FOSTERING COMMUNICATION AND COLLABORATION

The NIH CATALYST

A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

NATIONAL INSTITUTES OF HEALTH ■ OFFICE OF THE DIRECTOR ■ VOLUME 11, ISSUE 4 ■ JULY–AUGUST 2003

SARS: IMPACT AND RESPONSE SWIFT AND WORLDWIDE

by Fran Pollner

Fran Pollner

Front and Center: *NIAID Deputy Director John La Montagne (foreground left) and NIAID Director Anthony Fauci confer at the start of the SARS research colloquium at NIH on May 30. The meeting, Fauci said, "was put together as quickly as SARS has spread."*

A critical mass of international scientists converged at NIH May 30 to construct a research agenda to defeat severe acute respiratory syndrome (SARS). The global scourge had infected 8,439 people and killed 812 by the time the first recognized outbreak was declared contained a month later.

A global report from the World Health Organization, first-hand accounts of the Hong Kong and Toronto outbreaks, and lectures on coronavirus biology set the stage for five concurrent working groups to hammer out research recommendations by the end of the day.

This research agenda was speedily transferred to cyberspace at **<http://www.niaid.nih.gov/sars_meeting.htm>**, which also displays all the slides presented throughout the day; the plenary talks can also be viewed at **<http://videocast.nih.gov/ram/sars053003.ram>**).

SARS Coronavirus Could Resurface in Chilly Weather

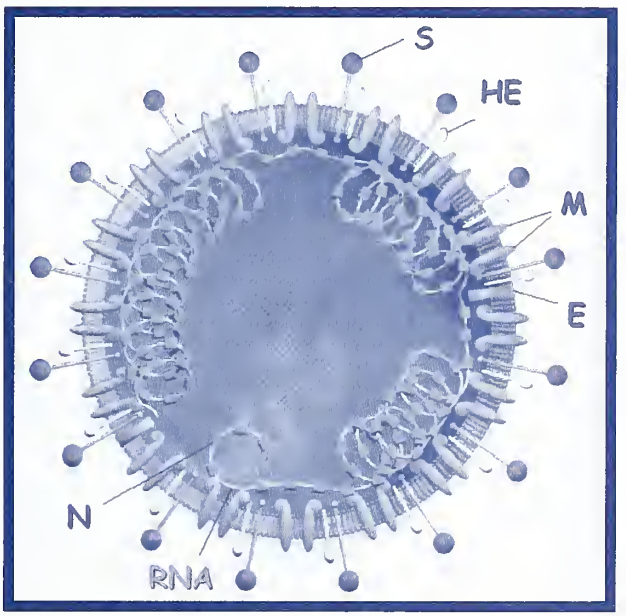
PROPOSED CC/NIAID PROTOCOL AIMED TO GO AT FIRST LOCAL RESURGENCE OF SARS

by Fran Pollner

The chain of events that led to a World Health Organization warning against traveling to Toronto began with the hospital spread of SARS from a patient and his wife. The couple passed the virus to 84 people in 31 hours.

Most of those infected, said Allison McGeer, director of infection control at Mount Sinai Hospital and a professor at the University of Toronto, had been "within droplet range for no more than one to two minutes."

Within days of this event, which turned out to be a rare example of a SARS "superspreader," 19 Toronto hospitals were affected by SARS, and every one of them wanted to be able to get a clinical trial going, McGeer recounted during a clinical research breakout session at the international SARS colloquium held at NIH May 30.



Adapted from Kathryn Holmes, "SARS-Associated Coronavirus, *NEJM* **348**:1948-1951, May 15, 2003; shown also during her talk on coronavirus virology and pathogenesis at the NIH workshop May 30

Structure of the Coronavirus Virion: *S = spike glycoprotein (the viral fusion protein), HE = hemagglutinin-acetylesterase glycoprotein, M = membrane glycoprotein, E = small envelope glycoprotein, N = nucleocapsid phosphoprotein*

"But there was no way they could get a clinical trial protocol through the ethics boards of 19 hospitals before the outbreak, which lasted a month, was over—not to mention that it's hard to focus on anything but treating during an outbreak. This is a major challenge," she said.

Many agreed that new mechanisms are needed for rapid—but careful—approval of national and international protocols to respond to such precipitous events.

Meeting the Challenge

Investigators generally view the next cold-weather flu season as a likely context for SARS resurgence. Collaborating scientists from NIAID and the CC are seeking IRB approval of a SARS clinical research protocol that would begin the instant the first patient in the metropolitan area thought to have SARS is referred to NIH as a study candidate.

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Catalyzing Team Science

Michael Gottesman

On June 23–24, 2003, the Bioengineering Consortium (BECON) at NIH held a symposium entitled "Catalyzing Team Science." This theme reflected the NIH Director's Roadmap focus on building multidisciplinary teams of the future. As a participant, I was asked to demonstrate ways in which the NIH intramural program has fostered team approaches to research. Team science has always been a strength at NIH, but recently we have developed several strategies for encouraging this approach.

Centers-based Co-localization Of Research Activities

NIH has 21 institutes and centers with intramural programs. As in academia, there is a tendency for each of these programs to develop its own resources, reducing the likelihood of interaction. To encourage trans-NIH team building, we have developed laboratory centers that are theme-oriented and co-locate scientists by research interests rather than administrative affiliation.

Examples include the Clinical Research Center, the in vivo Imaging Center, the Vaccine Research Center, the Porter Neuroscience Center (under construction), a Musculoskeletal Center (in planning), and a center focusing on the use of animal models to study disease (under discussion). This geographic co-location is based on ample evidence that interactions among scientists fall off dramatically as distance increases.

Because it is not always feasible to group scientists by research interest, NIH has also encouraged development of more virtual faculties of scientists who share research interests. Currently, there are close to 100 such special interest groups in the intramural program, including cross-cutting disciplines such as genetics, molecular biology and biochemistry, immunology, neuroscience, structural biology, cell biology, clinical research, and groups interested in specific model systems and technical approaches. This issue of the *Catalyst* includes the current list of these special interest groups.

Although it is the exception, rather than the rule at NIH, we are experimenting with joint appointments of individuals in two administrative organizations to encourage team science. Because of administrative oversight requirements, there is usually a primary appointment and a courtesy appointment, but the latter may be accompanied by commitment of resources and personnel to help build a team.

Recognition of Individual Accomplishment Within a Team

Recognizing individual team members is perhaps the most difficult problem facing academic and government institutions. One approach at NIH is the development of the Staff Scientist and Staff Clinician positions. These are accomplished scientists who do not control independent resources, but who support important NIH programs. Examples can be found in the National Center for Biotechnology Information in the National Library of Medicine, which is staffed primarily by Staff Scientists who work together to support bioinformatics at NIH, including PubMed and GenBank.

Staff Scientists are important team members in vaccine development programs at NIH, and Staff Clinicians make possible most of the groundbreaking clinical research in our Clinical Center. Staff Scientists are selected by individual ICs with overall institutional quality control and an institutional commitment to continue to employ the individual if performance is outstanding, even if a program disbands. In teams formed with Staff Scientists, there is at least one individual who is a tenured scientist who makes important programmatic decisions for the team.

NIH intramural scientists who control independent resources begin on a tenure track, and after six years (for laboratory-based scientists) or eight years (for clinical and population-based-research investigators), they are considered for tenure. At the NIH, tenure implies a permanent research position with resources subject to quadrennial outside review. The tenure decision at NIH, as at universities, is made by a central committee of peers, based on evidence of innovative, independent, and influential science.

In general, tenure-track scientists are encouraged to establish their independence, and often this is interpreted to mean that they should not publish extensively with their senior colleagues and mentors. This view is a clear disincentive to building team science (as it is in other academic settings). Approaches to deal with this problem include emphasizing recognition of the important contributions of each member of a team through presentations at scientific meetings, publishing as principal author in journals that are specific to the person's discipline, and extensively interacting with senior scientists in the person's field who can then appropriately attribute contributions to the team. Still, our tenure committees will need to be educated to recognize the critical nature of individual team members' contributions. For additional discussion of this critical issue, please see the July-August 1998 *Catalyst* (**http://www.nih.gov/catalyst/back/98.07/fostering.html**).

Other Resources Used To Promote Team Science

In addition to geographic co-location of scientists, which frequently requires significant investment of new resources, there are other resources that have been used at NIH to encourage team approaches. Small pools of funds, distributed on a competitive basis, encourage interaction of individual scientists with complementary interests. For example, for the past several years, NIH has sponsored "Bench-to-Bedside" awards, which support projects that pair lab-based scientists with more clini-

cally oriented scientists to create new translational research.

In addition, there is a fund to support intramural AIDS-targeted research (IATAP), with the specific goal of encouraging structural biologists to work with cell and molecular biologists to address HIV-related research problems.

Recently, in response to requests from the general scientific community, a stem cell characterization facility was established at the NIH to bring together experts in the biology and biotechnology of stem cells. Historically, NIH has supported several such central resources. These allow individual scientists to tap experts in many different fields. Examples include the Bioengineering and Physical Sciences Program, the Center for Information Technology, and the Veterinary Resources Program (see the July-August 2001 *Catalyst*; <**http://www.nih.gov/catalyst/2001/01.07.01/page5.html**>).

