FOSTERING COMMUNICATION AND COLLABORATION

The NIH CATALYST

A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

NATIONAL INSTITUTES OF HEALTH ■ OFFICE OF THE DIRECTOR ■ VOLUME 4, ISSUE 4 ■ JULY–AUGUST 1996

MCL, MOVING SAFETY AND SCIENCE FORWARD IN TANDEM

by Rebecca Kolberg

Improving safety and improving ease of scientific research are not necessarily mutually exclusive. Proof of that has just arrived on the south edge of the NIH campus in the form of a newly renovated facility for research involving pathogens that demand the highest levels of containment.

Although the new Maximum Containment Laboratory (MCL) is located in the same space as NIH's old Biosafety Level-4 (BL-4) facility in Building 41A, the difference between the old and new facilities extends far beyond a simple name change. Gone is the old "glovebox" approach, in which walls separated researchers from pathogens, forcing them to manipulate pathogen-exposed animals, samples, and equipment through bulky gloves inserted in fixed portholes. Inside MCL, researchers clad in plastic astronaut-like suits, with their own spiral breathing tubes hooked up to an outside air source, will be able to move about in relative freedom and conduct scientific and animal-care procedures more like they would in a normal lab.

Courtesy CDC

"We built MCL with flexibility in mind—although it may seem like an oxymoron to mention BL-4 containment in the same breath as flexibility," says Deborah Wilson, chief of the Occupational Safety and Health Branch in NIH's Division of Safety.

When it is completed later this summer, the $3.6 million MCL will be one of only three "suit-system" BL-4

continued on page 14.

FORWARD, CHARGE! CARD PROJECT GOES NIH-WIDE

by Celia Hooper and Rebecca Kolberg

A slim piece of plastic and a little shopping savvy is all it took to save an NCHGR lab more than $250,000. Although that may be a tough act to follow, the expansion of NIH's charge-card program will soon give hundreds more intramural scientists their own chance to save time and, possibly, big bucks.

On the basis of the results of a 30-card pilot program at NCHGR and NCI, NIH is moving ahead and offering all institutes, centers, and divisions (ICDs) the opportunity to allow their researchers to apply for their own charge cards, or purchase cards, as administrators prefer to call them. If efforts to automate the reconciliation and payment process proceed as planned, scientists who apply for the cards and undergo the required half-day training session should have their cards in hand by August, says Donald Kemp, an analyst in the Office of Procurement Management (OPM) who is coordinating the charge-card program along with staff from the Office of Financial Management (OFM), DCRT, and the Intramural Reinvention Working Group.

"We've tried to limit the 'thou shalt nots'," says Kemp, noting that since the pilot began, restrictions have been removed on using the cards to pay for NIH parking stickers and to rent meeting space. As of May 5, the 15 cardholders at NCI had made 704 purchases totaling about $251,000 and the 15 cardholders at NCHGR made 2,214 purchases totaling nearly $1.17 million. A complete audit by OPM of half of the card records for both institutes indicated that all purchases were justified.

Although some NCI scientists have reported problems tracking their purchase-card orders and reconciling them with monthly statements, NCHGR's Amy Pepper says she's found the additional bookkeeping duties to be well worth the effort. And Pepper knows what she's talking about: the lab technician has already saved the Immunological Genetics Section of NCHGR's Laboratory of Gene Transfer a quarter-million dollars with her smart use of the charge card. In the pre-card era, the lab bought the recombinant interleukin-2 (IL-2) that it uses to culture T cells from Life Technologies Inc. in Gaithersburg, Md., at a cost of about $250,000 a year. Now, armed with an NIH charge-card and a prescription written by an M.D., Pepper went to Giant Discount Pharmacy and bought a year's supply of IL-2 for $2,490—saving a cool $247,510.

