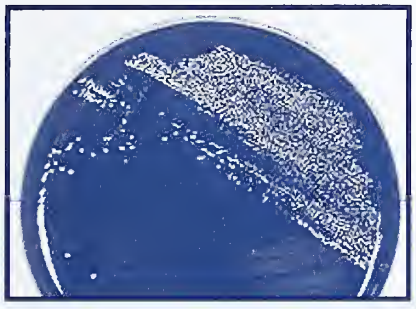
FOSTERING COMMUNICATION AND COLLABORATION

The NIH Catalyst

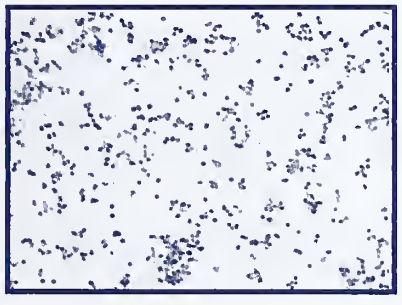
A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

NATIONAL INSTITUTES OF HEALTH ■ OFFICE OF THE DIRECTOR ■ VOLUME 15, ISSUE 4 ■ JULY–AUGUST 2007

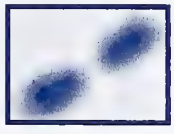
THE NEW KID IN TOWN



A buffered-charcoal yeast-extract (BCYE) plate showing the very first isolate of Granulibacter bethesdensis



Gram staining reveals a gram-negative coccobacillus, but standard microbiology laboratory procedures cannot identify the bacterium



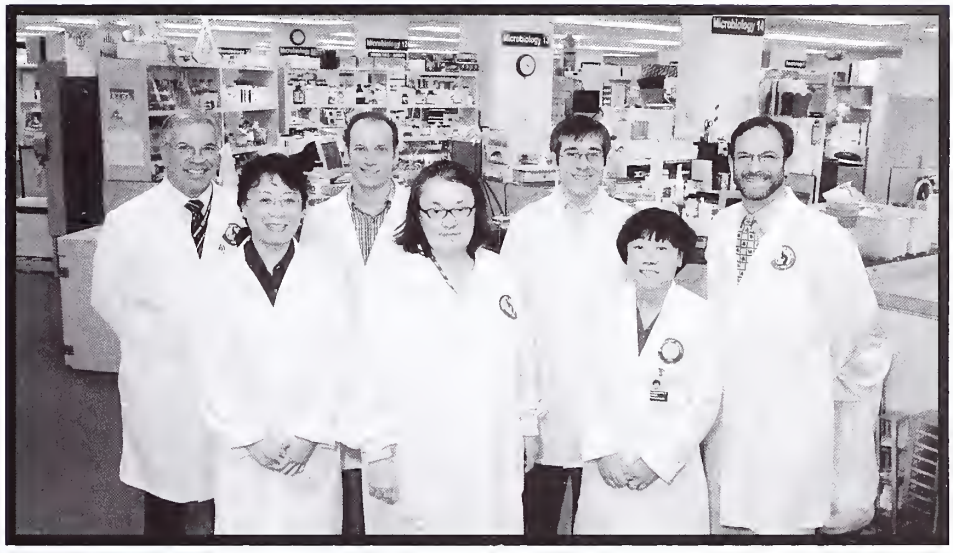
A pair of the newly discovered bacterium up close

Gene sequencing and biochemical profile reveal bacterium family, and further biochemical tests show the bacterium can grow on methanol (right), a clue to its natural environment

images courtesy of Adrian Zelazny

Bethesda Makes Another Name for Itself

CC, NIAID Researchers Uncover New Disease-Causing Bacterium



Ernie Branson

Lab Sleuths: *(left to right, back row) Patrick Murray, Adrian Zelazny, David E. Greenberg, and Steven Holland; (front row) Li Ding, Frida Stock, and Alexandra Wong*

by Christopher Wanjek

Bethesda, the famed healing bath of ancient Jerusalem and present-day home in Maryland to a certain collection of health institutes, has acquired one more historic attribute: There's now a bacterium named after it.

The newly identified bacterium is called *Granulibacter bethesdensis*, a tribute to the neighborhood where the discovery was made.

After a three-year investigation, researchers at NIAID and the CC determined that this bacterium was the cause of lymphadenitis in a patient with the rare genetic immune disorder known as chronic granulomatous disease (CGD).

The finding underscores bacteria-disease connections that still await discovery.

It took some sleuthing. *G. bethesdensis* is difficult to culture and is not only a new species but constitutes a whole new genus in a family of acetic-acid-producing bacteria never before associated with human disease. The bacterium's close cousins are used commercially in the production of vinegar.

The discovery also highlights the unique combination of talent and resources at NIH, in particular the close relationship among the CC's microbiolo-

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Postdocs: The Bread and Butter of NIH Research

Sharon Milgram

We all know what a great postdoc can do for a lab. Postdocs can bring new perspective and energy to our research programs; they can lead the charge in developing new technologies and establishing new collaborations; they can help maintain a positive lab environment and provide outstanding mentoring for summer students, postbacs, and grad students.

Strong postdocs also can be critical scientific colleagues who help us maintain our focus and strengthen our research programs. As the CC's Patrick Murray describes in the first-page story in this edition of *The NIH Catalyst*, the NIH is "blessed with bright fellows" who indeed enable many of the discoveries here.

The OITE works in collaboration with NIH ICs to oversee the recruitment and training of more than 3,800 postdocs, along with hundreds of graduate students, medical students, clinical fellows, postbacs, and summer interns. These young scientists often advance to be leaders in their chosen fields. Among NIH training alumni are several Nobel Prize winners and dozens of members of the National Academy of Sciences.

That said, identifying postdoc candidates and recruiting the very best of them to our labs is not always easy. Many new Ph.D. graduates have multiple offers and many outstanding opportunities, making postdoc recruitment a frustrating and time-consuming task.

I hope to share with you an NIH-wide plan to improve this system, which is off to a good start, and call upon you to keep the momentum going. In summer 2005, a committee of IC training directors and representatives of the OITE developed a plan to address the challenge of recruiting top postdocs. The committee proposed a two-day festival to the scientific directors that would bring 250 outstanding advanced graduate students to NIH.

In October of 2006, that plan was implemented as the first NIH National Graduate Student Research Festival (NGSRF). With help from former NIH postdocs and current members of FELCOM, we indeed hosted 250 advanced graduate students for two days of science and networking. They were selected from a list of nearly a thousand fine applicants. (See "Graduate Students Showcase Their Research at NIH—and Think about Coming Back for Postdoc Training," *The NIH Catalyst*, November-December 2006; <**http://www.nih.gov/catalyst/2006/06.11.01/page4.html**>.)

Festival participants presented their work at several poster sessions, interviewed with NIH PIs for positions, and toured the Bethesda campus. NGSRF participants also attended sessions on how NIH works, learned about exciting opportunities in the intramural research program, and heard from current postdocs, members of FELCOM, and recent alumni about professional and career development opportunities at NIH. They left not only with a positive impression of NIH in general but also with a better appreciation of the importance of NIH intramural research. It is hoped that the attendees will share their positive impressions with their colleagues at their home institutions, generating even more highly qualified postdoctoal applicants for NIH openings.

The event was highly successful from both sides; many PIs were excited about the quality of the students they had met, and some of the participants are now on campus working as postdocs. Ninety-seven percent of festival attendees who responded to a survey at the end of the event said that they would recommend the festival to a friend, and 71 percent said they were likely or very likely to accept a postdoctoral position at NIH if one were offered.

All participating NIH PIs agreed that this is a cost- and effort-effective way to recruit and interview potential postdoctoral fellows.

Plans are well underway for our second NGSRF, which will take place October 11 and 12. More than 600 applications were received, and we expect to invite up to 250 students to attend the festival. Applicants come from nearly 200 research institutions across the country and express interests ranging from nanotechnology to global public health, from tracking proteins to mapping the brain, and from molecular biology to behavioral studies.

You can help make the coming festival even more successful than last year's. Perhaps some attendee—or attendees, for that matter—would be a great fit with your lab? I encourage you to find out by participating in the festival. Go to the OITE website

<**www.training.nih.gov**>

and follow the "What's new" link to the NGSRF webpage to post a project and advertise research opportunities in your lab.

There is no need to view this as an official job posting, with all the regulations that that requires. Also, only festival invitees will have access to these postings. We will encourage festival participants to contact you directly to set up a meeting during the festival to discuss science, meet other members of your research group, and learn about opportunities in your lab. Then, come to the festival, meet our guests, and share your enthusiasm for the intramural research program.

See you at the National Graduate Student Research Festival this fall!

—Sharon Milgram
Director, OITE

'O Pioneers!': A Day to Celebrate the Visions of Pioneer Awardees —and announce the Newest Recipients

One researcher is using methods rooted in physics and engineering to understand the emergence of autoimmune diseases. Another is crafting new ways of observing protein folding inside living cells. And a third aims to build a catalog of the microbial organisms inhabiting the human body to help explain the roles of these communities in health and disease.

These scientists are among the 13 recipients of the 2006 NIH Director's Pioneer Award who will report on their research progress at the third annual Pioneer Award Symposium on Wednesday, **September 19.**

During the event in the Natcher Conference Center (Building 45), NIH Director Elias Zerhouni will also announce the newest group of awardees. The symposium agenda is at

<http://nihroadmap.nih.gov/pioneer/symposium2007/index.aspx>.

Attendance is free and registration is not required.

The NIH Director's Pioneer Award program is part of the NIH Roadmap for Medical Research and provides each awardee with $2.5 million in direct costs over five years to support highly innovative, and potentially transformative, research.

The goal is to identify scientists whose ideas could have especially significant impact but whose research proposals may be too novel or untested to fare well in the traditional peer-review process.

Researchers at all career levels and working in a broad range of disciplines—from engineering and mathematics to the behavioral and social sciences—are encouraged to apply, as long as they are interested in exploring biomedically relevant topics.

"The Pioneer Award supports particularly creative approaches to major biomedical research challenges," said Zerhouni.

"The program's annual symposium offers an exceptional opportunity to hear from an enterprising group of scientists whose cutting-edge research represents an important element of the NIH portfolio."

The symposium will begin at 8:15 a.m. with opening remarks by Zerhouni and Jeremy Berg, NIGMS director, who oversees the Pioneer Award program.

The symposium will conclude with a poster session and concurrent reception from 3:30 to 5:30 p.m. The posters will showcase the work of the 2004, 2005, and 2006 Pioneer Award recipients and members of their labs.

For more information on the 35 awardees and their research interests, see

<http://nihroadmap.nih.gov/pioneer/AwardRecipients.aspx>.

For an overview of the Pioneer Award and its history as part of the NIH Roadmap, see

<http://nihroadmap.nih.gov/pioneer/>.

Upcoming Talks by Last Year's Awardees

The talks by last year's year's awardees at the third annual NIH Director's Pioneer Award Symposium, **September 19** at Natcher Conference Center, will begin at 8:50 a.m. and end at 3:30 p.m. (with breaks and lunch interspersed). The speakers and the titles of their talks are:

- Karla Kirkegaard, Stanford University School of Medicine, Stanford, Calif.: "Dominant Drug Targets in RNA Viruses"
- Evgeny Nudler, New York University School of Medicine, New York: "New Approaches to Fight Bacterial Infections"
- David Relman, Stanford University: "It's a Jungle in There: Explorations of the Human Microbiome"
- Kwabena Boahen, Stanford University: "Neurogrid: Emulating a Million Neurons in the Cortex"
- Younan Xia, University of Washington, Seattle: "Putting Nanostructures to Work for Biomedical Research"
- Arup Chakraborty, Massachusetts Institute of Technology, Cambridge, Mass.: "Understanding Adaptive Immunity and Its Aberrant Regulation: A Crossroad of the Physical, Life, and Engineering Sciences"
- Lila Gierasch, University of Massachusetts, Amherst: "Moving the Protein Folding Problem from the Test Tube to the Cell"
- Gary Pielak, University of North Carolina at Chapel Hill: "Protein Biophysics Under Physiological Conditions"
- Thomas Kodadek, University of Texas Southwestern Medical Center at Dallas: "Monitoring the Immune System with Synthetic Molecule Microarrays: A New Route to Biomarker Discovery"
- Rosalind Segal, Dana-Farber Cancer Institute, Boston: "Proteoglycan Interactions with Sonic Hedgehog Are Selectively Required for Mitogenic Responses"
- James Sherley, Massachusetts Institute of Technology: "Making Human Adult Stem Cell Expansion Routine"
- Rebecca Heald, University of California, Berkeley: "Elucidating Mechanisms of Intracellular Scaling"
- Cheng Chi Lee, University of Texas Health Science Center at Houston: "Suspended Animation of Non-hibernating Mammals"

A Different Kind Of Peer Review

Photos and text by Christopher Wanjek

Visit the Clinical Center this summer, and you'll find that NIMH is working on ducks; NIDCR has reached a breakthrough on water lilies; and NIAID is perfecting quilts.

These institutes haven't changed research priorities. Rather, their researchers, exercising the other side of their brain, have created paintings, photographs, stained glass, and even origami for a new juried art exhibit called "Art Loves Science," on display in the Clinical Center until August 15.

Medicine and the arts have long intermingled. Paintings have graced the cover of JAMA since 1964 to emphasize the humanities in medicine. Many doctors, if not patrons of the arts, are active participants, as exemplified by the NIH Philharmonia and the NIH Community Orchestra.

Scientists (and others) appreciate the art of 30 of their colleagues at the opening reception June 14 of the Art Loves Science exhibition, which runs through August 15 at Gallery 3, first floor of the CC

NHLBI's Deanne Alpert, the impetus behind the show, transforms a tape dispenser into a work of art

Viruses dance on quilts for NIAID's Meggan Czapiga

NHGRI's Tyron Spady and his portrait of canine behavior

So it is perhaps not so strange that some NIH researchers have set aside their Matrigel medium for the more fanciful media of gouache and canvas.

The Clinical Center is well known for its contemporary art, an eclectic mix of media comprising about 3,000 original pieces mostly from local artists, displayed in eight galleries and along the building's vast network of corridors. The CC has its own art director, Crystal Parmele, who oversees procurement. Curator Lillian Fitzgerald designs and installs the exhibits and handles art sales. This latest exhibit, however, is the first to feature the art of NIH researchers exclusively.

Deanne Alpert, a postbac in NHLBI interested in painting and drawing, came up with the idea for an all-scientist exhibit upon realizing there were many musical programs at the NIH featuring local talent but nothing for the visual arts. She ultimately identified 30 other artists at the NIH interested in participating in a juried art show.

Many of the artists, like Alpert, draw inspiration from their scientific work. Alpert said that studying stained subcellular objects under the microscope has revealed striking shapes, patterns, and color combinations that she never would have

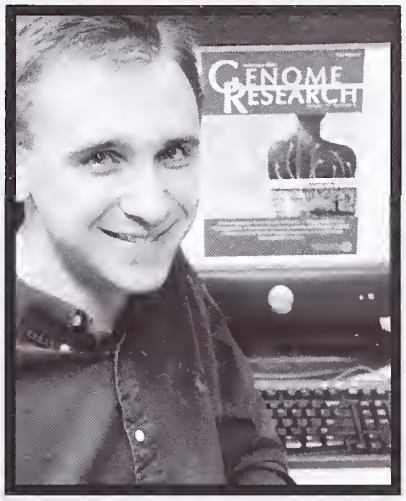
On Tenure Track

Ivan Ovcharenko is devising computational methods to cut through the so-called junk DNA in the human genome to find gene-regulatory elements concealed within.

He joined the NCBI's Computational Biology Branch this year after working as a scientist at the Lawrence Livermore National Laboratory in Livermore, Calif., for four years. With only about two percent of the three-billion-letter human genetic code known to correspond to proteins, his task of identifying and characterizing elements that regulate genes, hidden somewhere in the remaining 98 percent of the human genome, appears arduous.

But Ovcharenko has had some early success in applying evolutionary comparisons and sequence pattern analysis techniques to predict the location of gene regulators in so-called gene deserts—megabase-long stretches of DNA completely devoid of protein-coding genes.

Ovcharenko, who holds a doctorate in physics and mathematics, conducts his research much like a theoretical astrophysicist, using keen insight and computational muscle to predict patterns in nature and then partnering with molecular biologists to test his theories.



David Gilbert, DOE/Joint Genome Institute

Ivan Ovcharenko

He and his colleagues from the University of Chicago and the Lawrence Berkeley National Laboratory in Berkeley, Calif., for example, have devised a computational strategy to identify regulatory elements governing heart development during embryogenesis and to test them in vivo in transgenic mouse and zebrafish embryos. Encouragingly, many of the predicted elements were found to be driving gene expression in the heart region of developing mice and fish.

Ovcharenko uses gene-expression profiling, transcription factor binding-site analysis, and comparisons among vertebrate genomes to decipher sequence signatures for tissue-specific enhancers and repressors in the human genome. A major motivation for coming to the NIH was "the possibility to establish collaborations with researchers doing molecular biology and clinical studies," he said.

He sees a direct link between understanding the genomic encryption of gene regulators, often referred to as the second code of genomes, and developing disease screening techniques and ultimately cures, provided he gets together with the right bunch of researchers.

Ovcharenko is now working with researchers in NICHD, among other ICs. An overview of his recent work is captured in a cover article from February 2007 in *Genome Research* entitled "Predicting tissue-specific enhancers in the human genome."

—Christopher Wanjek

visualized otherwise. (Her piece in the show, a painting called "Tape Dispenser," admittedly didn't reflect this influence, but may have very well been inspired by the office supply shortage a few months ago.)

Tyrone Spady, a postdoc in NHGRI, has a photograph of his dog on display, called "Nya." His canine photographs were featured on several news media websites, such as ScienceNow and NPR, supporting the discovery by Elaine Ostrander's NHGRI lab of genes related to dog size and the muscle development of whippet race dogs. Spady studies canine behavior and is inspired by photographing the emotional complexity of dogs.

None of the pieces on display have overt scientific themes, aside from a quilt made by Meggan Czapiga, a staff scientist in the NIAID Biological Imaging Facility. Czapiga said she finds beauty in the color and shapes of viruses. Her quilt incorporates images taken straight off the confocal microscope of respiratory syncytial virus, the most common cause of bronchiolitis and pneumonia among infants.

A few of the researchers participating in the exhibit have extensive art training. Larry Bauer, a nurse consultant with the CC Patient Recruitment and Public Liaison Office, has a bachelor's degree in fine arts. His piece, called "Succulent #1," is a large, computer-enhanced photograph of a desert succulent. His use of saturated color produces a fantastical, dreamlike effect that makes the flower simultaneously familiar, even edible, yet all the while otherworldly.

The "Art Loves Science" exhibit is on the first floor of the Clinical Center in Gallery 3 near the lobby for PET and nuclear medicine. ■

Photo-enhanced enchanting desert flower, generated by the CC's Larry Bauer

Ed. Note: Exhibit art appears in color in the online *Catalyst.*

New Disease-Causing Bacterium

continued from page 1

gists and clinical investigators, who typically visit the microbiology lab every day to discuss their patient's infections.

"People are finding new bacteria all the time," said David Greenberg, an associate clinical investigator in the NIAID Laboratory of Clinical Infectious Diseases (LCID) and lead author on two papers describing the new bacterium.[1, 2]

A Rare Find

"But to find an organism that actually causes human disease, albeit in an immunocompromised population, is rare. That's what makes this very exciting."

Greenberg and his colleagues, led by Steve Holland, LCID chief, are now trying to understand what makes this bacterium virulent to CGD patients and whether it is implicated in other, more common diseases.

They also hope to determine what the immunodominant antigens are in order to develop a screening test. Such CGD research has provided insights into the nature of inflammation and immunology.

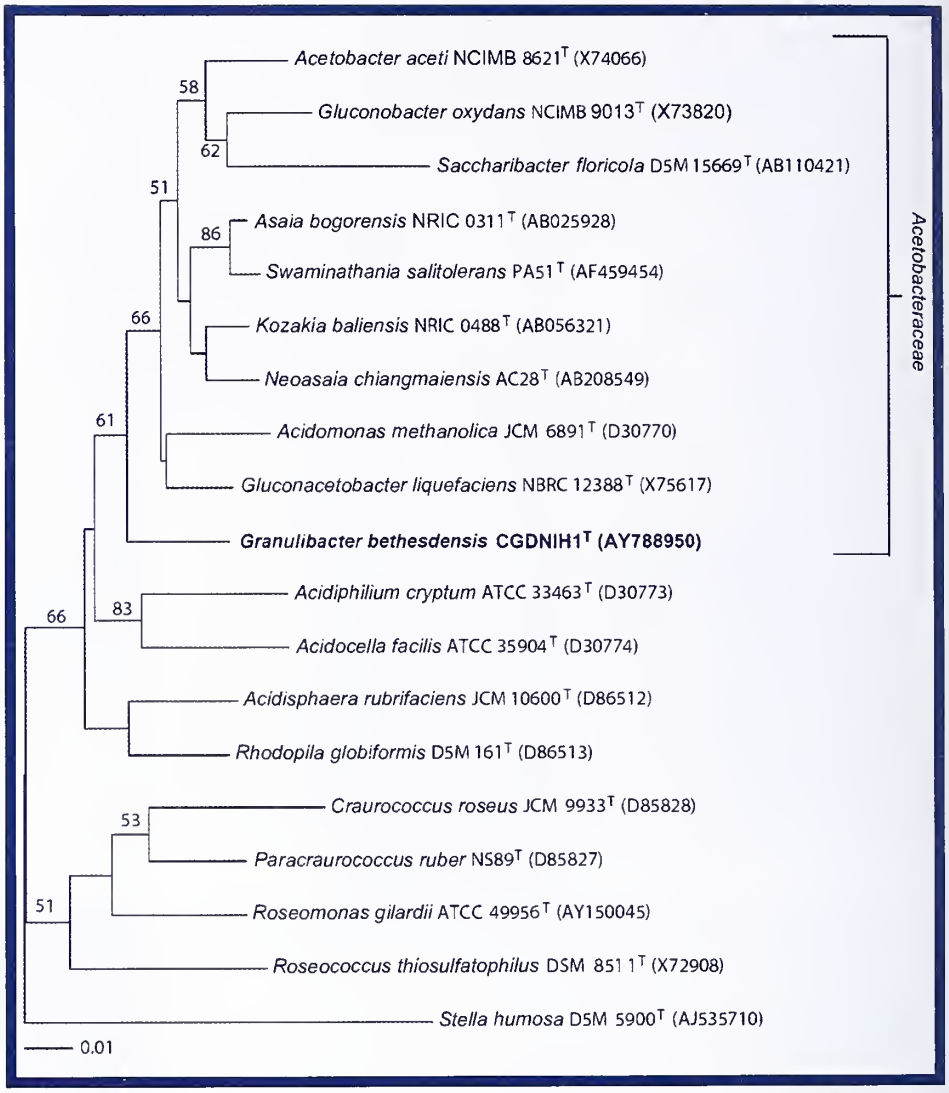
People with CGD are susceptible to serious infections of the lungs, lymph nodes, skin, and bone from seemingly unrelated bacteria and fungi. The CC is the leading research facility studying CGD, which affects about one in 250,000 people worldwide.

The CGD patient, who has since largely recovered but continues to be monitored, was first referred to the CC in 2003 after his doctors in his hometown could not determine the cause of his swollen lymph nodes.

Step 1: Culturing

Biopsies of the patient's lymph nodes were sent to to the microbiology lab, where Alexandra Wong, a medical technologist in the CC's Department of Laboratory Medicine, first discovered the bacterium growing in cultures of the biopsies.

Because many patients who come to the CC are immunocompromised and susceptible to a wide variety of infections, culture conditions are optimized for detection of bacteria that grow slowly or are fastidious. This was fortunate because this bacterium took five days to grow, about twice as long as most bacteria.



From D.E.Greenberg, et al., November 2006 (see footnote 2)

Sequencing of the 16s rRNA gene revealed that Granulibacter bethesdensis *constituted its own branch*

Traditional laboratory staining demonstrated this was a gram-negative bacterium, but standard biochemical tests couldn't pinpoint its identity.

For many labs, had they even been able to culture this bacterium, this point would have been the end of the road.

The CC-NIAID team, however, was confident that it was dealing with something unique and not simply a lab contaminant. The same bacterium was isolated from multiple biopsies, and gram-negative bacteria are not common lab contaminants.

So after consulting with Holland and Greenberg, Patrick Murray, chief of clinical microbiology at the CC, asked Adrian Zelazny, then a Fogarty fellow in the microbiology lab, to pursue other techniques for identifying the bacterium.

Step 2: Sequencing

Zelazny's first approach was to sequence the bacterium's 16S ribosomal gene, now a well-established test in the microbiology lab. These results were the first clue of the organism's uniqueness. Upon sequencing, the team found that the closest match was the Acetobacteraceae family, bacteria known to convert alcohol into vinegar.

"It still wasn't a very good match, so early on we had a sense we were deal-

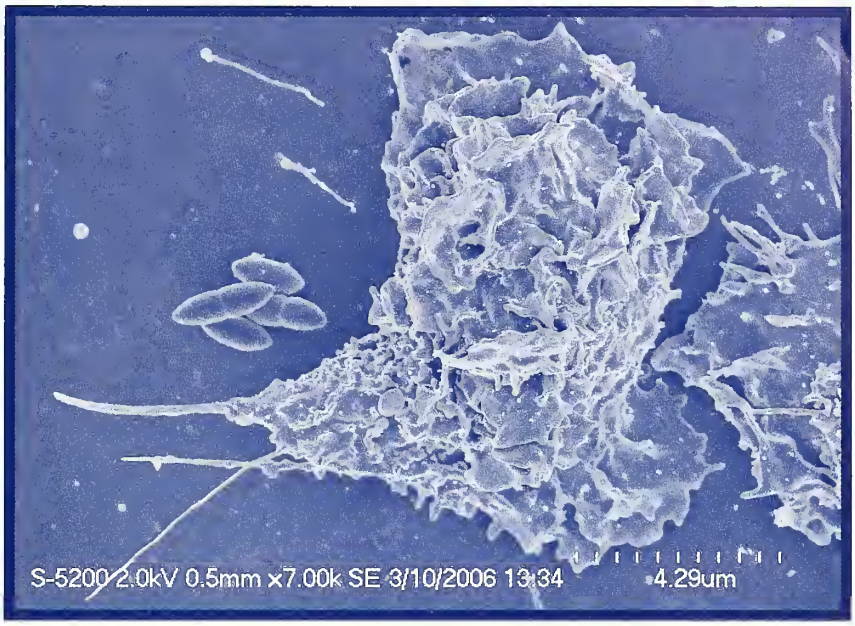
ing with something new," Greenberg said. "The question is, how do you figure out if you're dealing with a brand new species—or genus, for that matter?"

Zelazny, today a staff scientist in Holland's lab, subjected the mystery bacterium to more biochemical tests and compared the results to those from tests on the Acetobacteraceae family.

The team found that the bacterium expressed unique biological signatures. He then performed a polyphasic taxonomic study, which looks at the sequence of many genes, not just 16S. The final tests included DNA-DNA hybridization, a technique to measure the genetic distance between the new bacterium and members of the Acetobacteraceae family.

"The bacterium emerged as a distinct branch," Zelazny said, and the combination of sequencing and biochemical tests "proved it was a new member in the Acetobacteraceae family."

The outstanding question that remained was whether *G. bethesdensis* was the culprit causing lymphadenitis. Once again, the CC could accommodate.



Dave Dorward, Rocky Mountain Labs, NIAID

Scanning electron micrograph of a neutrophil about to engulf a Granulibacter bethesdensis *cluster*

Step 3: Demonstrating Pathogenicity

Years ago, Holland's lab had created a mouse model for CGD, a well-studied inherited disorder of phagocytic cells caused by a defect in the phagocyte NADPH oxidase, an enzyme responsible for creating the reactive oxidant superoxide.

Li Ding, a senior research assistant in Holland's lab, exposed the enzyme-deficient mice to *G. bethesdensis* and, sure enough, the mice developed a pathology similar to that of the original patient. More important, she could re-isolate the bacterium and grow it again, demonstrating how *G. bethesdensis* multiplied in the mice.

Further proof came after the team placed the sequence information into GenBank and word spread about the bacterium. *G. bethesdensis* was isolated from two more CGD patients with lymphadenitis at the CC and from a fourth patient with lymphadenitis in Houston. Working with Frida Stock, a research assistant in the microbiology department, the group has found that all the organisms are genetically distinct.

Greenberg is summarizing the four case studies in a third paper. So far, *G. bethesdensis* has not been isolated from the environment, but similar organisms grow on sugar cane and tropical fruit, essentially high-sugar environments where natural fermentation yields alcohol for the bacteria to feed on. Three of the four patients are from sunny climes; one is from tropical Panama. The original patient is from the north but developed his disease shortly after a visit to the Bahamas.

Many More Out There

"Why was [*G. bethesdensis*] discovered here?" Greenberg asked. "Probably because we have a spectacular microbiology lab. We have the means not only to identify things when they arise, but to take it to the next level and start asking questions: Is this really a pathogen, and how do you prove that?"

Murray attributed it to being "blessed with bright fellows" and "given the resources to pursue interesting research."

"There are a tremendous amount of diseases in the world for which there is no known etiology," Greenberg said. "And people have been suspicious that there may be an infectious connection. . . . At the end of the day there are disease-causing organisms that remain to be discovered. People should be on the lookout for them."

What's in a Name?

The naming of the new organism—carried out by Greenberg, Zelazny, Holland, and Murray—was nearly as tricky as its discovery.

The four liked the way *Granulobacter bethesdensis* rolled off the tongue, and, indeed, in the first published paper, issued April 2006,[1] they proposed this name. But by the time the second paper was issued, in November that year,[2] they had been informed that *Granulibacter,* with an *i*, is the proper word to accompany the Latin masculine adjective *bethesdensis*—and the name was changed accordingly.

Fungi are even harder to name, Murray joked. ■

Footnotes

1. D.E. Greenberg, L. Ding, A.M. Zelazny, F. Stock, A. Wong, V. Anderson, et al. "A novel bacterium associated with lymphadenitis in a patient with chronic granulomatous disease," *PLoS Pathogens* **2**, 28 April 14, 2006; online).

2. D.E. Greenberg, S.F. Porcella, F. Stock, A. Wong, P.S. Conville, P.R. Murray, et al., "*Granulibacter bethesdensis* gen. nov., sp. nov., a distinctive pathogenic acetic acid bacterium in the family *Acetobacteraceae*." *Int. J. Syst. Evol. Microbiol.* **56**, 2609 (2006).

Annual Update

Interinstitute Interest Group Directory

Web Access

Although not all the sites are up to date, nearly all the Interest Groups have websites that can be accessed through <http://www.nih.gov/sigs/sigs.html>).

Note: ** below indicates last year's listing—not verified or updated

Major Interest Groups

Cell Biology Interest Group
Meeting time: Not specified
Meeting place: Building 32, Library
Contact: Jennifer Lippincott-Schwartz
Phone: 301-402-1010; 301-402-1009
E-mail: <jlippin@helix.nih.gov>
ListServ: subscribe to CELBIO-L

**** Clinical Research Interest Group**
Meeting time and place: sponsors CC Grand Rounds once every other month
Contact: Cliff Lane
Phone: 301-496-7196
E-mail: <clane@nih.gov>

**** Genetics Interest Group**
Meeting time and place: Two all-day symposia a year to be announced
Contact: Dan Kastner
Phone: 301-496-8364
E-mail: <kastnerd@mail.nih.gov>
ListServ: subscribe to <GIG-L@list.nih.gov>

Immunology Interest Group
Meeting time (seminar): Each Wednesday (except summer), 4:15 pm
Meeting place (seminar): Building 10, Lipsett Auditorium
Contact 1: Ron Germain
Phone: 301-496-1904
E-mail: <rgermain@niaid.nih.gov>
Contact 2: Brian Kelsall
Phone: 301-496-7473
E-mail: <bkelsall@niaid.nih.gov>
ListServ: subscribe to IMMUNI-L by joining the interest group at its web site

**** Molecular Biology/Biochemistry Interest Group**
Meeting time and place: No regular meetings. IG heads meet yearly to consider WALS speaker nominations
Contact: Carl Baker
Phone: 301-435-1240
E-mail: <ccb@nih.gov>

Neuroscience Interest Group
Meeting time and place: Check website
Contact 1: Kenton Swartz
Phone: 301-435-5652
E-mail: <swartzk@ninds.nih.gov>
Contact 2: Bruce Cumming
Phone: 402-8097
E-mail: <bcg@lsr.nei.nih.gov>

Structural Biology Interest Group
Meeting time and place (2006-07): Usually 3rd Thursday, 4:00 pm, Building 50, first floor conference room; notices by e-mail and on the SBIG website
Contact 1: Anna Panchenko
Phone: 301-435-5891
E-mail: <panch@ncbi.nlm.nih.gov>
Contact 2: Doug Sheeley
Phone: 301-594-9762
E-mail: <sheeleyd@mail.nih.gov>
To register for e-mail announcements, join SBIG at <www.nih.gov/sigs/sbig>

Other Interest Groups

14-3-3 Proteins Interest Group
Meeting time: Usually the third Wednesday, 4:00–5:00 pm
Meeting place: Building 40, First-floor Conference Room
Contact 1: David C. Klein
Phone: 301-496-6915
E-mail: <kleind@mail.nih.gov>
Contact 2: Surajit Ganguly
Phone: 301-451-6399
E-mail: <gangulys@mail.nih.gov>

Advanced Technologies Interest Group
Meeting time and place: Check the website
Contact: Steven Hausman
Phone: 301-402-1691
E-mail: <hausmans@mail.nih.gov>

AIDS Interest Group
Meeting time and place: TBA
Contact: Leonid Margolis
Phone: 301-594-2476
E-mail: <margolis@helix.nih.gov>
ListServ: subscribe to AIDSINTG-L

Animal Well-Being Interest Group
Meeting time: quarterly
Meeting place: Building 14G, large conference room; occasionally hosts speakers on campus
Contact: Jim Weed
Phone: 301-435-7257
E-mail: <weedj@mail.nih.gov>

Apoptosis Interest Group
Meeting time: 1st Monday, 4:00 pm
Meeting place: Bldg 49, Room 1 50/59 AB
Contact 1: Richard Youle
Phone: 301-496-6628
E-mail: youle@helix.nih.gov
Contact 2: Yves Pommier
Phone: 301-496-5944
E-mail: <yp4x@nih.gov>

Behavioral and Social Sciences Interest Group
Meeting time: Varies; lecture series
Meeting place: See NIH Calendar of Events
Contact: Ronald Abeles
Phone: 301-496-7859
E-mail: <abeles@nih.gov>

Bioethics Interest Group
Meeting time: 1st Monday (except 3rd Monday following holidays; usually does not meet during summer), 3:00 pm
Meeting place: Natcher, Room D, or Building 31, conference room; check yellow sheet or web•site
Contact: Miriam Kelty
Phone: 301-229-5639; 301-496-9322
E-mail: <keltym@mail.nih.gov>
Sign up at <http://BIOETHICSinterestgroup@list.nih.gov/>

Biomedical Computing Interest Group
Meeting time: 1st three Thursdays, 3:00 pm; 4th Thursday, 5:30 pm (evening socials on 5th Thursdays; dark Aug & Dec)
Meeting place: Building 10, Room 2C116 (Medical Board Room)
Contact 1: Jim DeLeo
Phone: 301-496-3848
E-mail: <jdeleo@nih.gov>
Contact 2: Carl Leonard
E-mail: <cleonard@cc.nih.gov>
ListServe: subscribe to BCIG-L

Biophysics Interest Group
Meeting time and place: Holds seminars and conferences; does not meet regularly
Contact: Peter Basser
Phone: 301-435-1949
E-mail: <pjbasser@helix.nih.gov>

Biosciences Business Interest Group
Meeting time: Monthly, 12:00–1:00 pm
Meeting place: Building 37, 4th Floor Conference Room (4041/4107)
Contact 1: Val Bliskovsky
Phone: 301-435-7249
E-mail: <bliskovv@mail.nih.gov>

Calcium Interest Group
Meeting time and place: Not regularly scheduled at this time
Contact 1: Arthur Sherman
Phone: 496-4325
E-mail: <asherman@nih.gov>
Contact 2: Indu Ambudkar
Phone: 301-496-1478
E-mail: <iambudkar@dir.nidcr.nih.gov>
ListServ: Subscribe to CALCIUM-L

Cancer CAM Research Interest Group
Meeting time and place: Varies
Contact: Jeffrey White
Phone: 301-435-7980
E-mail: <jeffreyw@mail.nih.gov>

Chemistry Interest Group
Meeting time: Periodic seminars
Meeting place: Varies
Contact 1: John Schwab
Phone: 301-594-3827
E-mail: <schwabj@nigms.nih.gov>
Contact 2: Kenneth Kirk
Phone: 301-496-2619

Chromatin and Chromosomes Interest Group
Meeting time: One Tuesday a month, 4:00 pm
Meeting place: Building 41, Conf. Room
Contact: David Clark
Phone: 301-496-6966
E-mail: <clarkda@mail.nih.gov>

Chronobiology Interest Group
Meeting time: 1st Wednesday, almost monthly, 4:00–5:00 pm; check website
Meeting Place: Building 49, Rm 6A46, or USUHS Rm A2054
Contact: Steven Coon
Phone: 301-451-6622
E-mail: <coons@mail.nih.gov>

Clinical Applications of Stem Cells Interest Group
Meeting time and place: To be announced; see listing for Stem Cell Interest Group
Contact: Manfred Boehm
Phone: 301-435-7211
E-mail: <boehmm@nhlbi.nih.gov>

Clinical Pharmacology Interest Group
Meeting time: 2-3 times a year in conjunction with special lectures in the NIH Principles of Clinical Pharmacology course, 6:30– approx. 7:45 pm
Meeting place: Building 10, Lipsett Amphitheater
Contact 1: Juan Lertora
Phone: 301-496-9425
E-mail: <lertoraj@mail.cc.nih gov>
Contact 2: Donna L. Shields
E-mail: <dshields@mail.cc.nih.gov>