Education or Training Experiences That Promote Team Science

Graduate education frequently emphasizes individual scholarship with a sharp focus on a single important research problem. Team science requires broad knowledge of multiple disciplines so that team members can communicate effectively. At NIH, where many programs require interaction of people with backgrounds in multiple disciplines, it is often necessary to train postdoctoral fellows to function effectively in such teams. Training may include coursework in disciplines such as bioinformatics, clinical research, and integrative biology, as well as mentorship at the laboratory level.

NIH has recently initiated a Graduate Partnership Program in which graduate students interested in emerging disciplines matriculate at universities but do most of their research at NIH. Some of these programs involve co-mentoring in which an NIH scientist and a university faculty member with complementary skills work together with a single graduate student. We have recently established a joint fellowship program with NIST that emphasizes co-mentoring in biology and physical sciences.

If you have other ideas to encourage team science at NIH, please send a note to me.

—Michael Gottesman
Deputy Director for Intramural Research

Bread-and-Butter Dominates Director's Town Hall Meeting

by Nicole Kresge

Questions about the A-76—competitive outsourcing—process, NIH security, and a one-page addendum to employee performance contracts dominated the hour-long Town Hall meeting convened June 18 by NIH Director Elias Zerhouni.

The volume of e-mail about A-76 received in advance of the meeting reflected a fairly high degree of concern among NIH employees that their jobs were suddenly on the line, and Zerhouni had enlisted William T. Fitzsimmons, director of the NIMH Office of Resource Management and a member of the A-76 Steering Committee, to present an overview of the situation.

A-76 may strike some as a new concept, Fitzsimmons said, but it's actually been around since the Eisenhower years. The rationale behind it, he said, is that "if it's in the yellow pages—if it's something that you can contract out for and it's not part of your basic mission—then it's not the business of the government to compete with business." Thus, A-76 requires that for positions that have been classified as commercial-competitive, a bid must be prepared that contractors can compete for against the government.

To comply with the President's Management Agenda, NIH had to examine its workforce of 18,000 and determine which employees are doing jobs that could be done by a private contractor. It determined that about half of its workforce consists of "commercial employees."

Between 2002 and 2005, NIH will have to open 50 percent of these commercial-competitive positions to competition with the private sector. This year's competitions are in Facilities Management and Extramural Administrative Support jobs, for which proposals from the private sector are now competing with proposals from the current government staffs. The results should be known by late September, Fitzsimmons said, adding that federal employees have prevailed in most such competitions held so far in other agencies. However, even when employees do win, there may be job losses. NIH will find places for employees who lose their current jobs, he said.

Zerhouni expressed confidence that the NIH workforce—outstanding in his opinion—would come out ahead in the competitions.

Less than sanguine facilities management employees, however, said they felt they were placed at a competitive disadvantage by the federal hiring freeze, which prevents government managers from replacing people who have left, while private competitors are under no such constraints and can bid for a project at full workforce strength. A question on whether veterans' preference, seniority, or awards would be factors in what might be a scramble to keep current jobs could not readily be answered.

On NIH security, Robert Desimone, NIMH scientific director and chair of the Community Advisory Board on Security, reported that the group had developed the "First Principles of Security": 1) all the government rules and regulations will be followed, (2) protection against weaponized vehicles will be the highest priority, (3) employees will be treated differently from visitors, and (4) the application of security procedures has been changed so they run more smoothly.

The next stage of emergency preparedness is being implemented, he said, including shelter-in-place guidelines (see <**http://www.olao.od.nih.gov/employees/shelter_in_place.html**>), evacuation plans, and a recently purchased NIH emergency broadcast radio system. Operational plans for the "post-fence environment" and the new Visitors' Center are also in the works.

Several questioners focused on a new one-page addendum to job performance plans that requires that employees commit themselves to achieving specific HHS program and management objectives. What was the intent of this new requirement? How would they be implemented into job descriptions? What would be the consequences of refusing to sign the pledge?

Mike Rosenthal, of Human Resources, noted that, like A-76, this job-performance addendum came out of the President's Management Agenda. The employee's signature, he said, would reflect acknowledgment of the goals; supervisors will work with employees to incorporate those objectives applicable to their jobs. As for the consequences of not signing, he said, NIH management would deal with that issue.

These and other issues will continue to be addressed, Zerhouni said at the close of the meeting. One forum for this will be a "Director's Column" in *The NIH Record*. ■

CC Set To Go with First SARS Protocol

continued from page 1

The protocol encompasses three study cohorts comprising up to 200 individuals: SARS patients, their household contacts, and CC health-care workers.

"A major issue," said Henry Masur, chief of critical care medicine at the Clinical Center, "is how the virus is spread, and a major thrust of the study is determining from where, how much, and for how long the virus is excreted."

The protocol targets patients who have relatively mild disease when they are invited to enroll. It's anticipated that most of the patients would drive themselves to the Bethesda campus and be met at the perimeter and transferred via a dedicated negative-flow transport device (see photo, page 5). They would enter the hospital through a special entrance and be taken directly to a negative-flow room.

Blood, urine, feces, and respiratory secretions would be analyzed on a regular basis. Among the study goals listed in the protocol are:

- To evaluate and treat persons with SARS
- To elucidate the pathophysiology of SARS
- To characterize the immune response during SARS
- To evaluate diagnostic tests for the rapid identification of SARS in clinical specimens

Contacts: Household and Hospital

The second study population of family members and other close contacts would be enrolled and followed serially for evidence of the onset of viral excretion and correlation with the presence—or absence—of clinical symptoms. Data generated from this cohort should expand knowledge of the natural history of the disease, Masur said. "We'd have an unparalleled opportunity to study disease development virologically and immunologically from very early after exposure."

The third population—NIH health-care workers who come in contact with the study patients—would be followed to "make sure they are not acquiring the virus.

"While the risk of a hospital worker becoming infected is remote, that possibility does exist," Masur said. "Should that happen, the person would be moved into the other protocol group—but the hospital leadership and NIAID leadership have confidence in the caliber of our facilities and our staff and our ability to handle this virus better than can be done almost anywhere else." He noted that hospital epidemiologist and CC deputy director David Henderson, an associate investigator in the study, has discussed SARS transmission with involved hospital authorities in Canada and Asia and has concluded that the risk at the Clinical Center should be manageable, as has Cliff Lane, NIAID clinical director and the accountable investigator on the protocol.

The far greater danger to any hospital staff and to other patients, protocol leaders have observed, would be exposure to CC patients and staff who develop SARS through travel or personal contact and then enter the building for work or for treatment on protocols not related to SARS.

"Perhaps the most important lesson learned from the Toronto experience," Henderson said, "is that health-care workers at the front-line in an epidemic must have extremely high indices of suspicion for the diagnosis and proper management of highly contagious diseases such as SARS. Almost all instances of transmission occurred in settings in which the disease was not suspected." Conversely, once the disease was recognized, even institutions in developing countries with limited resources were able to contain the infection by careful adherence to traditional infection-control procedures.

Aside from CC excellence in infection control, other factors that argue for clinical SARS research at the CC are the NIH tradition and responsibility to respond to national health priorities, protocol investigators agree. They point to the response of the CC to the AIDS epidemic in the early 1980s, when there was considerable fear about having patients with HIV in hospital settings, as an example of meeting that obligation and advancing science and patient care in a perilous time.

Beyond the First SARS Protocol

The CC/NIAID investigators also envision two additional studies that could culminate in the development of a novel SARS therapy. The first would entail identifying patients who have recovered from SARS and bringing them to the Clinical Center to obtain plasma samples from them.

"The idea is that we can use these samples to make an immune serum globulin. We know that SARS patients make antibody to the virus," Masur said. "We would harvest that antibody, concentrate it, and remove potentially infectious elements." This potential product would be tested in a variety of in vitro studies and, if results warranted and the FDA approved, would then move into human testing.

In the current protocol, treatment is described in flexible terms:

"As there is no clear optimal therapy,

Fran Pollner

Teamwork: *(left to right) Henry Masur, CC critical care chief and an associate investigator in the CC/NIAID SARS protocol; John Beigel, CC clinical research fellow and protocol PI; and Cliff Lane, NIAID clinical director and the protocol's accountable investigator*

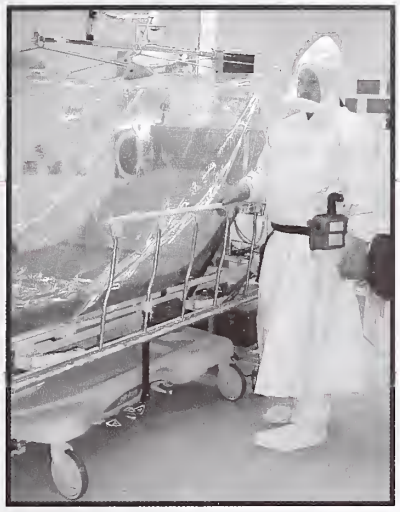
"We announced in April that we might bring SARS patients to the Clinical Center to participate in a study. We felt we have a fabulous environment scientifically—and a safe environment—to study SARS. But that possibility generated more e-mail to me than anything else in the eight years I've been Clinical Center director."