> "I THINK THE REAL VALUE OF THE CARDS IS IN THE TIME SAVED—TIME SAVED TO DO SCIENCE."
> —AMY PEPPER, NCHGR

What accounts for the mind-boggling price difference? Pepper says a Giant pharmacist told her the answer probably lies in the packaging that typically accounts for two-thirds to three-quarters of a drug's price. The IL-2 purchased from Giant came in bulk vials of 22 million units at $415 each, while the IL-2 from Life Technologies came in 5-mg vials of 25,000 units at $49 each. But what about quality? So far, Pepper says her lab has seen no difference between the expensive and cut-rate IL-2 when it comes to stimulating T-cell growth.

continued on page 14.

CONTENTS

CHANGING DEMOGRAPHICS OF NIH SCIENTISTS

Michael Gottesman

The commitment of the NIH intramural program to excellence in science goes hand in hand with our commitment to a diverse, talented scientific staff. The reports of the External Advisory (Marks-Cassell) Committee (1994), the Committee on the Status of Intramural Minority Scientists (see *The NIH Catalyst,* July 1994), and the Task Force on the Status of NIH Intramural Women Scientists (see *The NIH Catalyst,* June 1993) each pointed out deficiencies in representation of women and minority scientists at various levels of training and leadership at NIH. In this column, I report on some progress and problems on our path toward a multi-talented, multi-ethnic community of men and women scientists.

Although currently lacking a complete picture of the intramural program, we have a few windows through which we can gauge the changing demographics of our staff. The impression of a diverse population of NIH postdoctoral fellows is supported by the most recent data, which show an almost equal number of U.S. (IRTA) and foreign postdocs (visiting fellows), a goal established a decade ago when the IRTA program was initiated but achieved for the first time only last month. Our visiting fellows come from more than 80 different countries, providing NIH with a rich tapestry of different scientific training, points of view, and cultural heritage. The vast majority of these visiting fellows return home after their training through this scientific exchange. Our population of IRTA fellows has a gender distribution close to that of recent graduates in biological science, as evidenced by the self-identified pool of applicants for the Fellows' Awards for Research Excellence (FARE). About 35% of the applicants in this recent competition among NIH fellows for travel money were women, as were 32% of the award winners. Unfortunately, we do not have any reliable current information about the distribution of underrepresented minorities among our fellows.

WE ARE CURRENTLY REDOUBLING EFFORTS TO RECRUIT UNDERREPRESENTED MINORITIES INTO OUR TENURE-TRACK PROGRAM.

It is good to see the increasing visibility of minority and women postdocs and other scientists through the efforts of the Women Scientist Advisors, the Black Scientist Association, and the Asian/Pacific American Heritage Committee at NIH. Recruitment of minority fellows to NIH continues to be a high-priority goal. One area in which minority recruitment has been extremely successful is among our clinical associates. A two-year-old loan-repayment program for physicians from disadvantaged backgrounds who are participating in clinical research has led to the recruitment of 19 clinical associates, most of whom are underrepresented minorities.

NIH's future scientific leadership is reflected now among our tenure-track scientists. The establishment of a clearly defined tenure track two years ago has made it possible to get a clearer picture of the future demographics of NIH tenured scientists. The news is generally encouraging. Among the 202 current tenure-track scientists, 30% are women, 21% are minorities and 8.5% are underrepresented minorities (4% African American, 4% Hispanic, and 0.5% Native American). Lest we congratulate ourselves too hastily for this progress, it should be noted that current trends are *not* in the right direction. Of the 33 latest additions to the tenure track who were identified as a result of a search process carefully crafted to encompass both excellence and diversity, nine were women and six were Asian American, but, unfortunately, there were no underrepresented minorities. I find this statistic quite worrisome, and we are currently redoubling efforts to recruit underrepresented minorities into our tenure-track program.

The Central Tenure Committee now has a two-year track record in making recommendations for appointment to tenure. Forty-seven scientists have been considered by the committee, and 35 (74%) were approved at the time of first review. An additional six were approved after further review, bringing to 87% the overall approval rate of the committee. In the past two years, only three of the six women proposed for tenure received it. No underrepresented minorities were brought forward for tenure during this two-year period, but both of the Asian Americans brought forward were tenured. It is too soon to know the significance of these numbers since they represent small cohorts of scientists whose careers were initiated almost 10 years ago at NIH, but we are watching carefully to be sure that there is no inherent bias against either women or minorities achieving tenure at NIH. Of the eight Senior Biomedical Research Service scientists recruited from the outside over the past two years, two were women and one was Hispanic.

Parallel to these improvements, women at NIH have increasing representation among our section chiefs (18% this year compared with 13% in 1992) and lab and branch chiefs (10% this year compared with 4% in 1992). Compared with 1992, when NIH had only one female scientific director, two of our scientific directors are women today. In addition, two acting scientific directors are women.

One major problem that has made it difficult to evaluate the demographics, research interests, and productivity of NIH scientists is the lack of a uniform, central database from which such demographic data can be easily extracted. We are now planning to assemble such a database.

The statistics we do have now, however spotty, suggest that NIH is moving steadily but slowly toward our goal of a diverse and multi-talented community of scientists. Increased efforts to recruit, train, and retain our women and minority scientists will improve our ability to provide opportunities for a diverse group of highly motivated and capable individuals. This, in turn, will enhance the development of the novel ideas and strategies for the medical research to which NIH is dedicated. Our efforts must go forward at all levels of our scientific staff, and I urge all of you to become part of this process.

Michael Gottesman
Deputy Director for Intramural Research

CATALYTIC REACTIONS

Below are comments that we received for topics that were raised in the March-April issue.

On Kovac's letter about postdocs

As Paul Kovac said, many postdocs are weeping and bitter. Their reasons can be good. Examples known to me can often be traced to the behavior of a principle investigator (PI) who exhibits a limited grasp of the concepts of training, leadership, and people management. Also, many postdocs are in a panic because they realize that the job market is getting tougher every year. Many discover that they are not positioned to compete successfully. The latter is not always their fault and may not reflect their skills. Recently, one visiting scientist explained to me how they screen applicants for new posts at his university. First, they throw away all applications from NIH. NIH people have limited teaching experience and usually no grant-writing experience, so they are not worth interviewing. ...

Kovac suggests that NIH cannot be a bad place since "everybody wants to come here and stay here." Not everybody wants to come here. In fact, American postdocs generally do not want to come here. Interestingly, many postdocs take their position unopposed by other applicants. It should also be remembered that, whether it is a happy or unhappy place to be, NIH is safe—not because it is a good place, but because it nurtures and protects its tenured staff regardless of the level of their scientific or supervisory skills. On the outside, people have to compete, be productive, and write grants. Not here. By the time a postdoc discovers that NIH has its complications it is far too late to cut and run, and not all have the requisite imagination or drive to improve their own lots. ...

Perhaps some postdocs are insecure and unhappy because they are just no good and it is not the fault of bad old NIH at all. Certainly this is possible. I find myself happier with this place when I am working well, less happy when I am not working well. But even if the source of all this postdoc disgruntlement is based on their own deficiencies, NIH cannot be held free of blame. After all, how could it be that NIH attracts so many bad postdocs? Or is it that NIH cannot attract good postdocs? Whichever way you cut it, there must be big problems. NIH postdocs do not need "nannies and shrinks" [as Kovac contends], they need constructive debate on how to enhance the scientific atmosphere, how to improve the way PIs communicate with their staffs, and how to prepare for the competitive job market outside.

—Alastair S.H. Goldman, NCI

Both the evidence and I disagree with your evaluation of our intramural postdocs and training program. Where problems exist, there are many constructive ways in which fellows can improve the quality of their training at NIH. They can work with their labs to enhance communication and quality of science, they can work through the Fellows Committee to develop institutional solutions to generic problems, and, if all else fails, they can move to a different lab or institution. Much of your angst, however, seems to reflect a malaise that appears to be spreading among postdocs throughout the United States. It might help to remember that we are all part of an exciting process of discovery and that what we are doing is likely to result in the alleviation of human disease and suffering. There are few, if any, other careers that offer both the intellectual challenges and social benefits of biomedical research.

—Michael Gottesman, DDIR

On Dent cartoons

I felt compelled to throw in my two cents when I read the criticism of the Dent cartoon. Please keep the cartoon! I love it! Although I was never a postdoc, I am married to a former postdoc (now a senior staff fellow) at NIH and am quite familiar with the "life as a postdoc" experience. I really think the Dent cartoon has the exciting/frustrating/funny scenarios at NIH described to a "t." I find it really humorous, never offensive, and look forward to each new cartoon. ■

—Cathy Ribaudo, Office of Research Services

Microbial Ecology Conference

Scientists at an upcoming conference sponsored by NIDR, NIAID, and CBER will be focusing on the big principles governing small creatures. "Microbial Ecology and Infectious Disease," which will take place July 10–12 at the Pooks Hill Marriott in Bethesda, will highlight the commonalties in how microorganisms interact with their external environment.

Among the topics to be addressed are interactions between adhesins and receptors, microbial avoidance of host defense mechanisms, signaling within large populations of bacteria, and bacterial growth in complex environments. Speakers will include Joshua Lederberg and Elaine Tuomanen, Rockefeller University, New York; John Collier and John Mekalanos, Harvard Medical School, Boston; Julian Davies, University of British Columbia, Vancouver, Canada; Ananda Chakrabarty, University of Illinois at Chicago Medical Center; Barbara Iglewski, Rochester University, Rochester, N.Y.; and Jorge Galan, State University of New York at Stony Brook.

Eugene Rosenberg, a Fogarty scholar sponsored by NIDR, organized the conference. Registration forms are available at the Fogarty International Center (FIC), Room 202A, Building 16. For more information, contact FIC's Jack Schmidt (phone: 496-4161; e-mail: schmidtj@box-s.nih.gov). ■

Urgent Call for Comments on Commission on Research Integrity's Report

by Alan N. Schechter, NIDDK, and Joan P. Schwartz, NINDS

If adopted as federal policy, the recent recommendations of the Commission on Research Integrity would change significantly the way science is done at NIH and throughout the United States, especially with regard to resolution of disputes. Therefore, we feel it is imperative that as many scientists as possible read the commission's report and comment on its recommendations.

Health and Human Services (HHS) Secretary Donna Shalala established the Commission on Research Integrity (CRI) in 1993 after Congress directed her to form a panel to examine "issues of research misconduct and integrity." Congress specifically requested guidance in developing a new definition of research misconduct, an assurance process for institutional compliance with HHS regulations, processes by which to respond to and monitor related administrative processes and investigations, and a regulation to protect whistleblowers. The 12-member CRI, which was chaired by Kenneth Ryan of Harvard Medical School in Boston, spent two years holding hearings around the country and issued its final report last November. The report, entitled "Integrity and Misconduct in Research," covers three general areas: the definition of research misconduct, responsible whistleblowing, and administrative processes and investigations. Here is a brief summary of the recommendations and what we see as their implications for biomedical research.

Ralph Isenburg

Alan N. Schechter

Defining Research Misconduct

The current definition of research misconduct, adopted in 1989, was developed in response to a directive from Congress after several well-publicized cases of scientific misconduct. This definition—"fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research"—applies to all research funded by the Public Health Service, but not to that supported by the National Science Foundation or other federal agencies. Since its adoption, much concern has been raised about the vagueness of the "other practices" phrase.

One of CRI's main charges was to re-examine this hotly debated definition. To nearly everyone's surprise, instead of fine-tuning the currently accepted definition, the commission proposed a totally new definition, which it placed in the context of a broader category of professional misconduct. The definition states, "Research misconduct is significant misbehavior that improperly appropriates the intellectual property or contributions of others, that intentionally impedes the progress of research, or that risks corrupting the scientific record or compromising the integrity of scientific practices. Such behaviors are unethical and unacceptable in proposing, conducting, or reporting research, or in reviewing the proposals or research reports of others."

These phrases are followed by examples of misappropriation, interference, and misrepresentation. In the commission's judgment, these acts represent misconduct, but we believe the CRI's definition overextends the boundaries of misconduct to matters that would best be left alone or resolved by the individuals or institutions involved. For example, it appears that omission of relevant references in a scientific paper could be construed as misappropriation, and an editor's actions in declining a paper could be defined as interference. Although CRI's approach of applying the general principle that "scientists be truthful and fair in the conduct of research and the dissemination of its results" has attractive features, many scientists and professional societies have reacted with alarm to the commission's proposed definition because it appears to broaden unnecessarily the scope of misconduct.

Furthermore, CRI specifically notes that some authorship disputes might fall under the purview of misconduct. Thus, the new definition could result in a flood of authorship-dispute cases that are not deemed scientific misconduct under current definitions.

Ralph Isenburg

Joan P. Schwartz

Whistleblowing

The need to prevent retaliation against whistleblowers—people who report fraud, waste, and mismanagement—has been a concern of the federal government for the past decade. More recently, this concept has been extended to those making allegations of scientific misconduct—an uncharted area in which Congress asked CRI to propose some guidelines.

In its report, CRI strongly supported draft guidelines issued last November by the Office of Research Integrity (ORI). However, the commission added its own touch by drawing up "A Whistleblower's Bill of Rights," which it suggests be appended to the ORI's document.

Many concerns have been raised about the imbalance between the rights of the whistleblower and those of the accused, whether it be a scientist or an institution. The CRI "bill of rights" would provide significant protection to the whistleblower, but there is no comparable protection—or even acknowledgment—of the rights of the accused. Destroying a scientist's reputation through an unsubstantiated allegation that has been made public could be construed as a form of professional misconduct, and we believe measures that guard against this should be adopted. For example, standards for maintenance of confidentiality by all parties, with sanctions against those who break that confidentiality, are essential components of any dispute resolution, but they are not fully addressed in CRI's "bill of rights."

Administrative Processes

These sections of the CRI report cover many important issues, starting with how NIH intramural scientific misconduct cases will be reviewed. Other issues include 1) whether the results of all misconduct investigations–even those with no finding of misconduct–should be made public, 2) the increased potential for misconduct cases to overlap with civil and criminal procedures, 3) the suggestion that a law enforcement official be involved in all investigations, and 4) the proposal to assign retaliation cases to ORI, rather than allowing them to be handled through regular personnel channels.

Seeking Scientists' Responses

After receiving CRI's report, HHS Secretary Shalala appointed William Raub, who was formerly NIH's deputy director and is now Shalala's science policy adviser, to head a group that will recommend to her whether and how the CRI report should be implemented. This group is currently seeking input from scientists, and the NIH Committee on Scientific Conduct and Ethics would like to obtain as many comments from intramural researchers as possible. We will collate the comments and submit an unofficial response from the NIH community to the implementation group. Send your comments or suggested modifications to Alan Schechter (mail: Bldg. 10, Rm. 9N307: fax: 402-0101; e-mail: aschecht@helix.nih.gov). Copies of the CRI report can be obtained through HHS's Office of Research Integrity (phone: 301 443-3400; World Wide Web site: http://www.os.dhhs.gov/phs/ori). ■

ALTERNATIVE MEDICINE GOES INTRAMURAL

by Jennifer M. King

Most NIH scientists wouldn't blink an eye at the prospect of a half-dozen new postdoc positions being created in the intramural program. But what if those postdocs are studying alternative medicine?

Although many NIH researchers may find it difficult to accept the notion of even a small number of postdocs at the nation's leading biomedical research institution venturing into the realm of acupuncture, homeopathy, and herbalism, the head of the program, Wayne Jonas, says the move is no cause for concern. "The goal of the program is not to make a practitioner of alternative medicine. The goal is to expose them [the postdocs] to those areas so that they can begin to do good research," says Jonas, who became director of NIH's Office of Alternative Medicine (OAM) last summer. "We are not here to train natural healers. We are here to teach researchers."

In fact, Jonas says he has received some positive feedback from scientists on all rungs of the intramural ladder—from fellows to scientific directors. "There have been a lot [of NIH scientists] who have approached me and said, 'We're excited that you're doing this. We'd be very interested in it,'" he says.

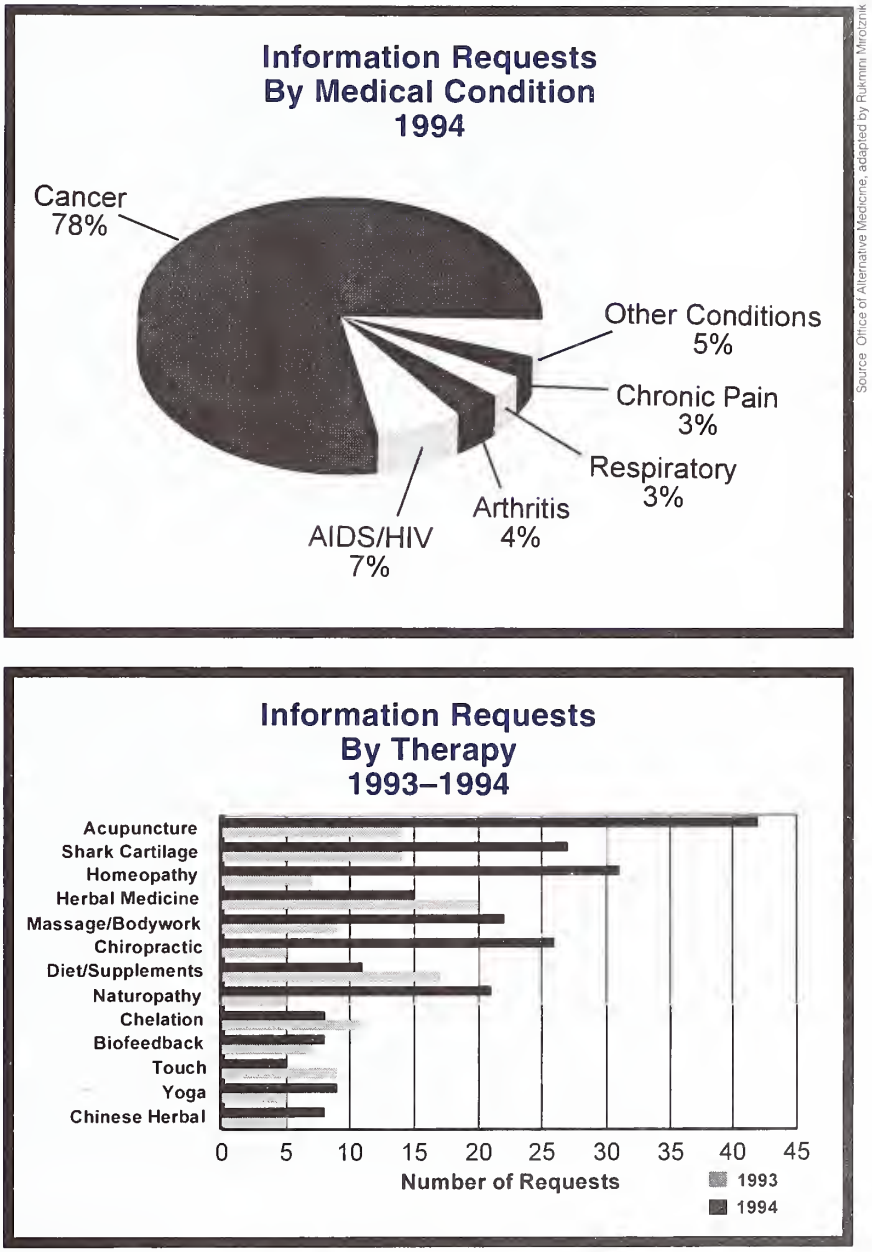
Under the $440,000- to $590,000-per-year program to be initiated in July 1997, OAM will make use of its own Individual Research Training Award (IRTA) or individual National Research Service Award (NRSA) funds to cover salaries and benefits of five to seven intramural fellows per year. