartilage as a cancer cure. Photo courtesy of Dr. Dwayne Meadows, NOAA/NMFS/OPR .

David Roberts, NCI Laboratory of Pathology

ents to aid in growth and ways to escape to new tissues. Many cancers secrete high levels of matrix metalloproteases, or MMPs, which essentially chop up the ECM, allowing the cancer cells unhindered movement to invade other tissues. Cancers also secrete angiogenesis factors to create new blood vessels so that nutrients and oxygen can be brought to the tumor.

Cartilage and the ECM have protection mechanisms in place to ensure that their environments limit the movement of invading cells, MMP activity and blood vessels formation. In addition to its structural components, ECM contains regulatory proteins that control how cells behave.

While the use of cartilage as medicine has not yet proven fruitful, NIH scientists have identified unique characteristics in cartilage that someday could be exploited to slow or stop cancer growth. The research hopes to bring out the shark in all of us.

"It's the normal ECM that is a physical and biochemical barrier that has to be overcome in order for metastasis to occur," said William Stetler-Stevenson, a senior investigator in NCI's Cell and Cancer Biology Branch. "There are components of the ECM that function to suppress the process and the events associated with growth, invasion and metastasis."

Stetler-Stevenson's group's studies of the anticancer properties of ECM have lead to promising new therapies and may reveal the initial anticancer effects that were observed using shark cartilage in cell-culture studies.

There Will be Blood, Or Not

David Roberts, head of the Biochemical Pathology Section in NCI's Laboratory of Pathology, has focused on two angiogenesis-inhibiting thrombospondin proteins that are released in the ECM, TSP1 and TSP2. These proteins bind to the components of the ECM and activate receptors that tell the cell not to grow or migrate. In many cancers found in animals and humans, levels are thrombospondin are reduced, which allows new blood vessels to form and deliver a supply of fresh nutrients to the tumor.

Therapeutics have been designed to block the angiogenesis pathway based on research from Roberts' lab and others. Although they have been proven somewhat effective, they are flawed. "They extend life by several months, but there is a problem because these patients get hypertension," he said.

Roberts' lab has shown that TSP1 is a potent antagonist to nitric oxide. The lab first observed that TSP1 was 100 times less effective in cell culture assays than it was when circulating in the bloodstream. They discovered if they added back nitric oxide to the cells, TSP1 increased in potency.

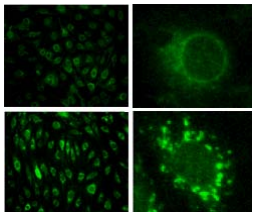
It is through inhibition of nitric oxide signaling that TSP1 is responsible for preventing angiogenesis. But "nitric oxide wears different hats in the vascular system," Roberts said. Nitric oxide is responsible, for example, for normal homeostasis of blood vessels by causing them to relax. When nitric oxide signaling is repressed, the blood vessels contract, which leads to high blood pressure.

Roberts' research has undoubtedly demonstrated that specific angiogenesis inhibitors will have to be selected more carefully to not interfere with blood pressure homeostasis.

The Matrix: Reloaded

Stetler-Stevenson works on a very different ECM protein that is a major soluble component of cartilage, called TIMP2, for tissue inhibitor of metalloproteases. As the name suggests, TIMP2 can bind and directly inhibit MMPs. MMPs are responsible for inducing cell proliferation in response to growth factors, signaling proteins that promote cell growth. Adding TIMP2 to cells inhibits MMPs, causing a reduction in growth even in the presence of growth factors.

As a result of the TIMP experiments, MMP inhibitors seemed like a great potential cancer therapy. "Drug companies invested hundreds of millions in MMP inhibitors that worked great in mouse models but had no effect in human cancers," said Stetler-Stevenson. Naively, it was not realized that MMPs are both positive and negative enhancers of growth and migration.



William Stetler-Stevenson of NCI's Cell and Cancer Biology Branch. His lab's latest research reveals: (top) when cells are immuno-stained with an integrin antibody, normal integrin is found distributed evenly on outer cell membrane; (bottom) when cells have TIMP2 added and immunostained with integrin antibody, TIMP2 causes the integrin to clump, causing programmed cell death to occur in the cells.

Stetler-Stevenson's lab created a version of TIMP2 with an extra alanine at the beginning of the protein that prevented TIMP2 from binding and inhibiting the MMPs. Surprisingly enough, this variation of TIMP2 was still able to prevent cell growth, demonstrating that TIMP2 had a function aside from MMP inhibitor. The lab soon determined that TIMP2 also binds to a cell receptor known as $\alpha 3\beta 1$ integrin, which sends signals to inhibit growth responses. This integrin response regulates normal homeostasis in the cartilage.

"Tumor cells make such a large and diverse spectrum of MMPs that acts as a sink, and the TIMP gets bound to all those and there is none left to act with the $\alpha 3\beta 1$ integrin," Stetler-Stevenson said. His group injected a small protein version of the TIMP2 with the extra alanine into tumors, which did not bind the MMPs, but bound $\alpha 3\beta 1$ integrin. The integrin then sent signals telling the tumors to not grow or migrate. These studies have been done successfully in cell culture and now the lab is moving on to mouse models.

"[TIMP2] is a good potential cancer therapeutic because it's an endogenous protein, and we're trying to use what the body already makes," Stetler-Stevenson said.

"People used to think that matrix proteins were just the glue that holds cells together," said Roberts. Sharks may have clued us in that there is something special about cartilage, and by focusing on cartilage and ECM biology, we may find cancer therapeutics right in our own bodies. ■

A Peek Inside Building 33

by Christiane Jost (NIAID) and Markus Elsner (NICHD), special to The Catalyst

What's going on in 33? It may seem that only a select few can swipe their ID, pass through the series of security checks and measures, and enter into a world of high-containment research on infectious diseases.

Others need to identify themselves to the guards from the outside via a video intercom and then navigate the metal detector like a common airline passenger, surrender cell phones should they have a camera, trade in their official NIH badge for a visitor's tag, and await escort.

Why the beefed-up security on a campus already surrounded by a fence? What kinds of pathogens are housed in there and what do Building 33 scientists do with them?

Actually, there's nothing secret about the research in Building 33, and no research in the NIH intramural program is classified. What goes on in Building 33 is similar to what goes on in any NIH lab: world-class research with the ultimate goal of saving lives and improving the quality of life.

The presence of Building 33 on the NIH Bethesda campus serves two purposes. One purpose is to expand and consolidate NIAID's research programs on viruses and bacteria that can cause serious and potentially lethal diseases and are transmitted by the inhalation route or by insect vectors, mainly mosquitoes.

The other purpose for the facility, however, was to expand the NIH's basic research on infectious diseases of global importance—those that occur naturally or those that may be caused by agents intentionally released through an act of bioterrorism. The anthrax attacks on U.S. Senate offices and news media outlets in September and October of 2001 alerted the public to the country's vulnerability to intentional dissemination of such pathogens.

The level of security in Building 33, as in any government facility, is dictated by the most dangerous pathogen samples housed within—in this case, anthrax, tuberculosis and other biosafety level 3 (BSL-3) agents. Hence the need for the guards and various security protocols, which may seem imposing or intimidating to some at the NIH who are use to a more open environment.

Although we cannot take you on a physical tour of Building 33, this article attempts to capture some of the intriguing research and facilities behind those closed doors.

Mycobacterium tuberculosis, it's back

Although the incidence rate of tuberculosis has been decreasing in high-income countries for decades, many African nations witnessed a tuberculosis epidemic in the 1990s, and the incidence rates have not decreased significantly. The disease is also prevalent in some Eastern European and Asian countries.

NIAID's Kanta Subbarao is developing strategies to combat a possible pandemic flu.

Especially worrisome is the fact that many of the new infections occur with bacteria that are resistant to the two main drugs used for tuberculosis treatment, accounting for over 20 percent of cases in some countries.

This problem is a major focus of Clifton Barry's research in Building 33. Because the emergence of multi-drug-resistant strains makes it important to develop new

Born from the Rubble of the September 11 Attacks

In September and October of 2001, on the heals of the grief, confusion and fear brought upon the nation by the September 11 attacks, five news media outlets and two U.S. Senate offices received envelopes sent through the U.S. postal service containing anthrax spores. Five people died in the attacks, and 22 others were infected with anthrax.

In February 2002, NIAID convened a Blue Ribbon Panel on "Bioterrorism and its Implications for Biomedical Research" to map out strategies for an efficient response to the bioterrorism threat. The panel's final report concluded that a "serious shortage of high-containment laboratories in which to perform experiments using dangerous pathogens" existed in the United States. NIAID's subsequent Strategic Plan called for, among other things, an expansion of the NIH's basic research capabilities on bioterrorism agents. This led to the incorporation of funding for the construction of three new high security research facilities in the 2003 budget. One was to be constructed on the main NIH campus, one in Fort Detrick, and one in Hamilton, Mont., at the Rocky Mountain Laboratories.

Construction in Bethesda commenced in November 2003 and was completed two years later. In a dedication ceremony in May 2006 the building was named in honor of a Republican Congressman from Florida, Charles William "Bill" Young, a strong proponent of biomedical research during his more than three decades in the House of Representatives. As chairman of the House Appropriations Committee he oversaw the doubling of the NIH budget from 1999 to 2004.

By March 2006, scientists began setting up the laboratories. Today about 90 percent of the space is occupied. Research ranges from basic science and vaccine development of (re-)emerging pathogens such as influenza virus and tuberculosis bacteria, to potential bioterrorism threats such as *Bacillus anthracis* or pox viruses. For the cost of $182.6 million, Building 33 provides 84,000 square foot in laboratory space, animal care facilities, offices and conference rooms to the NIH community. Most important, it more than tripled the available BSL-3 space on the NIH campus that is necessary for the work on highly pathogenic organisms.

The scientific focus of Building 33 is the development of medical protection and countermeasures against not only potential bioweapons but also potential and emerging public health threats. The United States does not have an offensive bioweapons program. President Nixon renounced the development and production of offensive bioweapons in 1969, and Congress ratified the "Biological and Toxin Weapons Convention" in 1975, making such work illegal.

NIAID's Clinton Barry studies tuberculosis.

antibiotics, his group concentrates on the identification of cellular components that can be efficient targets for new drugs. A trained chemist, Barry works on all stages of drug development, from the initial discovery of the target and the synthesis of potential inhibitors to testing in animals and early-stage clinical trials.

Barry's laboratory contains a chemistry and a molecular biology section, in addition to a BSL-3 part with a robotic system to test drug candidates in a high-throughput setup. "This is the only such testing system in the world in a BSL-3 setting, as far as I know," Barry said.

Barry moved from the Rocky Mountain Labs in Hamilton, Mont., in 1997, camping out at a NIH Twinbrook lab for several years. Among the main advantages of the Bethesda location, he cites the integrated research environment at the NIH campus and the ease of travel from Washington, which he says is especially important for maintaining his international collaborations with Korea and China.

This integrated research environment was one of the main arguments for choosing to build Building 33 in Bethesda.

Flu Anew

The influenza virus poses a challenge for the development of seasonal influenza vaccines every year. The high mutation and reassortment rate of the virus makes it difficult to develop a universal vaccine. A new vaccine is developed every year to protect against strains that are anticipated to be prevalent the next winter.

Although this approach has been very successful for seasonal influenza, the recent spread of new subtypes, as well as the fear of an influenza pandemic, have made it necessary to develop a strategy to generate vaccines against novel influenza virus subtypes. Kanta Subbarao is working on this major public health issue.