Cognitive Neuroscience Consortium
Meeting time: Every two months, last Wednesday, 4:15 pm
Meeting place: NSC Building, Room 2172 (starts September 2007; Extramural Program Directors' forum: last Friday every 3rd month, 3:00 pm, NSC Building, Conf. Room 2120, starts October 2007)
Contact: Emmeline Edwards
Phone: 301-496-9248
E-mail: <ee48r@nih.gov>

Critical Illness and Injury Interest Group
Meeting time and place: Varies (the next formal meeting will be held in conjunction with the Symposium on the Functional Genomics of Critical Illness and Injury, Nov. 14–15, Natcher; for details, see <http://www.strategic results.com/fg5>.
Contact 1: Anthony Suffredini
Phone: 301-402-3485
E-mail: <asuffredini@cc.nih.gov>
Contact 2: Scott Somers
E-mail: <somerss@nigms.nih.gov

Cytokine Interest Group
Meeting time: three to four symposia/year
Meeting place: Varies; one symposium/ year at NCI-Frederick
Contact 1: Daniela Verthelyi
Phone: 301-827-1702
E-mail: <daniela.verthelyi@fda.hhs.gov>
Contact 2: Thomas Wynn
E-mail: <twynn@niaid.nih.gov>

Data Resources Sharing Interest Group
Meeting time: 4th Wednesday, 3:00-4:30 pm
Meeting place: Rockledge 1 (6705 Rockledge Dr.), Room 5147
Contact 1: J.P. Kim
Phone: 301-435-0679
E-mail: <jpkim@nih.gov>
Contact 2: Marilyn Miller
Phone: 301-496-9350
E-mail: <millerm@nia.nih.gov>

** **Dendritic Cell Interest Group**
Meeting time and place: TBA
Contact 1: Uri Lopatin
Phone: 301-496-8490
E-mail: <ulopatin@niaid.nih.gov>
Contact 2: Brian Kelsall
Phone: 301-496-7473
E-mail: <bkelsall@mail.nih.gov>

** **Diabetes Interest Group**
Meeting time: ~ Every six weeks, usually Tuesday, usually 3:00 pm
Meeting place: Building 10, Lipsett
Contact 1: Eric Liu
Phone: 301-451-9809
E-mail: <ericliu@imil.nih.gov>
Contact 2: Derek LeRoith
E-mail: <derek@helix.nih.gov>

DNA Repair Interest Group
Meeting time: 3rd Tuesday, 12:30 pm
Meeting/Videoconference: Natcher, Room J; GRC (Baltimore), Room 1E03; FCRDC, Building 549, Conf. Rm. A; NIEHS (Research Triangle Park, NC) Building 101, Room B200; SUNY, Stony Brook; Univ. of Texas, M.D. Anderson Cancer Center, Smithville; Lawrence Livermore National Laboratory, Livermore, CA; Brookhaven National Laboratory, Upton, NY; Univ. of Michigan, Ann Arbor; Univ. of Kentucky, Lexington; Univ. of Pittsburgh, Pittsburgh, PA; Univ. of North Carolina, Chapel Hill; Oregon Health and Science Univ, Portland; Wake Forest Univ., Winston-Salem, NC
Contact 1: Kenneth Kraemer
Phone: 301-496-9033
E-mail: <kraemerk@nih.gov>
Contact 2: Vilhelm Bohr
E-mail: <vbohr@nih.gov>

Domestic Violence Research Interest Group
Meeting time and place: To be announced
Contact: John Umhau
Phone: 301-496-7515
E-mail: <umhau@nih.gov>

Drosophila Interest Group
Meeting time: 3rd Tuesday, 1:15 pm
Meeting place: Building 6B, Room 4B429
Contact: Jim Kennison
Phone:301-496-8399
E-mail: <James_Kennison@nih.gov>

Drosophila Neurobiology Interest Group
Meeting time: Every other Friday, 12:00 noon (check website for schedule)
Meeting place: Porter Neuroscience Research Center (Bldg 35), Room BB-1000
Contact: Chi-hon Lee
Phone: 301-435-1940
E-mail: <leechih@mail.nih.gov>

Drug Discovery Interest Group
Meeting time: Usually one Thursday a month, 3:00 pm
Meeting place: Building 37, 6th-floor conference room (Rm. 6041)
Contact: John N. Weinstein
Phone: 301-496-9571
E-mail: <weinstein@dtpax2.ncifcrf.gov>

Economics Interest Group
Meeting time and place: Varies
Contact 1: James A. Schuttinga
Phone: 301-496-2229
E-mail: <js41z@nih.gov>
Contact 2: Agnes Rupp
E-mail: <ar24f@nih.gov>

Emergency Preparedness and Biodefense Interest Group
Meeting time: 1st Thursday, 3:00 pm
Meeting place: Building 50, ground-floor conference room
Contact 1: Jeffrey Kopp
Phone: 301-594-3403
E-mail: <jeffreyk@intra.niddk.nih.gov>
Contact 2: Mike Bray
Phone: 301-451-5123
E-mail: <mbray@niaid.nih.gov>

End of Life Interest Group
Meeting time: 3rd Thursday, 3:00 pm
Meeting place: NINR Conference Room, 6701 Democracy Blvd., Suite 710
Contact: Alexis Bakos
Phone: 301-594-2542
E-mail: <bakosa@mail.nih.gov>

Epidemiology and Clinical Trials Interest Group
Meeting time and place: Varies (subscribe to ListServ for notices)
Contact: Martina Vogel-Taylor
Phone: 301-496-6614
E-mail: <martinav@nih.gov>
ListServ: subscribe to Epidem-L at <listserv@list.nih.gov>

Epilepsy Interest Group
Meeting time and place: Seminars and annual Data Blitz session announced by e-mail and at website
Contact: William Theodore
Phone: 301-496-1505
E-mail: <theodorw@ninds.nih.gov>

Epigenetics Interest Group
Meeting time: Last Thursday, 3:00 pm
Meeting place: EPN (6130 Executive Blvd.) Conference Room G
Contact: Mukesh Verma
Phone: 301-594-7344
E-mail: <Vermam@mail.nih.gov>

Flow Cytometry Interest Group
Meeting time: 2-3 times/year
Meeting place: Usually Building 10, Lipsett
Contact 1: William Telford
Phone: 301-435-6379
E-mail: <telfordw@mail.nih.gov>
Contact 2: James Simone
E-mail: <simonej@mail.nih.gov>

Interinstitute Interest Group Directory

Fluorescence Interest Group
Meeting time: Usually even Fridays, 4:00 pm; see website; join to receive upcoming events e-mail
Meeting place: Building 10, usually Room 5N264
Contact: Jay Knutson
Phone: 301-496-2557
E-mail: <jaysan@helix.nih.gov>
Contact 2: Dan Sackett
E-mail: <sackettd@mail.nih.gov>

Free Radical Interest Group
Meeting time: Monthly, in conjunction with the Oxygen Club of Greater Washington, D.C., Friday, 3:00 pm; annual regional symposium and banquet (20th Anniversary Symposia and Banquet to be held this year July 27; check website)
Meeting place: Radiation Biology Conference Room, Building 10, B2.5 level
Contact: Michael Graham Espey
Phone: 301-496-7511
E-mail: <SP@nih.gov>

Genomics and Bioinformatics Interest Group
Meeting time: Usually one Thursday a month, 3:00 pm
Meeting place: Building 37, 6th-floor conference room (Rm. 6041)
Contact: John N. Weinstein
Phone: 301-496-9571
E-mail: <weinstein@dtpax2.ncifcrf.gov>

Glycobiology Interest Group
Meeting time and place: Varies
Contact 1: Maria Manzoni
Phone: 301-846-1776
E-mail: <mm1070o@nih.gov>
Contact 2: Diana Blithe
Phone: 301-435-6990.
E-mail: <blithed@nih.gov>
ListServ: Subscribe to GLYCO-L@LIST.NIH.GOV

GTP Binding Proteins Interest Group
Meeting time: Irregular
Meeting place: FAES Social & Academic Ctr.
Contact: R. Victor Rebois
Phone: 301-496-9168
E-mail: <reboisv@nidcd.nih.gov>

Handheld Users Group (HUG)
Meeting time and place: check the website
Contact: Ben Hope
Phone: 301-594-6473
E-mail: <tallguy@nih.gov>

Hard Tissue Disorders Interest Group
Meeting time: Day varies, 9:30 am
Meeting place: Building 30, Room 117
Contact: Pamela Robey
Phone: 301-496-4563
E-mail: <probey@dir.nidcr.nih.gov>
Contact 2: Michael Collins
Phone: 301-435-1689

Head and Neck Cancer Interest Group
Meeting time and place: To be announced
Contact 1: Wendy Weinberg
Phone: 301-827-0709
E-mail: <wendy.weinberg@fda.hhs.gov>
Contact 2: Carter Van Waes
Phone: 301-402-4216
E-mail: <vanwaesc@nidcd.nih.gov>

**** Health Services Research Interest Group**
Meeting time: Quarterly (day, time, and place to be announced);
Contact: Jack Stein
Phone: 301-443-4060
E-mail: <js413y@nih.gov>

HIF (Hypoxia Inducible Factor) Interest Group
Meeting time: Quarterly
Meeting place: Building 10, Hatfield 2-3750
Contact: Tawnya McKee
Phone: 301-846-1943
E-mail: <mckee@ncifcrf.gov>
Website: <http://ccr.cancer.gov/faculties/faculty.asp?facid=457>

**** History of Biomedical Research Interest Group**
Meeting time: Second Tuesday, 1:00 pm
Meeting place: Varies; check web site
Contact 1: Office of NIH History
Phone: 301-496-6610
Contact 2: Buhm Soon Park
E-mail: <parkb@od.nih.gov>

HTS Assay Development Interest Group
Meeting time and place: Varies; check website
Contact 1: Ingrid Li
Phone: 301-443-1421
E-mail: <ili1@mail.nih.gov>
Contact 2: James Inglese
Phone: 301-496-7029
E-mail: <jinglese@mail.nih.gov>

Image Processing Interest Group
Meeting time and place: Distributed by e-mail and on <image.nih.gov>
Contact 1: Benes Trus
Phone: 301-402-7676
E-mail: <Benes_Trus@nih.gov>
Contact 2: Matt McAuliffe
Phone: 594-2432

Infectious Disease Imaging Interest Group
Meeting time: Tuesday or Thursday, 3:00 pm (check website)
Meeting place: Building 50, ground-floor Conference Room
Contact: Mike Bray
Phone: 301-451-5123
E-mail: <mbray@niaid.nih.gov>

Integrative Neural-Immune Interest Group
Meeting time and place: To be announced
Contact: Socorro Vigil-Scott
Phone: 301-496-9255
E-mail: <vigilscs@mail.nih.gov>

Integrative Neuroscience Interest Group
Meeting time: Alternate Thursdays, 4:00 pm
Meeting Place: Building 49, Room 1A51
Contact: Bruce Cumming
E-mail: <bgc@lsr.nei.nih.gov>

Inter-Agency Image-Guided Interventions Group
Meeting time: TBA
Meeting Place: NIBIB, 6707 Democracy Blvd, Bethesda, Suite 200, Room 223
Contact: John Haller
Phone: 301-451-4780
E-mail: <hallerj@mail.nih.gov>

**** In Vivo NMR Interest Group**
Meeting time: Varies
Meeting place: Building 10, Room B1N256
Contact: Jeff Duyn
Phone: 301-594-7305
E-mail: <jhd@helix.nih.gov>

Knowledge Management Interest Group
Meeting time and place: Announced prior to each meeting
Contact 1: Geoffrey Marsh
Phone: 301-594-9683
E-mail: <geoff@mail.nih.gov>
Contact 2: Paul Beatty
E-mail: <pbeatty@mail.nih.gov>

Lab Managers Interest Group
Meeting time: 2nd Thursday, noon
Meeting place: Building 40, Conference Room 1203
Contact: Dawn A. Walker
Phone: 301-402-7149
E-mail: <walkerd@exchange.nih.gov>
ListServ home page: <https://list.nih.gov/archives/locl.html>

Lambda Lunch (Bacterial and Phage Genetics)
Meeting time: Each Thursday, 11:00 am
Meeting place: Building 37, Room 6107/6041
Contact: Susan Gottesman
Phone: 301-496-3524
E-mail: <susang@helix.nih.gov>
Contact 2: Robert Weisberg
E-mail: <rweisberg@nih.gov>
Anonymous FTP site:FTP.CU.NIH.-GOV
directory "LAMBDA_LUNCH"

Light Microscopy Interest Group
Meeting time: Monthly, Tuesday, noon
Meeting place: Building 10, Room 4B51
Contact: James McNally
Phone: 301-402-0209
E-mail: <mcnallyj@mail.nih.gov>
Contact 2: Christian Combs
Phone: 301-496-0014

Mass Spectrometry Interest Group
Meeting time: 1st & 3rd Thursday, 10:30 am (check website)
Meeting place: Building 10, Room 7S235
Contact: Dawn Maynard
Phone: 301-402-6622
E-mail: <maynardd@mail.nih.gov>

Membrane Microdomains Interest Group
Meeting time: 1st Tuesday, 1:00 pm
Meeting place: Building 10, Room 9C209
Contact: Paul Roche
Phone: 301-594-2595
E-mail: <rochep@pop.nci.nih.gov>

Membrane Protein Interest Group
Meeting time: Usually one Tuesday a month, 1:00 pm; check website: <http://www.nih.gov/sigs/mpig>
Meeting place: Porter Neuroscience Building 35, Room BB1000
Contact: Reinhard Grisshammer
E-mail: <rkgriss@helix.nih.gov>

Microarray Users Group
Meeting time and place: Usually first Wednesday; Journal Club meets weekly or bimonthly, as the group decides
Meeting place: Varies
Contact: Katherine Peterson
Phone: 301-402-5678
E-mail: <petersonk@nei.nih.gov>

Mitochondria Interest Group
Meeting time: 1st Monday, 3:00 pm (excluding federal holidays)
Meeting/BREEZE WEB-conference: Building 2 Conference Room or other NIH campus sites; recent nodes for group viewing include NIEHS, Research Triangle Park, NC; GRC, Baltimore; VA Hospital, Cleveland; Podell Auditorium, Beth Israel Medical Center, NYC; Baylor Univ.,Texas; Louisiana State University Health Science Center
Contact 1: Steve Zullo
Phone: 301-435-2810
E-mail: <zullo@helix.nih.gov>
Contact 2: Nadja Souza-Pinto
E-mail: <souzan@mail.nih.gov>
Contact 3: Rao Divi
E-mail: <divir@mail.nih.gov>
Contact 4: Gerald McLaughlin
E-mail: <gmclaughlin@mail.nih.gov>

Molecular and Functional Optical Imaging Interest Group
Meeting time and place: Varies
Contact: Amir Gandjbakhche
Phone: 301-435-9235
E-mail: <amir@helix.nih.gov>

Molecular Modeling Interest Group
Meeting time: See <http://mmignet.nih.gov>
Meeting place: Building 12A, conf. rooms
Contact: Peter Steinbach
Phone: 301-496-1100
E-mail: <steinbac@helix.nih.gov>

Mood and Anxiety Disorders Interest Group
Meeting time: Tuesday, noon, 12-18 times a year
Meeting place: Varies (once speakers are set, the schedule is sent to members and interested persons; all sponsored lectures are listed on the NIH Calendar of Events)
Contact: Holly Giesen
Phone: 301-435-8982
E-mail: <giesenh@mail.nih.gov>

Motility Interest Group
Meeting time and place: Varies
Contact: Jim Sellers
Phone: 301-496-6887
E-mail: <sellersj@nhlbi.nih.gov>

Mouse Club
Meeting time: 1st Tuesday, 4:00 pm
Meeting place: Building 6A, Room 4A05
Contact: Heiner Westphal
Phone: 301-402-0545
E-mail: <hw@mail.nih.gov>

Muscle Interest Group
Meeting time: Irregular
Meeting place: Building 40, Room 1203 or 1205
Contact: Andres Buonanno
Phone: 301-496-0170
E-mail: <buonanno@mail.nih.gov>

Nanotech/Nanomedicine Interest Group
Meeting time and place: TBA
Contact 1: Kuan Wang
Phone: 301-496-4097
E-mail: <wangk@mail.nih.gov>
Contact 2: Jeffrey Forbes
E-mail: <forbesj@mail.nih.gov>

Neurodevelopmental Disorders Interest Group
Meeting time: 2nd Thursday, 12:30–1:30 pm
Meeting place: Building 10, Room 2-3330
Contact: Teresa Huggins
Phone: 301-435-3781
E-mail: <TeresaHuggins@mail.nih.gov>

Pain Interest Group
Meeting time: 2nd Tuesday, 3:30 pm
Meeting place: Building 49, Room 1A51
Contact: Michael Iadarola
Phone: 301-496-2758
E-mail: <miadarola@dir.nidcr.nih.gov>

PET Interest Group
Meeting time: Friday, 2:00 pm; see website for seminar listing
Meeting place: Building 10, Room 1-5674
Contact: Peter Herscovitch
Phone: 301-451-4248
E-mail: <herscovitch@nih.gov>

Phage-Tech Interest Group
Meeting time and place: Varies
Contact Rotem Edgar
Phone: 301-451-8820
E-mail: <edgarr@mail.nih.gov>

Pharmacogenetics Interest Group
Meeting time: Last Thursday, 3:30-5:00 pm
Meeting place: Rockledge 2
Contact: Pothur Srinivas
Phone: 301-435-0550
E-mail: <srinivap@mail.nih.gov>

Pigment Cell Research Interest Group
Meeting time: Usually 3rd Thursday, 12:30–2:00 pm; yearly day-long meeting most years; check the website
Meeting place: Bldg 49, Conf. Room 1A51
Contact 1: Marjan Huizing
Phone: 301-402-2797
E-mail: <mhuizing@mail.nih.gov
Contact 2: Tom Hornyak
Phone: 301-451-1926

Polyunsaturated Lipid Function Interest Group
Meeting time: Usually 1st Wednesday (resuming in September), 1:30 pm
Meeting place: 5626 Fishers Lane, Conference Room 3N-25, Rockville, MD
Contact 1: Norman Salem
Phone: 301-443-2393
E-mail: <nsalem@niaaa.nih.gov>
Contact 2: John Paul SanGiovanni
E-mail: <jpsangio@nei.nih.gov>

** **Prostate Cancer Interest Group**
Meeting time: Monthly, Friday, 4:00 pm
Meeting place: Bldg. 10 CRC, Room 2-3750
Contact: Marston Linehan
Phone: 301-496-6353
E-mail: <linehanm@mail.nih.gov>

Protein Trafficking Interest Group
Meeting time: 2nd Tuesday, 3:30 pm
Meeting place: Building 50, Room 2328
Contact 1: Manu Hegde
Phone: 301-496-4855
Email: <hegder@mail.nih.gov>
Contact 2: Peng Loh
Phone: 301-496-3239

Proteomics Interest Group
Meeting time: 1st Friday seminars
Meeting place: Building 50; check website; join listserv to receive seminar notices
Contact: Sanford Markey
Phone: 301-496-4022
E-mail: <markeys@mail.nih.gov>

RNA Club
Meeting time: 1st Tuesday (except July), 4:00 pm
Meeting place: Building 31, Room 2A48
Contact: Rich Maraia
Phone: 301-402-3567
E-mail: <maraiar@mail.nih.gov>

Interinstitute Interest Group Directory

** **Signal Transduction Interest Group**
Meeting time: Alternate Wednesdays, 5:00 pm
Meeting place: 5 Research Court, Conf. Room
Contact 1: John Northup
Phone: 301-496-9167
E-mail: <drjohn@codon.nih.gov>
Contact 2: James Battey
Phone: 301-402-0900

Stem Cell Interest Group
Meeting time and place: Monthly seminars to rotate through Baltimore, Bethesda, and Frederick campuses; check website
Contact 1: Nadya Lumelsky
Phone: 301-451-9834
E-mail: <nadyal@nidcr.nih.gov>
Contact 2: Colin Stewart
Phone: 301-846-1755
E-mail: <stewartc@ncifcrf.gov>
Contact 3: Manfred Boehm
Phone: 301-435-7211
E-mail: <boehmm@nhlbi.nih.gov>

Stroke Branch Interest Group/Seminar Neurovascular Case Conferences (year-round)
Meeting time and place: Wednesdays, either 8:30 am at Suburban Hospital or 8:00 am at Washington Hospital Center
Stroke Branch Seminars (September through May)
Meeting time: Thursdays 4:00 pm
Meeting place: Suburban Hospital Auditorium
Contact 1: Jose Merino
Phone: 301-435-9321
E-mail: <merinoj@ninds.nih.gov>
Contact 2: John Kylan Lynch
Phone: 301-451-7968
E-mail: <LynchJ@ninds.nih.gov>

** **Synaptic and Developmental Plasticity Interest Group**
Meeting time: Tuesday, every other month, 11:00 am
Meeting place: Building 35, Room BB1000
Contact: Bai Lu
Phone: 301-435-2970
E-mail: <bailu@mail.nih.gov>

Systems Biology Interest Group
Meeting time: 1st Thursday, 2:00 p.m., monthly seminars
Meeting place: Berliner Room, Building 10, Room 7S235
Contact 1: Eric Billings
Phone: 301-496-6520
E-mail: <billinge@nhlbi.nih.gov>
Contact 2: David Balshaw
Phone: 919-541-2448
E-mail: <balshaw@niehs.nih.gov>

** **Tobacco and Nicotine Research Interest Group**
Meeting time: 4th Wednesday, every other month, 2:00 pm (next meeting is July 27)
Meeting place: 6701 Rockledge Dr., Rooms 8115/8119, Rockledge 2 Building
Contact: Geraldine Anderson
Phone: 301-589-4020
E-mail: <andersong@mail.nih.gov>

Transcription Factor Interest Group
Meeting time: 1st Thursday (except July-Sept.), 2:00 pm
Meeting place: Building 50, ground-floor Conference Room (Room 1227)
Contact 1: Stoney Simons
Phone: 301-496-6796
E-mail: <steroids@helix.nih.gov>
Contact 2: Uli Siebenlist
Phone 301-496-8917
ListServ: subscribe to TFACTORS

Tumor Angiogenesis & Invasion Working Group
Meeting time and place: Posted at website
Contact 1: William Figg
Phone: 301-402-3622
E-mail: <wdfigg@helix.nih.gov>
Contact 2: Steven Libutti
Phone: 301-496-5049

Viral Hepatitis Interest Group
Meeting time: 2nd Monday, 4:15 pm
Meeting place: Building 10, Room 9S235 (Bunim Room)
Contact: Barbara Rehermann
Phone: 301-402-7144
E-mail: <barbarar@intra.niddk.nih.gov>

Virology Interest Group
Meeting time: 1st Thursday, 12:00 noon; minisymposium in November
Meeting place: Building 4, Room 433
Contact 1: Alison McBride
Phone: 301-496-1370
E-mail: <amcbride@nih.gov>
Contact 2: Carolyn Wilson
E-mail: <carolyn.wilson@fda.hhs.gov>
ListServ: Contact <CBuckler@nih.gov>

Washington Area NMR Interest Group
Meeting time: Three times a year, generally in December, February, and May
Meeting place: Building 5, Room 127, or the Cloister (Building 60) Lecture Hall
Contact: Daron Freedberg
Phone: 301-496-0837
E-mail: <daron_freedberg@nih.gov>

Washington Area Yeast Club
Meeting time: 2nd Wednesday, 4:30 pm
Meeting place: Building 6A, Room 4A05
Contact: Henry Levin
Phone: 301-402-4281
E-mail: <levinh@mail.nih.gov

Women's Health Special Interest Group
Meeting time: One Friday every other month, September through June, 11:30 am–12:30 pm
Meeting place: Building 1, Wilson Hall; upcoming meetings/seminars posted at website and announced through WHSIG list e-mails and NIH staff list e-mails
Contact: Vicki Malick
Phone: 301-496-7989
E-mail: <malickv@mail.nih.gov>

X-ray Diffraction Interest Group
Meeting time and place: See biweekly newsletter: <http://mcl1.ncifcrf.gov/nihxray/
Contact: Fred Dyda
Phone: 301-402-4496
E-mail: <fred.dyda@nih.gov>

Zebrafish/Xenopus Interest Group
Meeting time and place: Monthly, rotating through participating labs; space is limited
Contact: Tom Sargent
Phone: 301-496-0369
E-mail: <sargentt@mail.nih.gov>

IGs on the Horizon

Pediatric Neuroimaging Group
Contact: Lisa Freund
Phone: 301-435-6879
E-mail: <freundl@mail.nih.gov>

Mucosal Immunology Interest Group
Contact 1: Yasmine Belkaid
E-mail: <ybelkaid@mail.nih.gov>
Contact 2: Brian Kelsall
E-mail: <bkelsall@mail.nih.gov>
Contact 3: Warren Strober
E-mail: <wstrober@mail.nih.gov>

Peter Basser is planning on starting an **NIH Inventors' Interest Group**—"open to anyone who has ever submitted an Employee Invention Report (EIR) or aspires to."
Phone: 301-435-1949
E-mail: <pjbasser@helix.nih.gov>

Additions and/or Corrections?

Considering starting a new Interest Group? Contact Christopher Wanjek, OIR director of communications:
<wanjek@od.nih.gov>.
Need to correct your group's listing? Contact CIT's web publishing group:
<publish@cit.nih.gov>.

September Gala: NIH Research Festival Celebrates Its 20th Anniversary

The 2007 NIH Research Festival, to be held **September 25–28, 2007**, on the NIH Bethesda campus, also commemorates the 20th anniversary of this NIH Intramural Program showcase event.

This year's organizing committee is co-chaired by Alan Koretsky, NINDS, and Dan Longo, NIA.

The opening plenary session on Tuesday, September 25, at 9:30 a.m. in Masur Auditorium, features presentations on "Chromosomes in Modern Biology and Medicine."

Other events during this four-day showcase of the NIH Intramural Program include cross-cutting symposia and poster sessions; the 2008 FARE awards ceremony and reception; special exhibits on resources for intramural research; the job fair for NIH postdoctoral, research, and clinical fellows; the festival food and music fair; and the Technical Sales Association scientific equipment tent show.

All NIH investigators and Bethesda FDA/CBER investigators are invited to submit poster abstracts online through **July 30**. Posters in any area of research conducted within the NIH Intramural Program will be considered for presentation, but the organizing committee requests a limit of one poster submission per first author. Applicants will be notified of acceptance by e-mail in mid-August.

For a preliminary schedule of events and online poster registration, go to the NIH Research Festival website at

<http://researchfestival.nih.gov>.

For more information about poster registration, contact Paula Cohen or Amy Blackburn, Research Festival logistics co-coordinators, at

<researchfest@mail.nih.gov>.

Functional Genomics Of Critical Illness and Injury

The fifth symposium on the Functional Genomics of Critical Illness and Injury entitled "Forging a Critical Alliance: Are We Meeting the Need?" will be held **November 14–15, 2007** (8:00 a.m. to 6:30 p.m. and 8:00 a.m. to 5:30 p.m.), at the Natcher Conference Center. The conference is sponsored by NIGMS, the CC Critical Care Medicine Department, and the Critical Illness and Injury Interest Group.

The meeting will assemble acute- and critical-care specialists (intensivists from internal medicine, surgery, pediatrics, and anesthesiology), microbiologists, immunologists, cell biologists, molecular biologists, experts in high-throughput technologies, and computational scientists. Scientific presentations are scheduled for the first day and collaborative workshops the second day.

The deadline for abstract submission is **September 15**; registration for the meeting closes **October 15**. For additional information, go to

<http://www.strategic results.com/fg5>.

Role of Nitrite in Physiology, Pathophysiology, and Therapeutics

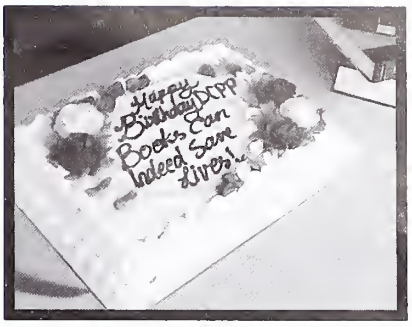
The second international meeting on the Role of Nitrite in Physiology, Pathophysiology, and Therapeutics—sponsored by NHLBI, NIDDK, CCMD, Wake Forest University in Winston-Salem, N.C., and the ORD—will be held **September 6–7, 2007** (8:00 a.m. to 6:30 p.m. and 8:00 a.m. to 5:30 p.m.), at the Natcher Conference Center.

The deadline for abstract submission is **July 22**; online registration closes **August 3**.

For more information, visit

<http://www.strategic results.com/nitrite2>.

Celebrating Global Disease Control



Evan Galloway

Food for thought

Books—especially when they're free and filled with vital health information— "can save lives," Roger Glass, director of the Fogarty International Center at NIH, told a gathering of international scientists, economists, and health policy experts who came to NIH June 11 to review the goals and accomplishments of the Disease Control Priorities Project.

The occasion was the one-year anniversary of the project's influential publication: *Disease Control Priorities in Developing Countries*, second edition (DCP2).

Dedicated to finding public health "best buys," the creators of the DCP2 aim to educate policymakers, philanthropists, and health advocates about the investments that save the most lives.

They suggest that some of the most cost-effective and sometimes overlooked lifesavers are childhood vaccinations, taxation of tobacco products, enforcement of traffic regulations, and the prevention and treatment of cardiovascular disease using cost-effective drugs, such as aspirin.

Donor skepticism of the value of investing in such endeavors can be overcome by the scientific information presented in books like DCP2, participants agreed. The Bill and Melinda Gates Foundation has promoted this book as required reading for individuals involved in funding health initiatives and for policymakers in governments seeking public health aid.

Moreover, all of the project's publications, including the 1400-page DCP2, can be accessed online for free at

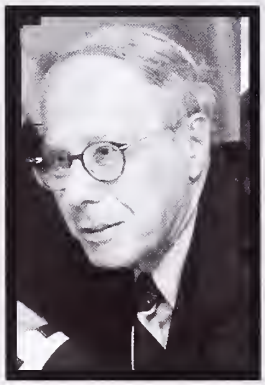
<http://www.dcp2.org>.

Anyone can create and download their own book with title page, selecting specific chapters from the DCP2. Promisingly, the DCP2 website has accumulated over a half-million site views in the past year, with 83 percent of the visitors coming from developing countries.

—Evan Galloway

Ed. note: The following commentary represents the views of the author and appears here under the auspices of the NIH Assembly of Scientists, which has been accorded a standing ViewPoint space in The NIH Catalyst. *Individuals who wish to write a column should contact a member of the ViewPoint editorial board (Abner Notkins, Harvey Alter, Edward Korn, Alan Schechter, Joshua Zimmerberg).*

Erosion of Freedom of Inquiry



Abner Notkins

What would tenured scientists view as true freedom of inquiry?

The answer simply put: To wake up in the morning with a new idea for an experiment in one's area of expertise and to initiate that experiment the same day with available resources and without having to seek administrative approval.

In fact, it is this unencumbered freedom to explore ideas that has led so many individuals into science as a career. The Intramural Research Program (IRP) at NIH for years has represented the best of this tradition—and still does today. But this tradition is under constant direct and indirect attack and requires vigilant protection.

Ironically, direct threats to freedom of inquiry sometimes come from the very source that deserves so much credit for making American science the envy of the world, the U.S. government.

Unfortunately, political considerations at times inform funding decisions, leaving scientists to choose to pursue either those well-funded research areas that are in current political favor or some poorly funded line of research that they consider more promising.

The IRP can create its own political problems. In an effort to satisfy an institute's often vocal extramural community and patient constituency, mission-oriented and translational studies frequently are favored over investigator-initiated basic and long-term research that doesn't have an immediate payoff.

This emphasis pressures scientists within an institute to conform to current priorities and can restrict curiosity-driven freedom of inquiry. Serendipitous findings also may create a dilemma: Instead of pursuing unexpected leads, a scientist may feel or actually be compelled to back away should these leads not fit into the mission or type of work currently favored by an institute.

A related problem is the pressure to conform that many tenured intramural investigators experience when an incoming institute director or scientific director wants to modify the scientific direction of the institute.

Because decisions on the yearly budget of intramural investigators generally are in the hands of a single individual—the scientific director—the pressure to conform to the changing thrust of an institute rather than to pursue one's own research ideas can be great. The lack of a readily available formal appeal process for investigators who feel that their budgets are inadequate or have been inappropriately reduced adds further pressure to conform, as does the lack of the option—available to extramural scientists—to seek funds from other public or private agencies.

Along the same line, candidates for tenure-track positions know that to be selected they must come up with projects that will be viewed as relevant to the particular institute's current direction. From the institute's point of view this certainly seems to make good sense, but it may not take full advantage of the candidate's scientific curiosity, creativity, and expertise—nor does it allow for truly free choice of projects.

Similarly, "big science" projects are revolutionizing biological research and expediting the achievement of specific goals, but at a price. Invariably, these projects limit freedom of inquiry for individual members of the "big science" research teams.

The threat to freedom of inquiry is not just politically and administratively based, but also can come from the scientific community itself. The peer-review process that has proved so important in evaluating the contributions of individual scientists and in maintaining the high quality of science can sometimes be one of the culprits.

Study sections are reluctant to support novel ideas and technologies that by definition have not already been proven. Grant applicants are well aware of this and stay away from "risky" projects in favor of "safe" projects. NIH intramural scientists face the same problem.

Although it is generally thought that intramural scientists have greater freedom to choose long-term "high-risk, high- impact" projects, intramural scientists increasingly are choosing safer projects to ensure a good review by the Board of Scientific Counselors.

These boards are made up of extramural scientists who, ironically, criticize intramural scientists for not choosing "high-risk, high-impact" projects, but punish them when the projects do not provide outstanding results. This, too, diminishes free choice.

As in all fields of endeavor, science too has its trends and fads that generate infusions of money from public and private funding agencies. The scientific community rewards investigators in these areas with invitations to present their work at meetings and publish their papers in prestigious journals.

Such actions can result in an exodus from true independent investigator-initiated research to trend-conformity. The scientific journals also contribute to this problem by favoring trendy papers, even to the exclusion of solid and important papers in other areas.

Some scientists and administrators have added further to the problem by taking the position that tenure, promotion, and support require publication in so-called high-impact journals (for example, *Science*, *Nature*, *Cell*).

It certainly is not the intention of the scientific community or the journals to dampen creativity or freedom of inquiry—and they almost certainly would dispute this accusation—but the end result is subtle, and often not so subtle, pressure on investigators to follow the trend.

Of factors that place restrictions on projects that an investigator might wish to pursue, one of the most distressing is the increasing bureaucracy that has evolved in government and academia in recent years.

Although often well-intentioned and in some cases perhaps necessary, the paperwork required to study pathogens, toxins, recombinant molecules, and even panels of stored sera that have identification markers can become so onerous that investigators choose not to do experiments in these areas.

The same applies to animal protocols that now require so much information—well beyond the original intent of ensuring that the animals are protected from undue pain and discom-

fort—that approval often takes months and becomes a stifling paperwork exercise.

The prohibition on outside consulting imposed on intramural scientists to avoid even the appearance of conflict of interest creates still another problem. It diminishes interaction with the extramural community, limits scientific exchange, and reduces opportunities to develop new technologies and therapies.

Similarly, the restrictions on travel, lecturing, editing, and serving on scientific boards—together with the cumbersome paperwork required to obtain approval for some of these activities—creates a negative environment that makes interaction with the academic extramural community more difficult than ever before.

Although freedom of inquiry is not and never has been totally open-ended—nor should it be—the cornerstone and success of the NIH intramural and extramural programs has been and remains bottom-up, investigator-initiated research. Anything that erodes this freedom, no matter how subtle, must be viewed with concern.

Many of the issues discussed here have become so ingrained and accepted that they are no longer readily recognized as the threats they truly are to freedom of inquiry. Restriction on freedom of inquiry will have an adverse effect not only on recruitment and retention of the current generation of scientists, but also on attracting the best of the next generations into science as a career.

How should the scientific community deal with these and future problems? Each issue is different and requires a separate solution. Decisions must be constantly weighed to find the balance that provides the best environment for creative endeavor. Open debate and constant appraisal and reappraisal would seem to be the best approach.

The NIH Assembly of Scientists provides a proactive venue for intramural scientists to express concerns and views. The AOS has worked successfully over the past couple of years with the NIH administration on the problems associated with the conflict-of-interest regulations. Equal attention and effort now should be placed on these many other problems that impinge on scientific creativity so that the NIH IRP maintains its great and successful tradition of freedom of inquiry.

—Abner Louis Notkins
Chief, Experimental Medicine Section
Oral Infection and Immunity Branch
NIDCR

People

Recently Tenured

Kevin Camphausen *received his M.D. degree from Georgetown University, Washington, D.C., in 1996 and completed a residency in radiation oncology at the Harvard Medical School Joint Center for Radiation Therapy, Boston, where he studied the interaction of angiogenesis inhibitors and radiotherapy in the Judah Folkman lab. He joined NCI in 2001 as a tenure-track investigator and is currently chief of the Radiation Oncology Branch.*

Christopher Wanjek

Kevin Camphausen

Approximately 75 percent of the 1.2 million patients diagnosed with non-skin cancers in North America in 2007 will receive radiotherapy during the course of their disease. Improving the efficacy of radiotherapy would therefore significantly contribute to the field of oncology.

Characterization of the processes regulating cellular radiosensitivity has led to the hypothesis that many of these cellular processes and signaling pathways can be targeted for interruption, thereby predisposing tumor cells to death.

The work in my laboratory and clinic focuses on two major projects: development of novel biomarkers of early failure after radiotherapy, and histone acetylation as a target for tumor-cell radiosensitization.

The first focus is the development of a noninvasive biomarker for tumor recurrence after irradiation. An early marker of recurrence would allow prediction of which patients harbor subclinical disease and may benefit from additional therapy, instead of the current practice of delivering treatment to every patient at moderate risk of recurrence.

Because tumor growth depends on angiogenesis, an increase in circulating angiogenic factors could identify patients at risk for persistent or recurrent disease. Although angiogenic factors have been explored as tumor markers, no study has explored their utility as a tumor marker across multiple tumor types or in patients receiving radiation.

Matrix metalloproteinases (MMPs) have been implicated in both primary and metastatic tumor formation. Marsha Moses and colleagues defined the presence of biologically active MMP-2 or MMP-9 in the urine of cancer patients as an independent predictor of organ-confined cancer. We developed an in vivo Lewis lung carcinoma (LLC) model to evaluate urinary MMP-2 as a biomarker for disease recurrence after irradiation.

We were able to detect biologically active MMP-2 as an early marker for lung metastases in C57Bl/6 mice that had been implanted with LLC and "cured" with local irradiation. This rise in MMP-2 activity was then used as a signal to begin adjuvant angiostatin therapy, which successfully reduced the metastatic burden.

With the knowledge that urinary MMP-2 levels reflect disease status in mice after irradiation, we sought to explore this finding in radiotherapy patients using two biomarkers, MMP-2 and VEGF (vascular endothelial growth factor).

A pilot study (02-C-0064) examining these two urinary biomarkers was opened in early 2002. We recently published early findings from this study. In samples obtained before radiotherapy, there were a greater number of MMPs detectable in the urine of patients with localized cancer than in that of normal controls (1.43 vs. 0.38). Similarly, patients with localized cancer had higher urinary VEGF levels than normal controls (317 vs. 131.6 pg/mg creatinine). Although the absolute values of these biomarkers were not able to predict clinical outcome, comparisons of the MMP or VEGF level on the last day of radiation with levels obtained at one-month follow-up were predictive of disease status at one year.

To validate the utility of these promising markers, patients with the same histology undergoing a homogeneous treatment regimen needed to be studied. Therefore, we initiated a prospective Phase II study (04-C-0200) in patients with glioblastoma multiforme (GBMs) undergoing radiotherapy to determine whether these urinary biomarkers add to the Radiation Therapy Oncology Group Recursive Partition Analysis, which uses clinical parameters to divide patients into subgroups based on historical survival. This study should be mature within the next year.

My second focus is the evaluation of histone deacetylase inhibitors as radiation sensitizers. Histone acetylation plays a critical role in modulating chromatin structure and regulating gene expres-

Recently Tenured

sion. The balance of histone acetylation is determined by the opposing actions of histone acetyltransferase (HAT) and histone deacetylase (HDAC).

In addition to slowing tumor-cell proliferation, the HDAC inhibitors sodium butyrate and trichostatin A have also been shown to enhance tumor-cell radiosensitivity. Their clinical utility, however, is limited by their pharmacologic characteristics.

Although several HDAC inhibitors have recently been developed that possess more favorable pharmacokinetic and toxicity profiles, their ability to increase tumor-cell radiosensitivity cannot be assumed. We have been examining these HDAC inhibitors and have found that several—including MS-275, CI-779, depsipeptide, and valproic acid (VA)—indeed appear to enhance the radiosensitivity of tumor cells.

Because of its potential for clinical application—oral bioavailability, a low toxicity profile, and penetration of the blood-brain barrier—we have conducted further studies with VA.

Our laboratory results suggest that VA-induced HDAC inhibition can lead to an enhancement of radiosensitivity both in vitro and in vivo. Our data further suggest that continuous exposure to VA is necessary to achieve the maximum enhancement.

Based on these findings, I initiated an NCI Phase II trial (06-C-0112) testing this agent as a radiation sensitizer in combination with temozolomide and radiotherapy in patients with newly diagnosed GBM.

David Clark *received his Ph.D. degree from the University of Cambridge, U.K., in 1986. He did his postdoctoral training with Gary Felsenfeld at NIH. In 1995, he joined the Laboratory of Cellular and Developmental Biology, NIDDK, as a tenure-track investigator. In 2003, he moved to the Laboratory of Molecular Growth Regulation, NICHD, where he is now a senior investigator and head of the section on Chromatin and Gene Regulation.*

The study of gene regulation is a prerequisite for understanding how cells respond appropriately to a changing environment, how they implement developmental programs, and how a defect in gene regulation can result in carcinogenesis. Gene activation involves the recruitment of a set of factors to a promoter in response to appropriate signals, ultimately resulting in the binding of RNA polymerase II and transcription.

These events must occur in the presence of nucleosomes, in which DNA is coiled around a central octamer of core histone proteins. Nucleosomes are compact structures capable of blocking transcription at every step. To circumvent this chromatin block, eukaryotic cells possess ATP-dependent chromatin-remodeling machines and histone-modifying complexes. The former use ATP to alter nucleosome structure and to move nucleosomes along DNA. The latter contain enzymatic activities that modify the histones to alter their DNA-binding properties and to mark them for recognition by other complexes, which have activating or repressive roles (the basis of the histone-code hypothesis).

Christopher Wanjek

David Clark

The current excitement in the chromatin field reflects the realization that chromatin structure is of central importance in gene regulation: The cell has dedicated complex systems to manipulate the repressive properties of chromatin structure to maximum effect. Furthermore, multiple connections between chromatin and disease are apparent.

We have developed a model system to investigate the remodeling and histone modifications that occur on gene activation. We purify native plasmid chromatin containing a model gene in its transcriptionally active or inactive chromatin states from yeast cells and compare their structures. Our studies provide a detailed and surprising picture of the events occurring in the chromatin structure on gene activation.

Frank DeLeo

We discovered that induction results in a remodeled chromatin domain that extends far beyond the promoter to include the entire gene. The formation of this domain requires the transcriptional activator and a remodeling machine. We propose that a highly dynamic chromatin structure is created, facilitating access to the DNA for initiation and elongation factors. Our current studies aim to increase our understanding of the structure and dynamics of remodeled chromatin domains.

In a second, related, project, we are investigating the biological function of the yeast Spt10 protein, which we believed initially to be a co-activator with histone acetyltransferase (HAT) activity that is recruited to promoters by activators. However, we discovered that Spt10p is in fact the activator of the histone genes, which has been sought after for many years.

Spt10p appears to be a rare example of an activator with a sequence-specific DNA-binding domain fused to a HAT domain. Our current aim is to place our observations in their biological context of cell-cycle regulation of the histone genes. In addition, we are investigating the implications of the homology we have observed between the DNA-binding domain of Spt10p and the zinc-finger domain of human foamy retrovirus integrase.

Frank DeLeo *received his Ph.D. in microbiology from Montana State University, Bozeman, in 1996 and carried out his postdoctoral training with William Nauseef at the University of Iowa, Iowa City, in the Department of Medicine. He joined the staff at NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Mont., in the fall of 2000 as a tenure-track investigator in the Laboratory of Human Bacterial Pathogenesis. He is currently a senior investigator and chief of the Pathogen-Host Cell Biology Section.*

My laboratory studies the interaction of human polymorphonuclear leukocytes (PMNs, or neutrophils) with pathogenic bacteria. Although most bacteria are killed readily by neutrophils, pathogens such as *Staphylococcus aureus* have evolved mechanisms to circumvent destruction by these key innate immune cells and thereby cause human infections. Therefore, a better understanding of the bacteria-neutrophil interface at the cell and molecular levels will provide information critical to our understanding, treatment, and control of disease caused by bacterial pathogens.

The Pathogen-Host Cell Biology Section conducts 1) a systematic molecular dissection of steps involved in pathogen-host interaction, with specific emphasis on the interaction of bacterial pathogens with innate host defense (neutrophils), and 2) research investigating mechanisms mediating evasion of innate immunity by pathogens of

special interest, such as methicillin-resistant *S. aureus* (MRSA).

During my first few years at RML, we used genomics strategies to discover a genetic program that links phagocytosis in human neutrophils with apoptosis. This research redirected our thinking about neutrophil function in the innate immune response.

Using similar genomics methodologies, we elucidated a global model of host cell-pathogen interaction, which is broadly applicable to many bacterial pathogens. Collectively, these studies lead to a new paradigm for the resolution of human bacterial infections.

Studies from our laboratory were also among the first to identify complex genetic programs in bacteria that circumvent human innate immunity to promote disease. This work, which comprises a series of studies, identified novel virulence factors in human bacterial pathogens.

Since late 2003, we have focused our research on the emerging problem of community-associated MRSA (CA-MRSA), which is epidemic in the United States. CA-MRSA causes disease in otherwise-healthy individuals, and these infections can be severe and/or fatal. The molecular basis for the increased incidence and severity of CA-MRSA disease is not known.

Work from our laboratory suggests that enhanced CA-MRSA virulence is linked to (or results from) evasion of killing by neutrophils, which likely underlies the ability of these pathogens to cause disease in otherwise-healthy individuals.

An *S. aureus* leukocyte toxin, Panton-Valentine leukocidin (PVL), is widely believed to be the cause of the increased severity and incidence of CA-MRSA infections. However, our recent studies indicate PVL does not play a major role in CA-MRSA disease. This unexpected finding will redirect the medical community toward other factors likely responsible for CA-MRSA infections.

Our efforts to understand MRSA pathogenicity are currently focused on identifying the proteins directly responsible for the type and severity of disease caused by these emerging human pathogens.

The long-term objective of this research is to develop and/or promote development of enhanced diagnostics, better prophylactic agents, and new treatments for emerging infectious pathogens such as CA-MRSA.

Aiyi Liu *received his Ph.D. degree in statistics in 1997 from the University of Rochester, Rochester, N.Y. He was a postdoctoral research fellow at St. Jude's Children's Research Hospital in Memphis, Tenn., and an assistant professor of biostatistics at Georgetown University Medical Center, Washington, D.C., before joining NIH in 2002 as a tenure-track investigator in the Biometry and Mathematical Statistics Branch, Division of Epidemiology, Statistics and Prevention Research (DESPR), NICHD. He is now a senior investigator in that branch.*

As an intramural investigator at NIH, I conduct independent statistical research and collaborate with investigators within and outside DESPR on design, analysis, and interpretation and publishing of biomedical studies.

Aiyi Liu

Sequential methods is one of my major research areas. Sequential methods, which allow a scientific hypothesis to be tested repeatedly at several time points using accumulated data, are frequently used in designing medical studies, particularly clinical trials, because they increase the ability to reduce sample size and to terminate inferior treatments as early as possible.

Independently or joined by other colleagues, I have published a series of papers addressing various issues in the design and analysis of a sequential trial, with particular focus on statistical inference upon termination of the trial.

It is well know that sequential sampling introduces bias to estimation of treatment effect. I derived some explicit formulas to evaluate the magnitude of such bias and found that the bias can be substantially reduced using a simple segmented estimation by shrinking the estimator toward zero for small treatment effect and subtracting a constant for large treatment effect. For two-stage phase II trials, I discovered that the bias can also be substantially reduced by simply subtracting an empirical estimator of the bias.

Clinical trials are usually designed to test hypotheses for a primary endpoint. However, data on secondary endpoints are also collected and need to be analyzed by taking into account the possibility of early stopping of the trial. I developed a simple bias-corrected confidence interval for the mean of a secondary parameter and showed the interval to have desired coverage probability. For a sequential phase II trial, I obtained several efficient estimators to reduce the bias in estimating a secondary probability. The methods can be used to obtain efficient estimation of the toxicity rate when the response rate is the primary endpoint in a phase II cancer clinical trial.

Power and sample-size calculation are integrated considerations in planning a medical study. Unfortunately, such calculation usually relies on correctly specified values of nuisance parameters, that is, parameters that are not related to the treatment difference but need to be dealt with in the study. The study can be severely underpowered if the specification is far from the truth. This situation calls for sample-size recalculation based on internal data. I investigated this issue for a bivariate phase II cancer trial to evaluate toxicity and response rate simultaneously, and also for studies comparing the accuracy of two diagnostic medical devices. I proposed several approaches to re-estimating the sample size to achieve the needed statistical power.

I have also been exploring statistical issues related to diagnostic devices (or biomarkers), such as receiver operating characteristic (ROC) curves analysis, which plots sensitivity and specificity. I found a linear function to combine several medical devices so that the sensitivity of the resulting diagnosis is maximized over a desired range of high specificity. I also developed several sequential methods to compare the diagnostic accuracy of medical devices.

Recently, I proposed and developed a two-stage testing procedure to evaluate the measurement errors of an instrument in measuring the level of disease-associated biomarkers. This procedure allows the investigator to assess the measurement error at an early stage and make decisions about whether more experiments are needed for further evaluation.

I am also interested in microarray data analysis. In order to extract information from a database with a large number of genes and a relatively small number of samples, I found an efficient way to perform principal components analysis (PCA) via grouping genes into several

Recently Tenured

blocks according to their correlation. Within each block, PCA is conducted and important gene expression features extracted. These selected features are then combined for further PCA. This new procedure, called "block principal components analysis," has the advantage of computational simplicity and is as efficient as ordinary PCA.