—John Gallin

"The facts of the evolution [of the SARS outbreak] show that when the medical staff is prepared, the chain of transmissibility is broken. The risk of spread in a hospital that is conducting a study is low."

—Anthony Fauci

CC Grand Rounds, June 17, 2003



Fran Pollner

Private Spaces: *The DeMistifier rolling bed/isolation unit, acquired to transport a SARS protocol patient from his or her vehicle to a secure CC entrance and up to the negative-flow room where the patient would be cared for—with CC respiratory therapy chief Dennis Brown in attendance, as would often be the case throughout the upcoming study. Brown is wearing the powered air-purifying respirator (PAPR) and protective gown, gloves, and foot gear that all involved health-care workers would don while participating in the study. Filtered air is delivered to the hood by tube from a pack worn around the waist; the hood is disposable and after each patient encounter would be discarded in the anteroom outside the negative-flow room. Brown says he is not too worried about his personal safety: "I wouldn't have signed on as a health-care provider—especially at NIH—if I didn't know some risk was involved." Brown and others, including hospital epidemiologist David Henderson, believe this risk is minimal based on the ability of hospitals in Asia and Toronto to control SARS once they understood and enforced the necessary precautions.*

and the data regarding optimal therapy for SARS [are] continually changing, two options will be presented to the patients regarding therapy. First, the patients may be treated as clinically indicated by best medical practice given our continually changing knowledge of SARS.

"Alternatively, patients may be enrolled in other protocols designed to evaluate therapies. These may be intramural protocols of the NIH or protocols from outside study groups for which the NIH is a collaborative center." ■

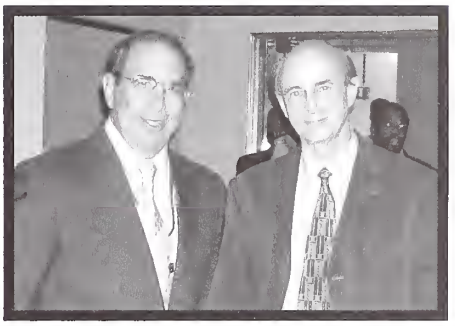
Celebrating 50 Years Of Clinical Research And Patient Care

Peter Kozel

The Clinical Center takes the cake: *A July 9th party began a year of celebration that culminates in summer 2004 with the opening of the Mark O. Hatfield Clinical Research Center.*

Peter Kozel

A Proud Circle: *(left to right) CC Director John Gallin, NIH Director Elias Zerhouni, and Deputy Director for Intramural Research Michael Gottesman are in fine humor before opening the festivities. During his talk later, Gottesman revealed to the world at large the kinds of items Gallin keeps in his office, including a walking hamburger, two windup Godzillas, an ambulatory purple dinosaur, two wind-up mice, a lounging frog and a hopping frog, two cool-dude raisins, and a walking nose. Why? Because Gallin exchanges toys with his pediatric patients when he goes on rounds—another way to care for them.*



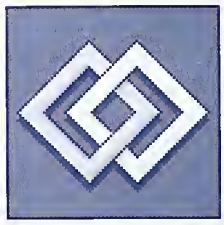
Fran Pollner

Institutional Memory: *For more than 30 years, Harvey Alter (right) has been divining the nature of elusive infectious enemies from his post in the CC's Department of Transfusion Medicine—and the world has witnessed the disappearance of post-transfusion hepatitis because of it. "I've enjoyed every moment," he said—that is, he added, until John Gallin (CC director, at left) asked him to reflect at this kickoff 50th-anniversary celebration. But Alter managed to get past his reluctance to take the stage by sprinkling his talk with bits of his tongue-in-cheek poetry—an ode to his then-arch nemesis that was neither hepatitis A nor hepatitis B, another to an old collegial rival, and a third—more recent and a bit more sentimental—to none other than the Clinical Center.*

Fran Pollner

The Bad Business Blues Band: *Beating back the rain for the CC celebration, David Rubinow (far right), NIMH clinical director, chief of the behavioral endocrinology section, lead (1963 Les Paul) guitar, and major warbler, with bandmates of 20+ years Richard Loewenstein on harmonica, Howard Feinstein on keyboard, Gary Gott on bass, and—sitting in for Rubinow's wife, Carly—Thomas Lombardo on drums.*

Interinstitute Interest Group Directory



Web Access

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

Major Interest Groups

Cell Biology Interest Group
Meeting time: Not specified
Meeting place: Building 32, Library
Contact: Jennifer Lippincott-Schwartz
Phone: 402-1010; 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: 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: 496-8364
E-mail: <tf60y@nih.gov>
ListServ: subscribe to <GIG-L@list.nih.gov>

Immunology Interest Group
Meeting time: Each Wednesday (except summer), 4:15 pm
Meeting place: Building 10, Lipsett Auditorium
Contact: Terry Fry
Phone: 402-0215
E-mail: <bfowlkes@nih.gov>
ListServ: subscribe to IMMUNI-L by joining the interest group at its web site

Molecular Biology/Biochemistry Interest Group
Meeting time: Yearly to consider speakers
Meeting place: Building 8, Room 122
Contact: Reed Wickner
Phone: 496-3452
E-mail: <wickner@helix.nih.gov>

Neuroscience Interest Group
Meeting time and place: Check website
Contact 1: Chip Gerfen
Phone: 496-4341
E-mail: <gerfen@codon.nih.gov>
Contact 2: Betsy Murray
Phone: 496-5625, X-227
E-mail: <eam@ln.nimh.nih.gov>

Structural Biology Interest Group
Meeting time and place: Usually 3rd Tuesday, 4:00 pm, Building 50; notices by e-mail and on the SBIG website
Contact 1: Sandford Markey
Phone: 496-4022
E-mail: <s.markey@nih.gov>
Contact 2: Susan Buchanan
Phone: 594-9222
E-mail: <skbuchan@helix.nih.gov>
To register for e-mail announcements, join SBIG at <www.nih.gov/sigs/sbig>

Other Interest Groups

AIDS Interest Group
Meeting time and place: Varies
Contact: Fulvia Veronese
Phone: 496-3677
E-mail: <veronesf@od.nih.gov>
ListServ: subscribe to AIDSINTG-L

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

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

Bioethics Interest Group
Meeting time: 1st Monday (except 2nd 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: 496-9322
E-mail: <mk46u@nih.gov>
Sign up at <http://BIOETHICSinterestgroup@list.nih.gov/>

Biomedical Computing Interest Group
Meeting time: Third Thursday, 3:00 pm
Meeting place: Building 10, Room 2C116 (Medical Board Room)
Contact 1: Jim DeLeo
Phone: 496-3848
E-mail: <jdeleo@nih.gov>
Contact 2: Susan Harris
Phone: 435-8721
E-mail: <sharris@mail.cc.nih.gov>
ListServe: subscribe to BCIG-L

Biophysics Interest Group
Meeting time and place: Varies (often Building 10, Bunim Room)
Contact: Peter Basser
Phone: 435-1949
E-mail: <pjbasser@helix.nih.gov>

Biosciences Business Interest Group
Meeting time: Monthly, lunchtime
Meeting place: Varies
Contact 1: Jonathan Sorger
Phone: 496-3208
E-mail: <jsorger@nih.gov>

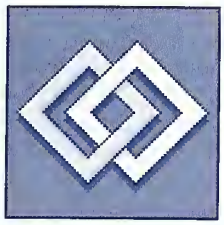
Birth Defects and Teratology Interest Group
Meeting time: Quarterly seminars
Meeting place: Videoconference between Bethesda and Research Triangle Park, N.C.
Contact: Megan Adamson
Phone: 443-4354
E-mail: <madamson@willco.niaaa.nih.gov>

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: 496-1478
ListServ: Subscribe to CALCIUM-L

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

Chemistry Interest Group
Meeting time: Periodic seminars
Meeting place: Varies
Contact 1: John Schwab
Phone: 594-5560
E-mail: <schwabj@nigms.nih.gov>
Contact 2: Kenneth Kirk
Phone: 496-2619

Chromatin and Chromosomes Interest Group
Meeting time: One Friday a month, 10:30 am
Meeting place: Building 50, 3rd-floor library
Contact: David Clark
Phone: 496-6966
E-mail: <djclark@helix.nih.gov>



Clinical Immunology Interest Group
Meeting time: Monthly, last Wednesday, noon
Meeting place: Building 10, Room 9S235
Contact: Oral Alpan
Phone: 402-3447
E-mail: <oalpan@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, 6:30–7:30 pm
Meeting place: Building 10, Lipsett
Contact: Donna Shields
Phone: 435-6618
E-mail: <dshields@mail.cc.nih.gov>

Cognitive Neuroscience Consortium
Meeting time: Every two months, last Wednesday, 4:15 pm
Meeting place: NSC Building, Conference Room A (starts September 2003; Extramural Program Directors' forum: last Friday every 3rd month, 3:00 pm, NSC Building, Conf. Room 2120, starts October 2003)
Contact: Emmeline Edwards
Phone: 496-9964
E-mail: <ee48r@nih.gov>

Cultural and Qualitative Research Interest Group
Meeting time: 2nd Tuesday of February, April, June, September, November, 9:30 am
Meeting place: As announced
Contact 1: Sabra Woolley
Phone: 435-4589
E-mail: <woolleys@mail.nih.gov>
Contact 2: Suzanne Heurtin-Roberts
Phone: 594-6655
E-mail: <sheurtin@mail.nih.gov>

Cytokine Interest Group
Meeting time: three to four symposia/year
Meeting place: Varies; one symposium/year at NCI-Frederick
Contact 1: Brian Kelsall
Phone: 496-7473
E-mail: <bkelsall@niaid.nih.gov>
Contact 2: Calman Prussin
E-mail: <cprussin@niaid.nih.gov>

Developmental Biology Interest Group
Meeting time and place: None scheduled
Contact: Tom Sargent
Phone: 496-0369
E-mail: <tsargent@nih.gov>
Contact 2: Peggy Zelenka
E-mail: <zelenkap@intra.nei.nih.gov>

DNA Repair Interest Group
Meeting time: 3rd Tuesday, 12:30 pm
Meeting/Videoconference: Natcher, Room H; 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, TX; Univ. of Texas, Galveston; Lawrence Livermore (CA) National Laboratory; Univ. of Michigan, Ann Arbor; Univ. of Kentucky, Lexington; Brookhaven National Laboratory, Upton, NY; Univ. of Pittsburgh
Contact 1: Kenneth Kraemer
Phone: 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: 496-7515
E-mail: <umhau@nih.gov>

Drosophila Interest Group
Meeting time: 3rd Tuesday, 1:15 pm
Meeting place: Building 6B, Room 4B429
Contact 1: Sue Haynes
Phone: 301-295-9791
E-mail: <shaynes@usuhs.mil>
Contact 2: Jim Kennison
E-mail: <Jim_Kennison.nih.gov>

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

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

Endocrinology Interest Group
Meeting time and place: Varies
Contact 1: George Chrousos
Phone: 496-5800
E-mail: <George_Chrousos@nih.gov>
Contact 2: Phil Gold
Phone: 496-1945

End of Life Research Interest Group
Meeting time: Typically Thursdays, 3:00 pm, on an as-needed basis
Meeting place: Natcher, room as available
Contact: Ann O'Mara
Phone: 496-8541
E-mail: <omaraa@mail.nih.gov>

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

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: 496-2557
E-mail: <jaysan@helix.nih.gov>
Contact 2: Dan Sackett
E-mail: <sackettd@mail.nih.gov>

Gene Therapy Interest Group
Meeting time: 2nd Thursday, 2:00 pm
Meeting place: Building 10, Lipsett Auditorium
Contact: Fabio Candotti
Phone: 435-2944
E-mail: <fabio@nhgri.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
Contact: John N. Weinstein
Phone: 496-9571
E-mail: <weinstein@dtpax2.ncifcrf.gov>

Glycobiology Interest Group
Meeting time and place: Varies
Contact: Diana Blithe
Phone: 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: 496-2007
E-mail: <reboisv@ninds.nih.gov>

Hard Tissue Disorders Interest Group
Meeting time: Day varies, 9:30 am
Meeting place: Building 30, Room 117
Contact: Pamela Robey
Phone: 496-4563
E-mail: <probey@dir.nidcr.nih.gov>
Contact 2: Michael Collins
Phone: 496-4913

Interinstitute Interest Group Directory

Head and Neck Cancer Interest Group
Meeting time: To be announced
Meeting place: Building 30, Room 117
Contact 1: Adrian Senderowicz
Phone: 594-5270
E-mail: <adrian.senderowicz@nih.gov>
Contact 2: Wendy Weinberg
E-mail: <weinberg@cber.fda.gov>

History of Biomedical Research Interest Group
Meeting time: Second Tuesday, 3:30 pm
Meeting place: Varies; check web site
Contact 1: Office of NIH History
Phone: 496-6610
Contact 2: Victoria Harden
E-mail: <hardenv@od.nih.gov>

Image Processing Interest Group
Meeting time and place: Distributed by e-mail and on <image.nih.gov>
Contact 1: Benes Trus
Phone: 496-2250
E-mail: <Benes_Trus@nih.gov>
Contact 2: Matt McAuliffe
Phone: 594-2432

Imaging Ligand Development Consortium
Meeting time and place: To be announced (every 3 months; steering committee meetings will be held every 2 months in the Neuroscience Center)
Contact: Jamie Driscoll
Phone: 443-5288
E-mail: <jdrisco1@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>

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

Java Interest Group
Meeting time and place: Announced through ListServe; join at <list.nih.gov/archives/java.html>
Contact 1: John Ostuni
Phone: 451-9935
E-mail: <ostuni@helix.nih.gov
Contact 2: Jai Evans
Phone: 496-9544
E-mail: <evansj@helix.nih.gov>

Knowledge Management Interest Group
Meeting time: 4th Wednesday, 2:30 PM (changes will be noted on NIH Calendar and KMIG website)
Meeting place: Building 12B, 2nd-floor Conference Room (directions posted at website)
Contact 1: Geoffrey Marsh
Phone: 301-594-9683
E-mail: <geoff@mail.nih.gov>
Contact 2: Paul Beatty
E-mail: <pbeatty@mail.nih.gov>

Lambda Lunch (Bacterial and Phage Genetics)
Meeting time: Each Thursday, 10:30 am
Meeting place: Building 36, Room 1B13
Contact: Susan Gottesman
Phone: 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"

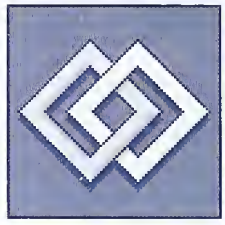
Light Microscopy Interest Group
Meeting time: Monthly, Tuesday, noon
Meeting place: Building 10, Room 4B51
Contact: James McNally
Phone: 402-0209
E-mail: <mcnallyj@mail.nih.gov>
Contact 2: Christian Combs
Phone: 496-0014

Mass Spectrometry Interest Group
Meeting time: 1st & 3rd Thursday, 10:30 am
Meeting place: Building 10, Room 7C101
Contact: Jeff Kowalak
Phone: 496-4242
E-mail: <jkowalak@intra.nimh.nih.gov>

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

Membrane Protein Interest Group
Meeting time: Usually one Wednesday a month, 1:00 pm; check website: <http://www.nih.gov/sigs/mpig>
Meeting place: Building 5, Room 127
Contact: Reinhard Grisshammer
E-mail: <rkgriss@helix.nih.gov>

Microarray Users Group
Meeting time and place: Varies
Contact: Katherine Peterson
Phone: 402-6537
E-mail: <petersonk@nei.nih.gov>



Mitochondria Interest Group
Meeting time: 1st Monday, 3:00 pm
Meeting/Videoconference: Natcher, Room H; NIEHS, Research Triangle Park, NC; GRC, Baltimore; NIST, Admin. Bldg, Room B113, Gaithersburg, MD; VA Hospital, Cleveland; Podell Auditorium, Beth Israel Medical Center, NYC; Baylor Univ.,Texas; Louisiana State University Health Science Center
Contact: Steve Zullo
Phone: 301-975-8984
E-mail: <zullo@nist.gov>
Contact 2: Salvatore Alesci
E-mail: <alescis@mail.nih.gov>

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

Molecular Recognition and Quantitative Interaction Interest Group
Meeting time: 1st Wednesday, 5:30 pm
Meeting place: Building 6A, Room 4A05
Contact: Robert Crouch
Phone: 496-4082
E-mail: <robert_crouch@nih.gov>

Motility Interest Group
Meeting time and place: Varies
Contact: Jim Sellers
Phone: 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: 402-0545
E-mail: <hw@helix.nih.gov>

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

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

Neurobiology Interest Group
Meeting time: alternate Fridays, 4:30 pm
Meeting place: Building 36, Room 1B13/17
Contact: Chip Gerfen
Phone: 496-4341
E-mail: <gerfen@helix.nih.gov>
ListServ: <http://intra.ninds.nih.gov/nig/>

Neuroinformatics Interest Group
Meeting time and place: To be announced
Contact 1: Stephen Koslow
Phone: 443-1815
E-mail: <koz@helix.nih.gov>
Contact 2: Barry Davis
Phone: 402-3464
E-mail: <barry_davis@nih.gov>

Pain Interest Group
Meeting time: Tuesday, 12:00 noon
Meeting place: Building 30, Room 117
Contact 1: Raymond Dionne
Phone: 496-0294
E-mail: <rdionne@dir.nidcr.nih.gov>
Contact 2: Michael Iadarola
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 1C520
Contact: Peter Herscovitch
Phone: 451-4248
E-mail: <herscovitch@nih.gov>

Phage-Tech Interest Group
Meeting time and place: Varies
Contact 1: Dean Scholl
E-mail: <dscholl@helix.nih.gov>
Contact 2: Carl Merril
Phone: 435-3583

Pigment Cell Research Interest Group
Meeting time: One Tuesday every other month, lunch meeting 12:00–1:30 pm; once a year a daylong meeting
Meeting place: Building 40, Room 1201-1203
Contact 1: Bill Pavan
Phone: 496-7584
E-mail: <bpavan@nhgri.nih.gov>
Contact 2: Marjan Huizing
Phone: 402-2797
E-mail: <mhuizing@mail.nih.gov

Polyunsaturated Lipid Function Interest Group
Meeting time: Usually 1st Wednesday of each month, as announced (journal club; resuming in September), 1:00 pm
Meeting place: Flow Bldg. Conference Room, Rockville, 12501 Washington Ave.
Contact: Norman Salem
Phone: 443-2393
E-mail: <nsalem@niaaa.nih.gov>

Prostate Cancer Interest Group
Meeting time: 2nd & 4th Tuesdays, 4:00 pm
Meeting place: Building 10, Room 2S235
Contact: Kathleen Simon
Phone: 496-6353
E-mail: <simonk@mail.nih.gov>

Protein Trafficking Interest Group
Meeting time: 2nd Tuesday, 3:30 pm
Meeting place: Building 50, Room 2328
Contact 1: Harris Bernstein
Phone: 402-4770
E-mail: <harris_bernstein@nih.gov>
Contact 2: Peng Loh
Phone: 496-3239

Proteomics Interest Group
Meeting time: Monthly 1st Friday seminars
Meeting place: Building 50; check website: <http://proteome.nih.gov>
Contact: Donita Garland
Phone: 496-6999
E-mail: <dgarland@helix.nih.gov>

Reactive Oxygen Species Interest Group
Meeting time and place: Monthly seminars with Oxygen Club of the Greater Washington Area (info via NIH Calendar, members' e-mail, and <Jayasree.Nath@NA.AMEDD.ARMY.MIL>)
Contact 1: Mike Chiueh
Phone: 496-3421
E-mail: <chiueh@helix.nih.gov>
Contact 2: Mike Espey
Phone: 496-7511

RNA Club
Meeting time: 1st Tuesday (except August), 4:00 pm
Meeting place: Building 41, Room C509
Contact 1: Carl Baker
Phone: 496-2078
E-mail: <ccb@nih.gov>
Contact 2: Susan Haynes
E-mail: <shaynes@usuhs.mil>

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

Stem Cell Interest Group
Meeting time and place: TBA; check website
Contact 1: Peter Gasper
Phone: 1-410-558-8260
E-mail: <gasperpe@grc.nia.nih.gov>
Contact 2: Kevin Becker
E-mail: <beckerk@grc.nia.nih.gov>

Stroke Branch Interest Group/Seminar
Meeting time: Thursdays 3:30 pm
Meeting place: Building 36, Conf. Room 1B13
Contact 1: John Kylan Lynch
Phone: 496-1187/1714
E-mail: <LynchJ@ninds.nih.gov>
Contact 2: Zurab Nadareishvili
Phone: 496-6231

Synaptic and Developmental Plasticity Interest Group
Meeting time: Wednesday, once a month, 12:00 noon
Meeting place: Building 49, Room 1A50
Contact: Bai Lu
Phone: 435-2970
E-mail: <lub@codon.nih.gov>

Systems Biology Interest Group
Meeting time: Every second Thursday, 3:00–4:30 pm (starting September 11, 2003)
Meeting place: Natcher, Room 2AS10
Contact 1: Victor Pollara
Phone: 402-1620
E-mail: <pollarav@mail.nih.gov>
Contact 2: Martin Meier-Schellersheim
Phone: 496-5046
E-mail: <mms@niaid.nih.gov>

Therapeutic Oligonucleotides Interest Group
Meeting time: Last Thursday, 4:00 pm
Meeting place: Building 10, Room 2C116
Contact: Yoon Cho-Chung
Phone: 496-4020
E-mail: <chochung@helix.nih.gov>

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

Interinstitute Interest Group Directory

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

Veterinary Interest Group
Meeting time: 3rd Thursday, 12:00 noon
Meeting place: Varies
Contact: Kay Jordan
Phone: 402-4547
E-mail: <ekj@helix.nih.gov>

Viral Hepatitis Interest Group
Meeting time: One Monday a month, 4:15 pm
Meeting place: Building 10, Room 1C726 (DTM conference room)
Contact: Marian Major
Phone: 301-827-1881
E-mail: <major@cber.fda.gov>

Virology Interest Group
Meeting time: 4th Tuesday, 12:15 p.m.; minisymposium in November
Meeting place: Building 4, Room 433
Contact 1: Alison McBride
Phone: 496-1370
E-mail: <amcbride@niaid.nih.gov>
Contact 2: Kathryn Carbone
E-mail: <carbonek@cber.fda.gov>
ListServ: Contact <CBuckler@nih.gov>

Washington Area Yeast Club
Meeting time: 2nd Wednesday, 4:30 pm
Meeting place: Building 6A, Room 4A05
Contact 1: Reed Wickner
Phone: 496-3452
E-mail: <wickner@helix.nih.gov>
Contact 2: Alan Hinnebusch
Phone: 496-4480
E-mail: <ahinnebusch@nih.gov>

WorldWideWeb Interest Group
This group is seeking someone to take on the administrative activities to keep the group going smoothly. Interested?
Contact: Dale Graham
E-mail: <degraham@helix.nih.gov>

Xenopus/Zebrafish Interest Group
Meeting time: Last Monday (except summer), noon
Meeting place: Building 6B, Room 429
Contact 1: Brant Weinstein
Phone: 435-5760
E-mail: <bw96w@nih.gov>
Contact 2: Ajay Chitnis
E-mail: <chitnisa@mail.nih.gov>

X-ray Crystallography Interest Group
Meeting time and place: See biweekly newsletter: <http://mcl1.ncifcrf.gov/nihxray/
Contact: Xinhua Ji
Phone: (301) 846-5035
E-mail: <jix@ncifcrf.gov>

New 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: Surajit Ganguly
Phone: 496-8423
E-mail: <surajit@codon.nih.gov>
Contact 2: David C. Klein
Phone: 496-6915
E-mail: <klein@helix.nih.gov>

Chronobiology Interest Group
Meeting time: 1st Wednesday, monthly, 4:00–5:00 pm
Meeting Place: Building 36, Room 1B13, or USUHS Rm A2054
Contact: Steven Coon
Phone: 496-8293
E-mail: <coon@codon.nih.gov>

Drosophila Neurobiology Interest Group
Meeting time: Every other Friday (roughly), 12:00–1:30 pm (starting Sept. 12)
Meeting Place: Building 36, Room 1B13
Contact: Howard Nash
Phone:402-1041
E-mail: <nash@codon.nih.gov>

Handheld Users Group (HUG)
Meeting time: Every third Monday, 3:00 pm
Meeting place: Building 10, NIH Library training room
Contact: Ben Hope
Phone: 594-6473
E-mail: <tallguy@nih.gov>

Lab Operations Interest Group
Meeting time and place: To be determined
Contact: Dawn Walker
Phone: 402-7149
E-mail: <walkerd@exchange.nih.gov>

Technology Transfer Interest Group
Meeting time: First Thursday each month, 3:30 pm
Meeting place: 6011 Executive Blvd., suite 325
Contact 1: Ted Roumel
Phone: 435-4074
E-mail: <RoumelT@od.nih.gov>
Contact 2: Norka Ruiz-Bravo
Phone: (301)-594-4499
E-mail: <ruizbran@nigms.nih.gov>

Tobacco and Nicotine Research Interest Group
Meeting time: Bimonthly (date and time vary)
Meeting place: Executive Plaza North
Contact: Matthew Fritts,
Phone: 301-594-6637,
E-mail: <frittsm@mail.nih.gov>

Women's Health Special Interest Group
Meeting time and place: Monthly, usually 11:30 am–1:00 pm; day and location vary; see website for upcoming lectures
Contact: Vicki Malick
Phone: 301-496-7989
E-mail: <malickv@od.nih.gov>

Addenda

Considering starting a new Interest Group? Contact* Celia Hooper: *<hooperc@od.nih.gov> or fax: 301-402-4303.

Need to correct your group's listing? Contact CIT's web publishing group: <publish@cit.nih.gov>.

Recently Tenured

Jenny Hinshaw *received her Ph.D. from Brown University, Providence, R.I., in 1990 and did her postdoctoral work at The Scripps Research Institute in La Jolla, Calif. In 1995, she became a tenure-track investigator at NIH in the Laboratory of Cell Biochemistry and Biology, NIDDK, where she is currently a senior investigator.*

My laboratory is interested in the dynamic process of membrane trafficking within eukaryotic cells. This process involves numerous specialized protein complexes and lipid domains. Over the past several years we have focused on one particularly intriguing set of proteins, the dynamin family of mechanochemical enzymes—a family of large GTPases that are potentially involved in nearly all cellular membrane stabilization and fission events. Dynamin itself is essential for receptor-mediated endocytosis, caveolae internalization, and trafficking to and from the Golgi.

Fran Pollner

Jenny Hinshaw

I first became curious about the role of dynamin in endocytosis when, as a postdoctoral fellow in Sandy Schmid's laboratory at Scripps, I discovered this protein was capable of self-assembling into ordered spirals. This work led to the hypothesis that dynamin assembles around the necks of coated pits in a spiral prior to membrane fission in endocytosis. The positioning of dynamin at the penultimate step in membrane fission further suggested that dynamin may play a direct role in formation of vesicles.

Zhang, P. & Hinshaw, J.E. *Nat. Cell Biol.* **3**:922-926 (2001)

Three-dimensional reconstruction of dynamin in the constricted state.

Three prominent densities are displayed in different shades of grey (head, stalk and leg) from the outer to inner radius with the inner leaflet of the lipid bilayer in the center.

Soon after I arrived at NIH, my lab demonstrated that dynamin undergoes a GTP-dependent conformational change causing constriction and fragmentation. We believe this represents a critical step in the process that occurs when clathrin-coated pits bud from the plasma membrane. This ability of dynamin to constrict and generate a force on the underlying lipid bilayer makes it unique among GTPases as a mechanochemical enzyme.

To determine the conformational changes that occur during dynamin-induced constriction, we then calculated the first three-dimensional map of dynamin in the constricted state using cryoelectron microscopy and helical reconstruction methods at a resolution of 20 angstroms. The 3-D map consists of a repeating **T** structure (dimer) along the tube axis, which can be divided into three distinct density peaks.

Based on previous biochemical results and the docking of X-ray crystal structures into our 3-D map, we were able to predict the location of each of dynamin's five distinct domains (GTPase, middle, Pleckstrin homology, GTP effector domain [GED], and proline-rich domain). Further analysis of the 3-D structure of dynamin allowed us to propose a mechanism of dynamin-induced membrane constriction: An interaction between GED and a GTPase domain from a neighboring dimer would lead to a decrease in both radial diameter and helical pitch.

In the near future, we hope to determine whether a common mechanism of action exists among all the dynamin family members. Additional dynamin family members have been implicated in numerous fundamental cellular processes, including other membrane fission events, antiviral activity, cell plate formation, and chloroplast biogenesis.

For example, a dynamin-related protein (Drp1) has been shown to localize to regions of mitochondria scission, and a plant dynamin family member, Arc5, has been elegantly shown to be involved in chloroplast division. Among all the dynamin proteins, self-assembly and oligomerization into ordered structures (such as rings and spirals) is a common characteristic and, for the majority, essential for their function. While they are continually being implicated in diverse functions of the cell, we would predict that all dynamin family members undergo similar conformational changes upon GTP addition.

Overall, understanding this unique family of large GTPases will provide valuable insights into the mechanism of fundamental cellular processes such as membrane fission and remodeling events.

Brian Kelsall *received his M.D. degree from Case Western Reserve University in Cleveland in 1986. He did an internal medicine residency at New York Hospital and an infectious disease fellowship at the University of Virginia in Charlottesville before joining the Laboratory of Clinical Investigation, NIAID, in 1992 as a postdoc in the Mucosal Immunity Section. He is currently a senior investigator in the Laboratory of Clinical Investigation, NIAID.*

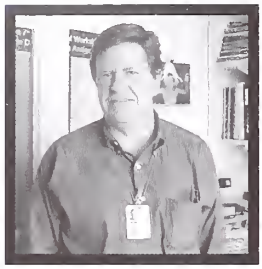
The mucosal immune system is marked by the necessity for precise regulation of positive and inhibitory immune responses. A host must respond to invading pathogens with the production of protective antibodies and cell-mediated immune responses, while, at the same time, controlling unnecessary responses to the myriad harmless foreign antigens that cross mucosal surfaces.

The major long-term goal of my laboratory is to develop a fundamental understanding of the factors that regulate the induction and maintenance of these disparate mucosal immune responses and to apply this knowledge to the development of novel mucosal vaccine strategies and treatments for mucosal inflammation.

After completing my internal medicine residency and a fellowship in infectious diseases that focused on mucosal immunity to *Entamoeba histolytica,* I came to NIH in 1992. As a postdoctoral fellow in Warren Strober's lab, I identified several populations of dendritic cells (DCs) in Peyer's patches, lymphoid structures that are primary sites for the induction of immune responses to antigens and microorganisms in the small intestine. DCs are now known to be a family of cells that are the major cells that present antigens to naïve T cells during a primary immune response. I demonstrated the importance of these cells for the induction of T-cell responses to orally administered antigens.

During my time as a tenure-track investigator, members of my laboratory demonstrated that DCs isolated from the Peyer's patch are unique among DCs from nonmucosal lymphoid organs in their ability to produce IL-10 and induce the differentiation of IL-10–producing T cells. IL-10–producing T cells can po-

Recently Tenured



Fran Pollner

Brian Kelsall

tently inhibit immune responses, suggsting that mucosal DCs are conditioned to induce such regulatory T cells.

We went on to identify four different subpopulations of DCs in the Peyer's patch, to study their phenotype and function, and to localize these populations to discrete regions of the Peyer's patch. With this information, we developed models for how different DC populations are involved in tolerance to oral antigens ("oral tolerance") and the induction of immunity to pathogens.

Most recently we applied this knowledge to study the role of DCs in immunity to murine reovirus. We discovered that submucosal DCs are able to process reoviral antigens directly from overlying infected apoptotic epithelial cells. In addition, we identified novel receptors on human DCs that are responsible for the direct uptake of reovirus and possibly other viruses. We are currently exploring ways to exploit these findings for the development of mucosal vaccines that target DCs.

A second focus of the lab, which relates directly to our studies of mucosal immunity, is the regulation of cytokine production by DCs and macrophages. In particular, we demonstrated that signaling via several disparate surface receptors can inhibit the production of cytokines, such as IL-12, that are key in driving T-cell differentiation into Th1 cells. Th1 cells are important for host defense as well as for pathologic intestinal inflammation in certain types of inflammatory bowel disease, such as Crohn's disease.

Translational leads are beginning to emerge from this work. For example, we showed that antibodies to and natural ligands of the β2-integrin CD11b/CD18 (complement receptor 3; CR3) can inhibit IL-12 production from human monocytes in vitro and suppress Il-12–dependent interferon-γ production in a mouse model of septic shock. Then, most recently, we demonstrated that anti-CR3 can be used for the treatment of ongoing intestinal and skin inflammation in murine models.

We also demonstrated a primary role for G-protein–coupled receptor signaling in the regulation of cytokine production from both DCs and monocyte/macrophages. G-proteins are divided into subfamilies (such as Gs and Gi) based on their particular signaling characteristics. For signaling by the Gs subfamily of G-proteins, we demonstrated that cholera toxin, which directly activates Gs, can suppress IL-12 production from antigen-presenting cells. For signaling by the Gi subfamily of G-proteins, we observed that Gi-signaling by the chemoattractants C5α and fMLP has a similar suppressive effect.

We went on to show the importance of the Gi2α G-protein subunit for this effect. Gi2α-/- mice have exaggerated Th1 responses to most stimuli and develop spontaneous Th1-mediated intestinal inflammation. We are currently exploring the intracellular mechanisms by which G-proteins regulate IL-12 production and the in vivo mechanisms responsible for the exaggerated Th1 responses in the Gi2α-/- mice.

In summary, my primary research interest is understanding how immune responses are generated and maintained at mucosal sites like the intestinal tract. My hope is that information generated by our studies will result in the development of novel vaccine strategies for infectious diseases and novel ways to treat inflammatory bowel disease.

Fran Pollner

Karl Pfeifer

Karl Pfeifer *received his Ph.D. in biology in 1988 from the Massachusetts Institute of Technology in Cambridge. His postdoctoral training was with Shirley Tilghman at Princeton University in Princeton, N.J. In 1995, he joined NICHD and there began the Section on Genomic Imprinting, where he is now a senior investigator.*

Genomic imprinting represents a curious defiance of normal Mendelian genetics. Mammals inherit two complete sets of chromosomes, one from the mother and one from the father, and most autosomal genes will be expressed from both the maternal and paternal alleles. Imprinted genes, however, are expressed from only one chromosome, in a parent-of-origin-dependent manner.

Because silent and active genes are present in a single nucleus, the differences in transcriptional activity cannot be explained by the presence or absence of critical transcription factors. Instead, the transcription of imprinted genes represents a clear situation in which epigenetic mechanisms restrict gene expression. Imprinting, therefore, is a great model system for looking at the role of DNA modifications and chromatin structure in maintaining developmentally appropriate patterns of gene expression.

Imprinting is also of interest because imprinted genes are frequently associated with disease and developmental disorders. This is due to two unique vulnerabilities. First, imprinted genes are in some sense functionally haploid. For example, mutations in a maternal-specific gene, such as *p57KIP2*, will be completely dominant when on the maternal chromosome. However, the same mutation will be completely recessive when paternally inherited, thus allowing a way for the allele to persist in the population.

Second, imprinted genes are susceptible to disruptions in the imprinting process itself. If a cell loses track of the parental origins of its chromosomes, imprinted genes will be twofold over-expressed or completely unexpressed.

Our section is investigating a cluster of genes on the distal end of mouse chromosome 7. This cluster includes the *H19* and *Igf2* genes, which share developmentally complex patterns of gene expression but are reciprocally imprinted. *H19* is expressed only from the maternal chromosome while *Igf2* is paternal-specific.

We have focused on using genetic analyses with the goal of understanding three aspects of imprinting of these genes: establishment of the primary imprinting mark during gametogenesis, maintenance of this mark (or its secondary derivatives) during the many cell divisions and differentiation, and conversion of the imprinting mark into appropriate transcription patterns.

Our general approach has been to use molecular analyses to identify candidate DNA sequences that are likely to play a role in regulating gene expression and then testing the roles of these sequences by loss-of-function (knockout) and by gain-of-function (knockin) mutagenesis. Most importantly, we have defined a 2.4 kb region that lies between *H19* and *Igf2* that has three functions. First, it marks the chromosomal origin of the locus. Second, it functions as a DNA methylation-dependent transcrip-

tional insulator that prevents expression of the maternal copy of *Igf2*. Third, it acts as a methylation-dependent transcriptional silencer that blocks expression of the paternal *H19* allele.

Much of our current work is trying to understand the role of DNA methylation in imprinting. While such methylation clearly plays a role in regulating transcription of imprinted genes, we have been surprised to learn that its role in establishing the parental origins is much less certain. Identifying the true imprint, a mark that can be stably maintained during cell division but can be readily erased and reset each generation, is a key goal of our research.

We have also been interested in regulation and function of the *Kcnq1* gene, also in the distal chromosome 7 cluster. This gene has great significance in medical genetics. Chromosomal translocations with breakpoints in the human *KCNQ1* have been associated with Beckwith-Wiedemann syndrome (BWS), a fetal overgrowth syndrome, whereas point mutations in *KCNQ1* are associated with long QT syndrome (LQTS), a predisposition to cardiac arrhythmias.

Our curiosity about this gene was initially raised when we noted that BWS but not LQTS is inherited in a parent-of-origin fashion. We have generated mouse mutant lines to understand the etiology of these two diseases. LQTS is associated with loss of function mutations in *Kcnq1*, with the phenotype only apparent postnatally. LQTS is not parent-of-origin dependent because *Kcnq1*'s imprinting is developmentally regulated: after birth, both alleles are expressed. The etiology of BWS appears to be quite a bit more complicated: It is not loss of *KCNQ1* gene activity but a general disruption in normal embryonic imprinting patterns of several genes in the locus that is critical.

LQTS episodes in humans are very much induced by specific stresses, and we have also demonstrated this in our mouse model. A major goal of our current *Kcnq1* research is now directed toward understanding the molecular basis for this stress dependence.

Allan Saul *received his Ph.D. from the University of Queensland, Australia, in 1979, and then joined the Queensland Institute of Medical Research, Brisbane, pursuing the role of red cell polymorphisms on susceptibility to malaria and the development of malaria vaccines. From 1984 to 1986, he was a visiting scientist in the Laboratory of Parasitic Diseases, NIAID, returning to the Queensland Institute of Medical Research to head a Malaria and Arbovirus Unit. Over the next 13 years, he studied the epidemiology of malaria in Southeast Asia, the development of sustainable malaria control programs, and the development of malaria vaccines, culminating in a successful Phase 2 trial in Papua New Guinea. This trial was the first to show evidence of efficacy with a recombinant protein vaccine directed against blood-stage malaria parasites. In 2000, he joined the Malaria Vaccine Development Unit (MVDU), NIAID, where he is the co-director.*

Malaria kills a million children each year and makes hundreds of millions of people sick. The parasite has become resistant to standard antimalarial drugs, and unfortunately, as new drugs are introduced, resistance soon follows. The lack of health care in many endemic areas also makes it difficult to deliver treatment, especially when that requires frequent medication. Malaria vaccines directed against more new targets could make a big difference in the battle against this costly disease.

Allan Saul

We are developing two types of recombinant protein–based vaccines: one directed against blood-stage parasites that cause the disease, and the second against mosquito-stage parasites that transmit malaria from one person to another.

Several promising vaccine candidates have been identified; however, a major bottleneck has been getting these from the laboratory through Phase 1 safety and immunogenicity studies and Phase 2 studies in malaria-infected people to see whether they work.

Normally, a pharmaceutical company would accomplish these tasks, but, given the development effort required and the lack of a profitable market for malaria vaccines, public sector input is required. At the MVDU, we have developed something akin to a biotechnology company within the NIH to move the malaria vaccines through development. Our generic technology units provide the expertise for vaccine production and testing as well as product specialists who concentrate on individual vaccines.

We currently have six antigens either in clinical trials or undergoing the preclinical testing that may lead to trials. Several other antigens are in the pipeline and are likely to enter clinical trials in the foreseeable future.

We face two major technical challenges: formulation and human testing. In a vaccine, antigens are delivered in a formulation containing an adjuvant—a substance that stimulates the immune response. Although vaccines have been formulated with adjuvants for more than 70 years, the immunology underlying adjuvant activity is poorly understood. As a result, formulation is highly empirical. Developing formulations that will work with mixtures of antigens is even more complicated. We will put a major effort into studying adjuvant design and action to make this less hit-and-miss.

It takes a surprisingly large number of trials to test the vaccines we are producing. We plan about 30 Phase 1 trials in the United States over the next few years, leading to trials in countries where malaria is endemic. In collaboration with the University of Mali, we have developed a field-testing site in Mali, Bamako, and we will establish additional sites in other countries burdened with malaria .

Although the program is largely developmental, I am also pursuing several basic research questions. These include the nature of protective immunity in malaria; the impact of antigenic diversity on protective immunity; and the effect of new control measures, especially vaccines, on the population dynamics of malaria.

Yun-Bo Shi *received his Ph.D. from the University of California at Berkeley in 1998 under John E. Hearst and obtained his postdoctoral training under Donald D. Brown at the Carnegie Institution, Baltimore, MD. In 1992, he was recruited as a tenure-track investigator to head the Unit on Molecular Morphogenesis at NICHD. He is currently a senior investigator in the Laboratory of Gene Regulation and Development (LGRD), NICHD.*

My laboratory has been interested in understanding the molecular mechanisms of tissue remodeling and organogenesis during postembryonic development in vertebrates. Despite enormous improvement made in our understanding of the molecular mechanisms gov-

Recently Tenured

Fran Pollner

Yun-Bo Shi

erning embryogenesis from studies in various animal models, the progress in the study of postembryonic development has been hampered by the lack of proper developmental systems. We have chosen the thyroid hormone–dependent metamorphosis of *Xenopus laevis* as a model with which to study postembryonic development.

Amphibian metamorphosis is similar to postembryonic development in higher vertebrates in many aspects. An important advantage of this model system is its absolute requirement for thyroid hormone, which is also critical during the mammalian postembryonic period (from a few months before to a couple of years after birth in humans). Furthermore, this process takes place externally in free-swimming tadpoles. Thus, one can easily manipulate the process by simply changing thyroid hormone levels in the tadpole-rearing water or even in organ or primary cell cultures.

This model system allows one to avoid the complications associated with studies on fetal development in mammals, in which the fetuses enclosed in the uterus are inaccessible to manipulations. In the uterus, the effects of any treatments or manipulations may also trigger changes in both the embryos and the fetal environment due to maternal response, thus making it difficult to interpret the outcome.

Our research focuses on two early steps during *Xenopus laevis* metamorphosis by taking advantage of its total dependence on thyroid hormone. These are:

- How thyroid hormone receptors regulate thyroid hormone–response genes during development
- What roles the thyroid hormone–response genes play during tissue remodeling

In the first area, we first carried out several in vitro and in vivo studies on the functions of thyroid hormone receptors and their expression profiles during development. These led us to propose a dual-function model for thyroid hormone receptors in development—that is, as transcriptional repressors when thyroid hormone is absent to ensure a proper growth period before metamorphosis, and as transcriptional activators when thyroid hormone is present to initiate the gene regulatory cascade that leads to metamorphosis.

To validate the model in vivo, we used the chromatin immunoprecipitation (ChIP) assay to study the receptor binding to endogenous target promoters in developing animals. We were able to show, for the first time in any developing animal, that thyroid hormone receptors bind constitutively to target genes in vivo.

Furthermore, using the same ChIP assay, we have shown that the binding of the receptor leads to local recruitment of co-repressor complexes and histone deacetylation in the absence of the hormone. Upon thyroid hormone treatment of the tadpoles, which induces metamorphosis, the co-repressors are released and co-activators are recruited, leading to local histone acetylation and gene activation. These studies provide direct in vivo evidence in a vertebrate developmental system for an important role of cofactor complex in chromatin remodeling and gene regulation by thyroid hormone receptors.

In the second area, we have identified and characterized a large number of genes activated by thyroid hormone during metamorphosis. In particular, we have provided strong support for the involvement in tissue remodeling of a group of thyroid hormone–induced genes encoding matrix metalloproteinases in cell fate determination (cell death vs. cell proliferation and differentiation). More importantly, we have shown in organ cultures that the matrix metalloproteinase stromelysin-3 is required for larval epithelial apoptosis and adult epithelial migration during intestinal remodeling.