It can take several years to develop a new vaccine, but a pandemic will require an immediate response. Subbarao's group works on generating and evaluating candidate vaccines for all 16 known subtypes of the influenza A virus. Even if those vaccines prove not to be an exact match for any given strain of the respective subtype, experience with these vaccines should provide valuable lessons and make it possible to significantly speed up the development of antigenically matched vaccines.

And Anthrax, of Course

Stephen Leppla's lab is performing major research on *Bacillus anthracis*, a.k.a. anthrax, the bacterium that prompted health authorities and politicians to expand the government's research on emerging bioterrorism threats.

Anthrax was one of the first biological weapons, developed by the U.S., the Soviet Union and other countries in the 1940s and 1950s. The potential dangers of anthrax were highlighted with the 2001 anthrax attacks.

NIAID's Stephen Leppla studies anthrax.

Leppla's group researches the basic cell biology of the anthrax toxins. The group is especially interested in the receptors responsible for the uptake of the toxins and in how the processing of toxins by the cell contributes to their mechanism of action. His lab has generated mutants of one of the toxins for development of new and safer vaccines, which are now in clinical trials. (You may have noticed flyers on the NIH Bethesda campus asking for volunteers in an anthrax vaccine study).

While Leppla's research so far has had to rely on plasmids with single proteins or attenuated strains, moving into Building 33 will eventually provide him with lab space to perform experiments with virulent bacteria. Leppla is very conscious of the security requirements connected to working with potentially dangerous organisms. He especially stressed the importance of strict screening and training of personnel.

Animal Facilities

An essential part of the Building 33 resources is the integrated animal facility. Scientists can perform animal experiments under animal-BSL-3 conditions using "select agents," which are pathogens and toxins that the DHHS or USDA considers a serious threat to public health. (Refer to http://dohs.ors.od.nih.gov/select_agents_main.htm for the list.)

Staff in Building 33 are trained in animal care under ABSL-3 conditions. One assistant facility manager estimated that she had about nine months of specialized training. Standard procedures like infections or inoculations are often done by the animal technicians or research support specialists rather than the scientists themselves. Before being allowed to work with animals on their own, scientists are required to undergo additional training and have to have a proven record of animal handling.

Built to Last

Despite its light appearance with large windows and airy spaces, Building 33 was specifically planned with the possibility of a terrorist attack in mind. The building is set back from the surrounding streets, and physical barriers make it impossible to directly approach it with a vehicle. The construction included several different architectural features that protect the physical integrity of the building even under heavy impact or stress.

The design of BSL-3 laboratories themselves makes an unintentional release of bacteria and viruses extremely unlikely. Before reaching the actual laboratory one passes through two doors with an anteroom in-between. The microorganisms are handled in special biosafety cabinets that ensure product, personnel and environmental protection.

The laboratories are kept at a negative air pressure. This ensures that even in the unlikely event that pathogens are present in the laboratory air as aerosols, they are kept inside the confined laboratory area. All exhaust air is filtered through a series of High Efficiency Particulate Air Filters (HEPA) that remove more than 99.997 percent of all particles larger then 0.3 micrometers. The complexity of the air management can be appreciated by the fact that, despite its height, Building 33 has only three floors of laboratories. The interstitial space between the stories actually consists of maintenance floors that house the machinery for air pressure control and exhaust filtering.

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Colleagues

Recently Tenured

Peter R. Rapp *received his Ph.D. from the University of North Carolina at Chapel Hill in 1986 and conducted postdoctoral training at the Salk Institute for Biological Studies in La Jolla, Calif., where he was later promoted to Staff Scientist. He subsequently held faculty positions in the Center for Behavioral Neuroscience at the State University of New York, Stony Brook (1993–1997), and the Departments of Neuroscience, and Geriatrics and Adult Development, and the Kastor Neurobiology of Aging Laboratories at the Mount Sinai School of Medicine in New York (1997–2008). At Mount Sinai he served as Interim Chair of the Department of Neuroscience (2006–2008) and Co-Director of the Graduate Training Program in Neuroscience. Rapp joined NIH in July 2008 as Senior Investigator and Chief of NIA's Laboratory of Experimental Gerontology and head of the Neurocognitive Aging Section.*

Research in the Neurocognitive Aging Section (NAS) aims to understand the mechanisms of normal cognitive aging as a basis for developing effective therapeutic interventions. Our early studies in nonhuman primates succeeded in establishing a basic neuropsychological profile of aging, and we have now turned attention to the specific nature of decline, with the aim of defining effects on the component processes of declarative/episodic memory. An important goal is to test the working hypothesis that age-related decline results from large-scale restructuring of the neural networks that support normal memory. Toward this end, young and aged monkeys receive periodic high-resolution, structural MRI and corresponding fluorodeoxyglucose PET scans over the course of neuropsychological testing. Metabolic activity in the prefrontal cortex and medial temporal lobe system is then evaluated in relation to individual variability in the cognitive outcome of aging. The incidence of menstruation and urinary hormone profiles are also tracked, enabling analysis of the behavioral and imaging results in the context of naturally occurring ovarian failure.

Other collaborative studies in nonhuman primates take advantage of the uniquely valuable translational potential of this animal model. Although available evidence indicates that aging modulates the cognitive and neurobiological effects of ovarian hormone manipulation, this proposal has proved difficult to test in women. Studies currently underway in monkeys are therefore designed to compare the cognitive effects of multiple hormone replacement strategies, modeled on regimens available for clinical use in women. These investigations establish a unique framework of behavioral data for related collaborative initiatives focusing on the neurobiological effects of ovarian hormone manipulation.

Age-associated cognitive decline in humans prominently involves disrupted interactions between multiple memory-related brain systems. Ongoing studies in my lab are among the first to explore this issue in an aged rat model, using a plus-maze procedure and quantitative in situ hybridization for plasticity-related gene *Arc* to test the possibility that deficits in cognitive flexibility are coupled with functional network reorganization across the prefrontal cortex, dorsal striatum and hippocampus.

Current perspectives implicate alterations in plasticity mechanisms as a basis for cognitive aging. Related evidence indicates that promoting chromatin rearrangement permissive for gene transcription by pharmacological means enhances hippocampal long-term potentiation and benefits memory. These results predict that treatments targeting epigenetic transcriptional control may improve the neurocognitive outcome of aging. My lab is testing this proposal in both rats and nonhuman primates, coordinating behavioral assessment with the analysis of relevant molecular signatures of successful aging. Other studies are examining the resting basal status of epigenetic transcriptional control and the dynamic regulation of these mechanisms under learning activated conditions.

Progress in research on neurocognitive aging is critically supported by advances in understanding the fundamental structure and organization of memory in brain. Based on this perspective, and guided by the consensus that the medial temporal lobe system is critical for normal episodic memory, an additional line of investigation in my lab aims to identify the information-processing functions of the primate hippocampus that mediate this capacity. In these studies, subjects are tested across a battery of both standard and novel tasks, manipulating demands on candidate properties of episodic memory: 1) the temporal organization of memory, 2) memory for spatial and nonspatial context, 3) "autobiographical" memory, and 4) the relational organization of memory. Taken together, these investigations are expected to substantially advance our understanding of the structure and organization of medial temporal lobe memory in primates and, ultimately, fuel research on a variety of conditions in which memory is prominently affected. §

Javed Khan *obtained his bachelor's degree in 1984 and his master's degrees in 1989 in immunology and parasitology at University of Cambridge, England. He subsequently obtained his M.D. there and the postgraduate degree of MRCP (Membership of the Royal College of Physicians), equivalent to board certification in the United States. After clinical training in internal medicine and pediatrics as well as other specialties, he received a Leukemia Research Fellowship. In May 2001, Khan joined the NCI Pediatric Branch as a tenure-track investigator and became tenured in April 2008.*

The overall mission of my research is to leverage the power of genome-wide high-throughput "omic" approaches to improve the outcome of patients with high-risk cancers, with a focus on neuroblastoma, the most common solid extra-cranial tumor of childhood. My research program has four primary goals:

- to apply high-throughput genomics and proteomics to characterize high-risk neuroblastoma for the purpose of identifying and validating biomarkers and therapeutic targets, and translating them for clinical use;
- to develop ligands for delivery of therapeutic agents targeting the genome (i.e., chemical genomics);
- to decipher the complex interactions of DNA, mRNA, miRNA and protein with the cancer phenotype through integration, mathematical modeling and bioinformatic analysis (i.e. systems biology of neuroblastoma);

• to develop cross platform genomics databases for public release of data to stimulate collaborative research and maximally utilize high-quality data generated by our section and other investigators in the field.

My lab has applied DNA microarray techniques, artificial neural networks and other computational algorithms to identify gene-expression profiles that can diagnose the small, blue, round cell tumors of childhood as well as predict outcome in patients with neuroblastoma. Using DNA copy number changes detected by Comparative Genomic Hybridization, we have modeled how these neuroblastoma tumors progress and have provided the first proof that they do not progress from low-stage to high-stage tumors. We have molecularly characterized a large panel of pediatric xenografts that are currently used to screen new drugs for treating these malignancies. We are investigating the role of miRNAs in the development and progression of pediatric cancers, and we have mapped miRNA *mir-34a* to *1p36*, a region frequently deleted in MYCN-amplified neuroblastoma and which controls the expression level of MYCN itself. We are spearheading the use of next-generation whole-genome sequencers to perform mutational analysis, methylation and mRNA and miRNA profiling of pediatric solid tumors.

Recently my research team was awarded a grant from the Therapeutically Applicable Research to Generate Effective Treatments (NBL-TARGET) Initiative to identify targets for neuroblastoma. This is a collaboration among the NCI, Children's Hospital of Philadelphia, Children's Hospital Los Angeles and the Children's Oncology Group. We also recently have launched the NanoBioSensor Initiative to develop devices for the detection of nucleic acid hybridization using carbon nanotube and silicon nanowire transistors for diagnostic purposes. This is a collaboration among the NCI, University of Maryland and NASA. §

Back with the NIH Crew

From America to England to China and back again with a young Olympian scientist in dual training

There is an Olympian amongst us. No, it's not Michael Gottesman. As many of you have heard by now, Gottesman fouled out of the final round of the U.S. Men's Basketball qualifying trials after a scuffle with Kobe Bryant over his relentless Hack-a-Shaq antics.

Jamie Schroeder, a member of the US-Rowing Senior National Team as well as the NHLBI Laboratory of Cardiac Energetics, competed in the Beijing Olympics, placing 5th in the Men's Quad Scull, a sprinting two-kilometer race in which the Polish team ultimately captured the gold. The 27-year-old Schroeder also competed in the 2004 Athens games as part of the Men's Four.

Schroeder is participating in the NIH Oxford/Cambridge Scholars Program, an accelerated training program in which science students undertake research projects at the NIH and at either Oxford University or Cambridge University. Schroeder is also pursuing combined Ph.D./M.D. training. He is within a year of completing his Ph.D. at Oxford, and he will be transitioning to medical school at Johns Hopkins School of Medicine.

At Oxford—in addition to being a victorious Oxford Blue in the annual, storied Boat Race between Oxford and Cambridge—Schroeder developed a real-time motion-correction device to control a two-photon excitation laser-scanning microscope. He is using this tool to overcome drifting motion, a major barrier to time-course imaging of living perfused tissue.

At the Laboratory of Cardiac Energetics, Schroeder will continue tweaking his microscope and testing it in vivo, with an emphasis on heart muscle cells. As proof of concept, he has imaged the exposed tibialis anterior muscle of anesthetized mice. His team could directly assess the sarcomere lengths and mitochondrial energy state of both slow- and fast-twitch muscle fibers in the same field, along with the regional capillary flow. He hopes this quantitative muscle model can examine the effects of various physiological perturbations and provide unique in vivo insight into factors that affect the oxidative capacity of heart and skeletal muscle. The microscope can track perturbations at the cellular level and to some degree the subcellular level over an acute period of one to ten seconds, maintaining consistent resolution. Once perfected, this technique should be useful for drug and proteomic studies.

The vigorous scientific and physical training begs the question: Does Olympic-level rowing and earning a Ph.D. and M.D. constitute a triathlon?

Schroeder is part of the Physiology section of the Laboratory of Cardiac Energetics, led by Bob Balaban. The Oxford/Cambridge Scholars Program is coordinated by the NIH Graduate Partnerships Program. Refer to <http://gpp.nih.gov> and <http://oxcam.gpp.nih.gov> for more details. ■

—C. Wanjek

Jamie Schroeder of NHLBI and the NIH Oxford/Cambridge Scholars Program, with fellow members of the U.S. Olympic Rowing Team. Schroeder is second man in.

[The editor would like to note that he himself came within 10 seconds of breaking the world record for the 100-meter dash.]

Colleagues

On Tenure Track

Leslie Baier is a molecular biologist studying diabetes and obesity among the Pima, a group of Native Americans in southern Arizona who suffer from diabetes rates in excess of 50 percent. Baier is head of the Diabetes Molecular Genetics Section in the Phoenix Epidemiology and Clinical Research Branch (NIDDK). By studying the Pima, Baier hopes to uncover the genetic underpinnings of obesity and diabetes in all peoples.

Leslie Baier

Obesity and diabetes appear to be polygenetic diseases exacerbated by poor diet and inactivity. Yet identifying which genes underlie these diseases has proven to be challenging, Baier said. Variants of gene *TCF7L2*, for example, are highly associated with diabetes in Caucasians and many other ethnic groups, but Baier's group has found these variants are rare and do not have a role in increasing diabetes susceptibility in the Pima population. Conversely, Baier's group has found that variants of gene *HCRTR2*, an orexin receptor that influences eating behavior, are common among Pima but absent among Caucasians.

Baier's current work mostly involves genome-wide association studies. Using a 100,000-SNP chip, her group revealed the *HCRTR2* variants as well as variants of *A2BP1*, involved in body weight. Baier's group is pursuing follow-up studies from genotyping of a million-SNP chip using the same set of approximately 900 subjects. She is also involved in the genotyping of prediabetic patients at the NIH Clinical Research Center, where she and NIDDK colleagues are searching for disease predictors in about 600 patients. By analyzing SNPs of prediabetic patients with known phenotypes such as insulin resistance and decreased insulin secretion, Baier seeks to minimize the number of false-positives in gene-association studies for diabetes and obesity.

The Pima, as with many indigenous groups, have born witness to radical negative lifestyle changes in the past 100 years brought about by an encroaching outside culture. The name "Pima" comes from the word *pimo*, meaning "I don't understand," something this group said often to Spaniards in their early encounters. Nearly 500 years later, NIDDK is hoping to bring some understanding about diseases affecting the Pima and society at large.

Robert Nelson has worked with the Pima Indians of Arizona for over 20 years, studying type 2 diabetes with a particular focus on kidney disease. He is a member of the Diabetes Epidemiology and Clinical Research Section in NIDDK's Phoenix Epidemiology and Clinical Research Branch.

Robert Nelson

Nelson has helped identify the course and determinants of kidney disease in persons with type 2 diabetes. In the past, type 2 diabetes was primarily a disease of the elderly, but in recent years, it has increasingly been diagnosed in younger patients, who often develop the end-stage complications of diabetes, including kidney disease, in midlife. Nelson is involved in numerous projects to characterize kidney disease in type 2 diabetes. His early work focused on defining the frequency of kidney disease and its risk factors in the Pima Indians. In the early 1990s he and his colleagues began measuring glomerular function and reported on the hemodynamic changes within the kidney that occurred with the onset of diabetes and with the progression of diabetic kidney disease. By the late 1990s Nelson was performing kidney biopsies and was conducting morphometric studies of kidney structure that helped identify the loss of podocytes, or visceral epithelial cells, as an early predictor of progressive glomerular injury.

His group is also conducting clinical trials to identify medicines that slow the progression of diabetic kidney disease and outcomes studies that show that improvements in diabetes care are related to slowing in the progression of diabetic kidney disease. This year, Nelson received a Bench-to-Beside award to identify molecular markers of kidney disease development and progression and an ADA Clinical Research Award to complete the morphometry on over 120 kidney biopsies from one of his clinical trials.

[Editor's note: Leslie Baier and Robert Nelson have had long, distinguished careers at NIDDK, and they have become tenure-track investigators as part of a renewed effort by the Intramural Research Program to create a more definable career track for clinical scientists.]

—text by C. Wanjek

Iain Fraser, a biochemist and molecular biologist interested in mechanisms of cell signaling, arrived at NIH in August to set up a cell and molecular biology group in NIAID's new Program in Systems Immunology and Infectious Disease Modeling (PSIIM). At the heart of Fraser's efforts here will be the design, implementation and interpretation of screening efforts to identify and characterize the interactions among the components in immune-cell signaling networks, that could then be modeled using the software generated by the PSIIM computational biology team. A native of Scotland, Fraser spent the last eight years at Caltech, where in 2005 he became co-director of the Alliance for Cellular Signaling (AfCS) Molecular Biology Laboratory.

Iain Fraser

At Caltech, Fraser worked on a range of AfCS projects generating comprehensive data sets to model signaling networks in mouse macrophages. He led projects to develop sophisticated nucleic-acid-based reagents for RNA interference, subcellular localization studies, protein-protein interactions and fluorescent biosensors, and applied these technologies to assess how the activity state of the macrophage is altered through G–protein coupled receptor activation with a variety of ligands. He has been interested recently in mechanisms whereby the specificity of signaling crosstalk is controlled through local organization of signaling enzymes by scaffold proteins, drawing on earlier postdoc experience at the Vollum Institute in Portland, Ore.