I have now begun to examine several new research areas, including sequential and adaptive design methods for studies in diagnostic medicine, sequential ranking and selection of diagnostic biomarkers, and a new model for survival and ordinal data. With the continued excellent support of my branch chief and division director, I look forward to making more contributions to the science of statistics.

Enrique Schisterman *received his Ph.D. in epidemiology from the State University of New York at Buffalo in 1999 and completed his postdoctoral training in epidemiological methods at the Harvard School of Public Health in the Department of Epidemiology. In 2002, he came to NIH as a tenure-track investigator in the Division of Epidemiology, Statistics, and Prevention Research, NICHD. He is currently a senior investigator in the division.*

Enrique Schisterman

My current research interests are twofold: 1) I have a long-standing interest in reproductive and perinatal epidemiology, and 2) I am working on developing analytical tools that are closely tied to etiological questions. In pursuit of the first interest, I am in the midst of conducting two studies.

The Effects of Aspirin on Gestation and Reproduction (EAGeR) trial is a multisite, double-blind, placebo-controlled, randomized trial that will evaluate the effect of daily low-dose aspirin on all phases of reproduction beginning at preconception and continuing throughout pregnancy, including implantation and live births.

We plan to recruit 1,600 women preconception and actively follow them for two menstrual cycles or until becoming pregnant, whichever comes first. Active follow-up entails collection of questionnaire data as well as regular specimen collection. Women who do not become pregnant within the first two cycles will remain in the study under passive follow-up for four cycles or until pregnancy occurs, whichever comes first.

Study volunteers will be followed throughout gestation, and pregnancy outcomes will be recorded. Our main outcome is spontaneous abortion, which we hypothesize will be decreased in the aspirin arm compared with the placebo arm. Aspirin is a primary target of interest because of its anti-inflammatory, vasodilatory, and platelet-aggregation inhibition properties.We expect to be in the field by July 1, 2007.

The second epidemiological study is the BioCycle study, which is a longitudinal assessment of the effects of endogenous hormones (that is, estrogen and progesterone) on biomarkers of oxidative stress and antioxidant status during the menstrual cycle.

Specifically, we measured $F_2$8-isoprostanes, TBARS (thiobarbiturate acid reactive substances), and total plasma protein carbonyls as markers of oxidative stress; fat-soluble antioxidant vitamins, water-soluble vitamin C, and the major antioxidant enzymes were measured as markers of antioxidant defense. We assessed oxidative stress, hormones, and antioxidant levels at specific times during the menstrual cycle that represent the days with the greatest hormonal variation. The study recruited and completed follow-up on 259 women, and we are now in the midst of analyzing the data gathered.

In addition to these trials, I have explored and am currently exploring pooled-sample designs because they provide practical and cost-effective solutions for investigating oxidative stress as a mediator of reproductive outcomes.

I am also involved in developing new methods for estimating the receiver operating characteristic (ROC) curve and the accompanying Youden index accounting for measurement error, selection bias, and information bias.

Finally, I am interested in methodological research focused on the assessment of biomarkers and exposure data, consideration of the limits of detection, statistical modeling of causal effects, and design studies with pooled biospecimens.

Julie Segre *received her Ph.D. degree in genetics from the Massachusetts Institute of Technology, Cambridge, in 1996, working with Eric Lander at the inception of the MIT Genome Center. She was then a Damon Runyon–sponsored postdoctoral fellow in the laboratory of Elaine Fuchs at the University of Chicago, where she developed an interest in skin biology. In 2000, she was awarded a Burroughs-Wellcome Career Award in Biomedical Research and joined NIH as a tenure-track investigator. She is currently a senior investigator and head of the Epithelial Biology Section, Genetics and Molecular Biology Branch, NHGRI.*

Maggie Bartlett

Julie Segre

Combining classical genetics techniques and modern genomic tools, I study gene-environment interactions at the skin surface. I study the formation of the skin barrier during development, which is necessary to prevent the escape of moisture and the entry of infectious agents.

The skin barrier is established in utero at 32 weeks (resulting in an incomplete barrier and increased risk for dehydration and infection in children born preterm—about 2 percent). The skin barrier is maintained throughout life and reestablished after trauma such as abrasion or wounding.

Even when the skin regrows, the ensuing scar at the site of trauma continues to exhibit a mild barrier deficiency compared to uninvolved skin for as along as one year.

We modeled in animals the establishment of the skin barrier during development and the interaction of the pathways regulated by the transcription factors, KLF4, GATA-3, and the glucocorticoid receptor.

We showed that mice with increased gap junctional communication exhibit mild barrier impairment under homeostatic conditions. After wounding, an inability to restore the barrier arrested the wounds in the hyperproliferative state and resulted in immune cell infiltration.

These studies suggest that the signal to restore the homeostatic balance between proliferation and differentiation after regrowth of the skin is restoration of the barrier and that, in its absence, the skin enters a pathologic state resembling psoriasis.

Psoriasis is a common postnatal skin disorder, affecting 2 percent of the population in the United States; its typical age of onset is in the third decade. Wounding is an initiating event in a significant percentage of psoriatic patients and is clinically referred to as the isormorphic phenomenon.

Our future goal is to evaluate the hypothesis that skin microbial diversity (a mix, for instance, of bacteria, fungi, and archae) plays a role in many common dermatological conditions, including atopic dermatitis (eczema). The onset of atopic dermatitis is typically within the first year of life and affects about 15 percent of children in the United States. More than half of patients with severe atopic dermatitis will progress to develop asthma and/or allergic rhinitis (hay fever), disorders with significant morbidity and mortality.

There are two classical explanations for the role microbes play in skin disease: 1) A specific microbe colonizes the skin to disrupt the balance of commensal microflora, and 2) microbes release toxic substances or invade cells to induce an inflammatory response directly.

In fact, there are numerous possibilities of how microbial communities contribute to human health and disease. However, culture-dependent skin sampling methods are incomplete assessments of microbial diversity and thus are insufficient to fully address these basic questions.

We propose to use novel genomic methods to sample skin microflora directly and shed light on the above conjectures in both normal and diseased dermatologic states.

We genomically classify the phylum and genus of the bacteria by sequencing the 16S rRNA genes directly from skin biopsies and will characterize the full bacterial genomes with metagenomic sequencing.

The genetic program to specify, maintain, and heal the skin is complex. However, the skin is an ideal system in which to perform genetic and genomic experiments because it offers easy access to diverse human skin disorders, excellent animal models, and well-developed cell and organotypic culture systems.

Giorgio Trinchieri *received his medical degree from the University of Torino, Italy, in 1973. He was a member of the Basel Institute for Immunology (Basel, Switzerland) and an investigator at the Swiss Institute for Experimental Cancer Research (Epalinges sur Lausanne, Switzerland). From 1979 to 1999 he was at Wistar Institute in Philadelphia and became Hilary Koprowski Professor and Chairman of the Immunology Program; he was also Wistar Professor of Medicine at the University of Pennsylvania in Philadelphia. He was director of the Schering Plough Laboratory for Immunological Research in Dardilly, France, and an NIH Fogarty Scholar at the Laboratory for Parasitic Diseases, NIAID, before becoming director of the Cancer and Inflammation Program (CIP) and chief of the Laboratory of Experimental Immunology at NCI in August 2006.*

As CIP director, I oversee the operations of two major NCI intramural laboratories, the Laboratory of Experimental Immunology and the Laboratory of Molecular Immunoregulation.

Giorgio Trinchieri

These two laboratories constitute the major immunologic component of the CCR's newly announced inflammation and cancer initiative, which spans the NCI's campuses in Frederick and Bethesda and seeks to partner NCI's expertise in inflammation and immunology with its cutting-edge cancer etiology and carcinogenesis program.

My research interest has always focused on the interplay between inflammation/innate resistance and adaptive immunity and on the role of pro-inflammatory cytokines in the regulation of hematopoiesis, innate resistance, and immunity.

My focus now is on the role of inflammation, innate resistance, and immunity in carcinogenesis, cancer progression, and prevention or destruction of cancer.

Recent studies are shedding a new light on how innate resistance, as an integral part of inflammation, participates in oncogenesis and tumor surveillance.

For a long time, innate resistance was considered a primitive nonspecific form of resistance to infections that was eclipsed by the potent and specific acquired immunity of higher organisms.

More recently, it has been recognized that innate resistance is not only the first line of defense against infections but also sets the stage and is necessary for the development of adaptive immunity.

Advances in cancer biology now reveal that what used to be considered the defensive mechanisms of innate resistance and inflammation are indeed manifestations of tissue homeostasis and control of cellular proliferation that have many pleiotropic effects on carcinogenesis and tumor progression and dissemination.

The interaction of the inflammatory mediators and effector cells with carcinogenesis and tumor progression is complicated and results in effects that either favor or impede tumor progression.

In my own group and in collaboration with the other CIP investigators, research on the interface between inflammation, natural resistance, and adaptive immunity in the mouse and in humans will focus on:

1) The molecular and cellular mechanisms regulating the activity of dendritic-cell subsets, particularly the type I interferon-producing plasmacytoid dendritic cells, as well as conventional dendritic cells, and their cross-activating interaction with other inflammatory cell types, NK cells, and T cells

2) The role of plasmacytoid dendritic cells in the regulation of immune response and tolerance in experimental models of cancer, autoimmunity, and infections

3) The molecular, structural, and signaling aspects of receptors that recognize pathogens—particularly Toll-like receptors, cytoplasmic NOD and RIG-I–like receptors—and other surface receptors and their synergism or antagonism in the regulation of the inflammatory response

4) The immunosuppressive tumor environment that results in alternate activation of macrophages and myeloid cells and paralysis of dendritic cells, with an emphasis on the role of IL-10 and STAT3 activation

5) Treatments aimed at reversing the immunosuppressive environment, combined with others to activate innate resistance or modulation of the inflammatory response for antitumor therapy

6) Using genetic or chemical models of colon and skin carcinogenesis to explore the role of inflammation-related gene products, such as tumor necrosis factor, IL-12, IL-23, IL-27, IL-10, IL-17, IL-22, Toll-like receptors and their signaling molecules. ■

Catalytic Reactions?

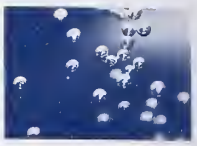
If you have a photo or other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation that scientists might appreciate that would be fit to print in the space to the right, why not send it to us via e-mail: catalyst@nih.gov>; fax:402-4303; or mail: Building 2, Room 2E26.

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

In Future Issues...

- Iron Regulation
- MRI and Heart Attacks
- Nursing Research

Kids' Catalyst: All That Fizz



Summer's here, and it's a good time to take science outside. We'll need some small plastic bottles of carbonated water that you can buy in a grocery store (how many and how large is up to you, but at least two—and the ones I used were 500 ml), at least three times as many large balloons, a cup of vinegar, a cup of baking soda, two clear cups, and a small nail.

Combining baking soda and vinegar happens to make a great cleaner. And vinegar smells a lot better than bleach, but just like bleach, you sure don't want to get it in your eyes, so be careful.

Before you head outside, think about what we know about carbonated water already. It dances on the tongue, you can watch the bubbles rise in a glass, and if you drink it fast enough . . . well, the carbonation can come back in unexpected ways. But we're going to do a bit more.

Fill one of your clear cups halfway with tap water and the other halfway with carbonated water, and place the two cups in the freezer. We'll come back to them later (but think about how the frozen results might be different). Now, outside we go.

With a small nail, carefully perforate the cap of the carbonated-water bottle you just opened. About 15 holes will do. Stretch the balloon mouth across the top of the cap. This will be our receptacle for the gas that comes from the carbonated water, and preparing it ahead of time allows us to catch as much as possible.

Mark the liquid level of the unopened bottle, and open it carefully. It will start to bubble immediately because the pressure has changed inside the bottle. When you safely have the top off, screw on the other cap with the balloon attached to it. And shake!

It won't take long to see the balloon expand, and if you shake the bottle enough, the balloon will become larger than the bottle itself. Lots of gas in there. But we can do more.

Now let's see what happens when we mix vinegar and baking soda. Place two tablespoons of baking soda and one tablespoon of vinegar (easiest with a funnel) into an empty bottle. Stand back (or you may find yourself covered in vinegary bubbles), get your balloon ready, and repeat the same procedure.

After you've cleaned up a bit, come back inside and look at the frozen water versus the frozen carbonated water that you placed in the freezer about an hour ago. You'll see a layer on top of the frozen carbonated water, but what is it? Thaw the glasses and note the water level, and also how fizzy the formerly frozen frothy water is. (Say that one quickly!)

If you have any leftover bottles of carbonated water, freeze them (unopened), along with another bottle full of tap water. It won't explode in the freezer, as cans can, because the bottle is plastic, but after these two are frozen you will see just how much frozen water expands.

Have fun with your carbonated water, see the mountain of bubbles created with vinegar and baking soda, and enjoy the warm weather!

—Jennifer White

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