Both thyroid hormone receptors and matrix metalloproteinases play important roles in human development and pathogenesis. However, it has been difficult to study the in vivo functions and the underlying mechanisms of these important proteins during postembryonic development due to the lack of good model systems. Thus, our findings are not only critically valuable for the understanding of frog development but also have important implications in higher vertebrates, including humans.

Our current research in both areas is directed toward functional analyses of these genes by using a relatively new transgenic approach in frogs to determine the roles of these genes in the transformations of different organs. To understand how these genes exert their effect on development, we plan to:

- Investigate the roles of different cofactors in gene regulation by thyroid hormone receptors through a combination of molecular analysis in vivo and transgenic studies
- Isolate and functionally characterize substrates of matrix metalloproteinases during metamorphosis.

James Troendle *received his Ph.D. from University of Maryland, College Park, in 1992 and joined the Biometry and Mathematical Statistics Branch of the Division of Epidemiology, Statistics, and Prevention Research, NICHD, as a staff fellow. He was converted to tenure track in 1997 and is now a senior investigator.*

My primary research at NIH has been in developing methods for multiple hypothesis testing, while controlling an appropriate error rate. Simple methods based on the Bonferroni inequality allow one to safely test several hypotheses with control of the overall chance of a spurious finding. However, such methods lack power, largely because they fail to exploit the correlation between the test statistics. Furthermore, controlling the chance of a spurious finding is too stringent a requirement in some cases. In these cases, methods that allow for a few spurious findings can be much more powerful.

The effect of correlation on the conservatism of Bonferroni methods is potentially great. Such methods control the chance of a spurious finding regardless of the correlation. As a consequence, the methods become more conservative as the correlation increases.

My motivating example was an analysis of 55 minor malformation types in babies born to diabetic and nondiabetic women. In this analysis we wanted to know which of the 55 malformation types are associated with having a diabetic mother. To determine this, one must test all 55 hypotheses that a particular malformation is not associated with having a diabetic mother. Because the presence of one malformation type is correlated with the presence of another malformation type, Bonferroni multiple testing methods are conservative. Less conservative (and therefore more powerful) methods can be ob-

tained by comparing the observed test statistics to the multivariate distribution obtained by permuting the vectors of malformation indicators. Permutation methods implicitly use the correlation by working with the intact vectors of outcomes. Doing so permitted us to conclude that two of the 55 malformations in the infants were linked to having a diabetic mother.

James Troendle

Recently, interest in multiple testing of this sort with data on gene expression from microarrays has increased dramatically. Each microarray can have up to about 10,000 gene expressions. In microarray studies, one typically does not mind having a few spurious findings because the results will have to be confirmed in later studies. In this case, multivariate permutations can be used to conduct multiple hypothesis testing (while controlling the number of spurious findings) far more powerfully than by using Bonferroni methods. With my colleagues Ed Korn, Lisa McShane, and Richard Simon of NCI, I have developed a method to perform such tests on microarray data. Software for the procedure is available in BRB-ArrayTools of NCI at <**http://linus.nci.nih.gov/BRB-ArrayTools/**>.

My current research is in extending permutation methods to allow for adjustment of covariates, while still controlling an appropriate error rate. For example, in the malformation analysis above it is known that certain malformations are associated with weight and that weight is in turn affected by diabetes. Therefore, it is important to see whether the malformations that are linked to diabetes are so only because of their relationship with weight. Adjustment for such covariates is important, especially in observational studies that can be greatly affected by confounding

Charles Vinson *received his Ph.D. from the University of Virginia in Charlottesville in 1987 and did postdoctoral work at the Carnegie Institution of Washington on the grounds of the Johns Hopkins University in Baltimore, Maryland. He joined the Laboratory of Biochemistry in NCI in 1991. He became a senior investigator in 2002 and is now chief of the Gene Regulation Section in the Laboratory of Metabolism.*

My interests are in the area of the structure and function of B-ZIP transcription factors. There are approximately 60 genes in the human genome that contain the B-ZIP protein motif. Each monomer of the B-ZIP dimer is a long bipartite α-helix. The COOH-terminal half either homodimerizes or heterodimerizes via a leucine zipper coiled coil motif to bind sequence-specific DNA. The NH-terminal half binds DNA in a sequence-specific manner.

My research in NCI started with a detailed analysis of the amino acids that regulate the stability and dimerization specificity of B-ZIP proteins. We did a double-mutant thermodynamic analysis and calculated coupling energies for charged amino acids in the γ and ε positions that lie across the leucine zipper interface. More recent work has examined the contribution of amino acids in the α position to dimerization specificity. These data have allowed us to predict dimerization partners of all human B-ZIP proteins, predictions that have been recently verified using protein microchip technology.

Fran Pollner

Charles Vinson

We have used our insight into the leucine zipper structure to design a dominant negative protein that acts in a dimerization-specific manner to inhibit the DNA binding of B-ZIP proteins. Such a reagent would inhibit the function of all structurally related B-ZIP proteins and overcome the redundant functions of many mammalian proteins. The leucine zipper itself could be a possible dominant negative protein. But such a reagent does not work because DNA binding stabilizes the B-ZIP dimer.

To overcome this limitation, we designed an acidic amphipathic protein sequence to replace the basic region. These A-ZIP protein constructs form heterodimers with B-ZIP proteins. The designed acidic amphi-pathic protein forms a coiled coil with the basic region of the B-ZIP motif, stabilizing the heterodimer up to 5.0 kcal/mol per dimer. The A-ZIP dominant negatives can totally inhibit the DNA binding of a B-ZIP protein in an equimolar competition.

We are now expressing these dominant negatives in transgenic mice. Our first transgenic mouse expressed a dominant negative that inhibits both the C/EBP and AP-1 family of transcription factors using a fat-specific promoter. These mice are born with no fat tissue, the only such mouse yet reported. The metabolic consequences of having no fat are profound. The mice overeat because they do not have leptin, a fat-derived hormone that acts as a satiety signal, and this results in profound type 2 diabetes.

To have more experimental control over expression of these dominant negatives, we are presently using the tetracycline system that allows us to control expression of the dominant negative. We have generated mice that express A-FOS, A-CREB, A-C/EBP, and A-USF, dominant negatives that heterodimerize with and abolish the DNA binding of JUN, CREB, C/EBP, and USF respectively.

We can express these dominant negatives in a tissue-specific manner by crossing these mice to mice that express the tetracycline transactivator under the control of a tissue-specific promoter.

Expression of these dominant negatives in skin or heart during development results in lethality. Expression of these dominant negatives in the adult mice does not produce a phenotype. We are collaborating with the Stuart Yuspa group at NCI to study carcinogenesis in the skin of these mice.

We find that the A-CREB mice do not get tumors and the A-FOS and A-C/EBP mice produce sebaceous tumors instead of the typical papillomas. We are examining these models in more detail to understand how these dominant negatives are preventing malignant papillomas.

We have also expressed A-FOS in the striatum of the brain. In collaboration with Ron Paletzki, NIMH, we have demonstrated that these mice have enhanced sensitization and preference for cocaine. We are now modulating the expression of A-FOS during the sensitization paradigm to determine when A-FOS expression is critical for sensitization to cocaine.

We will continue to determine whether expression of these dominant negatives ameliorates or exacerbates pathological states in the adult. ■

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 2W23.**

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

In Future Issues...

- More Details On Research Roadmap
- A Progress Report On Stem Cells
- Mouse Cancer Genetics

Kids' Catalyst

[Consider this the launch of what will be the occasional "Kids' Catalyst," our response to the reader suggestion that the back page present something to whet the scientific appetite of NIH offspring. This one is geared to the older end of the K–12 set (and maybe to their parents as well)—Ed.]

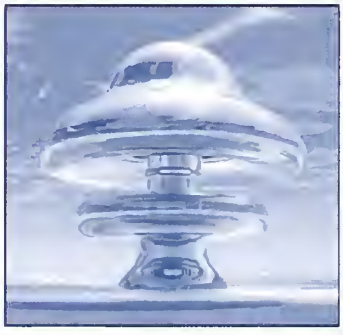
Screensaver Skirmish

If your computer does nothing but display, well, junk while you're eating dinner, there is another way. Be forewarned that the sights on this website are quite compelling, so you may be neglecting your homework for . . .

Periodic Art: <http://www.chemsoc.org/viselements/index.htm> Royal Society of Chemistry, London. I always thought periodic charts were kinda neat. All of those numbers and letters, meaning something, but . . . isn't it time for lunch? Turning away is not so easy with this stunning combination of chemistry and art. This is a collection of element-appropriate artistic renderings that get to you, and you mysteriously know where gold is. If you spend another second you will find the American flag, and you just have to roll over it to find out why. Download the screensaver and you'll have a different element waiting for you when you come back. It's an alluring alchemy that some of your more eclectic art and chemistry teachers might also appreciate.

—Jennifer White, NIGMS

Here are three of the 132 creations of the Visual Elements Periodic Table. *Can you guess which elements they represent?*



The NIH Catalyst is published bi-monthly for and by the intramural scientists at NIH. Address correspondence to Building 2, Room 2W23, NIH, Bethesda, MD 20892. Ph: (301) 402-1449; fax: (301) 402-4303; e-mail: <catalyst@nih.gov>

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