"The integrated nature of the PSIIM is what appealed to me in accepting this position," Fraser said. His experience with the AfCS emphasized the importance of combining groups with wet lab expertise alongside data analysis and computational teams dedicated to generating quantitative models of cellular responses. This, he said, permits an iterative process of data generation, model development, experimentation directed by model predictions and model refinement, which has great potential to provide new insight to biological processes. He hopes that the PSIIM program will develop a set of quantitative tools and computational approaches that will be invaluable, not only to answering questions in the field of immunology and infectious disease, but to researchers in all biomedical disciplines. "We would like to show the NIH community what is possible by taking this approach," he said.

A Peak Inside Building 33

continued from page 13

Security Prior to Security

Although the engineering measures are essential they are far from sufficient. "The human factor is big," said Jeff Potts, the Safety and Occupational Health Manager in Building 33. And the "human factor" has two important sides.

One is the general reliability of the personnel working in the building. To avoid terrorists, criminals or emotionally unstable persons gaining access to highly dangerous pathogens, all employees have to undergo a background check by the Department of Health and Human Services (DHHS). Additional security clearance is needed to work with select agents.

In this case, both the FBI and DHHS conduct independent investigations into the personal history of each scientist. Even a bad college prank years ago can lead to a restriction of access to the microorganisms.

Equally important is that the day-to-day work is performed in a manner that guarantees optimal safety. Although an accidental release of pathogens to the environment is basically unheard of, accidental infection of scientists in the laboratory are very rare nationwide, but do happen. However, not a single incident of exposure of the people outside the lab was recorded in an internal review of more than 3 million hours of BSL-3 and -4 work at the NIH.

BSL-4 in the Offing

Prior to the construction of Building 33, NIAID did perform BSL-3 research on the Bethesda campus. The new facility has quadrupled its space of dedicated BSL-3 lab space, providing an additional 14,300 square feet.

NIAID remains committed to two BSL-3/BSL-4 facilities at Fort Detrick and Rocky Mountain Laboratories. Construction is now underway on the Fort Detrick Integrated Research Facility, a $105 million 100,000-gross-square-foot building to house laboratory space for animal research, radiology equipment, mechanical space and a waste-handling area. Construction is complete on the $66.5 million 47,000-net-square-foot BSL2, 3, 4 Integrated Research Facility at Rocky Mountain Laboratories. ■

Jeff Potts is the Safety and Occupational Health Manager in Building 33.

Biosafety Levels

Level	Agents	Practices	Facilities and Equipment	Examples
BSL-1	These agents are not generally associated with disease in healthy people.	Good microbiological practice: - Hand washing - No eating or drinking - "Sharps" precautions - Biohazard warning signs	Doors, sinks	*Bacillus subtilis*, *Naegleria gruberi*, infectious canine hepatitis virus
BSL-2	Indigenous moderate-risk agents that are present in the community and associated with human disease of varying severity.	BSL-1 plus - Training for all lab personnel in handling pathogenic agents, supervision by scientists competent in handling pathogenic agents - Most work may be performed on a bench top; procedures that might result in splashes or aerosols must be conducted in Class I or II - Biological Safety Cabinets (BSCs) - Biosafety manual defining any needed waste decontamination or medical surveillance policies	BSL-1 plus - BSCs or other physical containment devices - Lab coats, gloves, and face protection as needed - Open benchtop - Autoclave available	Hepatitis B virus, HIV, Salmonellae, Vaccinia virus, Dengue virus, some influenza strains
BSL-3	These agents are associated with human disease and may cause illness by spreading through the air (aerosol) and/ or cause diseases that may have serious or lethal consequences.	BSL-2 plus - All work must be done in BSCs - Decontamination of all waste - Decontamination of lab clothing before laundering	BSL-2 plus - Physical separation from access corridors - Class I or II BSCs or other physical containment devices - Controlled access - Protective lab clothing, gloves, and respiratory protection as needed - Self-closing, double-door access - Exhaust air is not recirculated - Negative airflow into laboratory - Design includes back-up/redundant systems	*Mycobacterium tuberculosis*, St. Louis encephalitis virus, and *Coxiella burnetii*, West Nile virus, some influenza strains, *bacillus anthracis*, *Mycobacterium tuberculosis*, St. Louis encephalitis virus
BSL-4	Dangerous and exotic agents posing high individual risk of life-threatening disease, which may be transmitted via the aerosol route and for which there is no available vaccine or therapy.	BSL-3 plus - Clothing change before entering - Shower on exit - All material decontaminated on exit from facility	BSL-3 plus - Separate building or isolated zone - Dedicated supply and exhaust, vacuum, decontamination systems - Other requirements outlined in NIH/CDC publication "Biosafety in Microbiological and Biomedical Laboratories" - All procedures conducted in Class III BSCs or Class I or II BSCs in combo with full-body, air-supplied, positive- pressure personnel suit	Marburg virus, Congo-Crimean hemorrhagic fever virus

Source: adapted from NIAID fact sheet

Up for the Challenge?

NIH Director's Challenge Award Program for FY 2009: Call for Applications

This message announces the NIH Director's Challenge Award Program for FY 2009. The program aims to encourage collaboration among intramural investigators from multiple ICs, and to support innovative and high-impact research. We plan first to select several general research topics and then to request specific applications in these research areas.

We are now accepting nominations for the research areas to be considered. Send your suggestions by email to Dr. Chuck Dearolf, OIR, at dearolfc@od.nih.gov, and put "Director's Challenge Topic" as the subject heading. Include a short (half- to one-page maximum) justification for your topic, indicating the merits and potential of the research field and how such research could take advantage of strengths or unique aspects of the NIH intramural program. We welcome input from individual investigators and from Scientific Interest Groups. Last year's topics related to three ongoing trans-NIH initiatives: Systems biology; Imaging; and Immunology, Autoimmunity and Inflammation. The deadline for submission of topics for the 2009 awards is Friday, October 17.

Once the research topics are determined and announced, applications on these topics can request up to $250,000 per year, for one or two years, and funds can be spent on personnel, equipment, and supplies. A total of $1.5 million will be awarded. Applications must relate to one of several designated scientific areas, which will be selected from suggestions submitted by intramural investigators.

The successful topics will be chosen by the Scientific Directors at the end of October. The OIR will then announce a call for applications, which will include more information on the application process and on the review criteria. The deadline for Letters of Intent will be November 28, and full applications will be due January 16, 2009. The applications must include tenured and/or tenure-track PIs from at least two ICs.

If you have any questions, contact Dr. Chuck Dearolf, Assistant Director, Office of Intramural Research, by email or at 301-402-1225. ■

And the Winners Are...

As mentioned in the editorial from the May-June 2008 issue of *The Catalyst*, the NIH Intramural Program has a new funding source called the NIH Director's Challenge Awards. Dr. Zerhouni has provided $1.5 million in new intramural funds to stimulate highly innovative and potentially high-impact research. The program is expanding in FY2009.

For FY2008, the awards were targeted to projects related to three existing trans-NIH initiatives: The Center for Human Immunology, Autoimmunity, and Inflammation, or CHI; the Imaging Initiative (Molecules to Cells); and the Systems Biology Initiative (Molecular Networks). Nine projects involving investigators from 11 ICs were awarded funding. These are listed below with the lead investigators in order of award amount.

- CHI, $500,000 (Neal Young, NHLBI)
- A Trans-NIH RNA interference facility, $440,000 (Chris Austin, NHGRI; Brian Oliver, NIDDK; and the RNAi Committee)
- Real-time imaging of vesicle fusion and retrieval at sub-diffraction limited high spatial resolution, $142,000 (Ling-Gang Wu, NINDS; Albert Jin, NIBIB; Cheng Sun, Northwestern University)
- Confocal Nanoscopy beyond the diffraction barrier in the subwavelength nanoscale, $115,000 (Amir Gandjbakhche NICHD; Paul Smith, NIBIB; Ilko Ilev FDA)
- Development of a Cryo-PhotoActivation Localization (cryo-PALM) Microscope, $103,000 (Catherine Galbraith, NIDCR; Jennifer Lippincott-Schwartz, NICHD; James Galbraith, NINDS; Thomas Reese, NINDS)
- Label-free imaging of biochemical processes in live cells, tissues and viruses using high-definition infrared microspectroscopy, $75,000 (Sergey Leikin, NICHD; Edward Mertz, NICHD; Marian Young, NIDCR)
- Proposal for a JAK-STAT initiative, $60,000 (Lothar Henninghausen, NIDDK; Warren Leonard, NHLBI; John O'Shea, NIAMS; Alfred Singer, NCI; Danielle Thierry-Mieg, NCBI; Jean Thierry-Mieg, NCBI)
- Visualization of calcium channel activity in single living cells, $50,000 (Thomas Balla, NICHD; James Russell, NICHD; Nikolai Soldatov, NIA; Larry Samelson, NCI)
- The development of a novel method for monitoring gene expression by MRI, $15,000 (Henry Levin, NICHD; Alan Koretsky, NINDS)

Charles Dearolf (dearolfc@mail.nih.gov), an Assistant Director for Intramural Research, oversees the Challenge Awards. He will lead the solicitation of ideas from senior and tenure-track investigators for exciting topics that deserve additional support. We will select several and then issue a call for proposals that both relate to one of the topics and bring together investigators from multiple ICs. Successful projects can receive two years of support for up to $250,000 per year. ■

New Center, New Award, New Jobs

The Center for Human Immunology, Autoimmunity, and Inflammation is recruiting for multiple positions. The goals of the Center are to gain a better understanding of shared immune pathophysiologies that underlie specific diseases and the role of inflammation in a wide variety of common disorders, including cancer, atherosclerosis, rheumatic syndromes, and neurologic degeneration, and to rapidly translate new knowledge into improvements in diagnosis and treatment of disease in support of the core NIH mission to improve human health.

Applications must be received by November 30, 2008. Openings include:

- Scientific Manager / Chief Operating Officer
- Experts in bioinformatics, computer science, and systems biology
- Expert in proteomics
- Staff Physician
- Protocol Specialist
- Staff Assistant

More information is available at <http://www.nhlbi.nih.gov/about/jobs>.

The SIG Beat

News from and about the NIH Scientific Interest Groups

Mitochondria Mini-Symposium, November 19

The Mitochondria Interest Group is organizing an all-day mini-symposium on November 19, culminating with a WALS lecture by Leonard Guarente of MIT, titled "Sirtuins, Aging and Disease." The meeting will take place in Masur Auditorium, Building 10 on the NIH Bethesda campus. All are welcome to attend. Abstract deadline is October 15.

The mini-symposium is titled "The Interaction and Independence of Sirtuins and Mitochondria: A few NIH Perspectives." Sponsors include the National Institute on Aging, National Institute on Drug Abuse, the Office of Dietary Supplements, and the Office of Intramural Research.

Poster setup and registration begins at 7:45 a.m. Session I is 8:30 to 10:00 a.m. with three speakers: Karen Usdin (NIDDK), "The Dark Side of SIRT1"; John Hanover (NIDDK), "Sirtuins and O-GlcNAc: Interwoven threads in the fabric of the cellular stress response"; and Chuxia Deng (NIDDK) with a title to be announced.

Following a networking break and poster session, Session II begins at 10:30 a.m. with three speakers: Curtis Harris (NCI), title TBA; David Gius (NCI), "SIRT3 is a mitochondrial tumor suppressor gene"; and Barry Hoffer (NIDA), "Premature aging in POLG knock-in Mice".

Following lunch and poster session, Session III begins at 1:00 p.m. with three more speakers: Catherine Wolkow (NIA), "IIS and FOXO signaling in C. elegans: Unraveling the webs of direct and indirect targets that regulate longevity and diapauses"; Mark Mattson (NIA), "Adaptive stress response pathways in neurons"; and Toren Finkel (NHLBI), "Sirtuin regulation of mitochondrial function".

A networking break and poster session at 2:30 p.m. will lead to the WALS lecture by Guarente. Contact Steve Zullo of the NIH Center for Scientific Review at zullost@csr.nih.gov for more information.

New SIG: Retinal Disease Interest Group (RDIG)

The process of vision is initiated in the retina, which is the most accessible part of the central nervous system, supplying over 30 percent of the sensory input to the brain. Not surprisingly, visual (and specifically retinal) dysfunction is observed in numerous syndromic and inherited genetic diseases. The goal of RDIG is to promote interactions among scientists interested in biology, pathogenesis and treatments of syndromic diseases involving visual dysfunction or diseases of the neuronal tissues. Everyone is welcome to join and participate in lively discussions. The SIG leader is James Friedman (friedmanja@mail.nih.gov; 301-443-6758). Meeting times are generally the second Tuesday of the month (except in August).

Anita B. Roberts Lecture with Jennifer Lippincott-Schwartz

Jennifer Lippincott-Schwartz will give a seminar entitled "Emerging Fluorescence Technology for the Analysis of Protein Localization and Organelle Dynamics" on October 30 at 11:30 a.m. in Lipsett Amphitheater, Bldg. 10.

The presentation is the fifth lecture in the Anita B. Roberts Lecture Series: Distinguished Women Scientists at NIH, sponsored by the NIH Women Scientist Advisors Committee and Office of Research on Women's Health announces. The series highlights outstanding research achievements of women scientists in the NIH Intramural Research Program.

Lippincott-Schwartz uses live cell imaging approaches to analyze the spatio-temporal behavior and dynamic interactions of molecules in cells. These approaches have helped to change the conventional "static" view of protein distribution and function in cells to a more dynamic view that integrates information on protein localization, concentration, diffusion and interactions that are indiscernible from protein sequences and in vitro biochemical experiments alone. Lippincott-Schwartz's projects cover a vast range of cell biological topics, including protein transport and the cytoskeleton, organelle assembly and disassembly, and the generation of cell polarity. Analysis of the dynamics of fluorescently labeled proteins expressed in cells is performed using numerous live cell imaging approaches, including FRAP, FCS and photoactivation. Most recently, her research has employed photoactivation localization microscopy, or PALM, which enables visualization of molecule distributions at high density at the nano-scale.

This seminar series is dedicated to the memory of Anita B. Roberts, chief of the NCI Laboratory of Cell Regulation and Carcinogenesis from 1995 to 2006. Prior to her death in 2006, Roberts was a research leader at NIH for 30 years. She was a pioneer in the field of carcinogenesis, autoimmune disease and wound healing, specifically contributing to much of our current knowledge of the transforming growth factor-β. Her published work is among the top 50 most-cited research papers, and she is the second most-cited female scientist in the world. This lecture series honors her role as an exceptional mentor and scientist. ■

Behavioral and Social Scientists Unite on November 12

The Office of Behavioral and Social Sciences Research (OBSSR) and a trans-NIH planning group are organizing a first-ever NIH-wide retreat for behavioral and social scientists, on November 12, 2008, at the Natcher Conference Center. Organizers expect over 300 attendees from across NIH. Confirmed speakers include NIMH Director Tom Insel, NIDA Director Nora Volkow and NIH Deputy Director Raynard Kington.

The goals of this brain-storming retreat include social networking and the sharing of common goals, as well as a discussion about scientific opportunities and what might lie ahead for this community as it applies innovative research and improves collaboration.

The retreat opens with a welcoming address at 8 a.m. by OBSSR Acting Director Christine Bachrach, followed by a Town Hall Meeting, "A Framework for the Future of BSS at NIH," and various breakout sessions throughout the day.

Registration deadline is Nov. 6. More information available at <http://conferences.thehillgroup.com/obssr/NIHretreat/>, or contact Dana Sampson of the OBSSR at sampsond@od.nih.gov.

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: Building 2, Room 2E26.

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

In Future Issues...

- Collaborations and the Ombudsman
- Exit Interview with NIH Director Zerhouni
- Pain Relief

NIH Director's Seminar Series, 2009-2009 Schedule

October 3: Susan Buchanan, Ph.D., Laboratory of Molecular Biology, NIDDK
"Import and Export Across the Bacterial Outer Membrane"

November 7: Daniel Appella, Ph.D., Laboratory of Bioorganic Chemistry, NIDDK
"Synthetic Scaffolds to Target Biological Macromolecules"

December 12: Javed Khan, M.D., Pediatric Oncology, NCI
"Translational Genomics in Neuroblastoma"

January 16: Rafael de Cabo, Ph.D., Laboratory of Experimental Gerontology, NIA
"Interventions for Healthy Aging and Longevity: Is There a Fountain of Youth?"

February 20: Ramanujan Hegde, MD, Ph.D, Cell Biology and Metabolism, NICHD
"Secretory and Membrane Protein Biosynthesis in Health and Disease"

March 6: Ling-Gang Wu, M.D., Ph.D., Synaptic Transmission Section, NINDS
"Multiple Modes of Exocytosis and Endocytosis at a Central Synapse"

April 3: Mirit Aladjem, Ph.D., Laboratory of Molecular Pharmacology, NCI
"DNA Replication: Start Right, Proceed with Caution."

May 1: Tom Misteli, Ph.D., Laboratory of Receptor Biology and Gene Expression, NCI
"Genome Cell Biology: How Genomes Function in the Cell Nucleus"

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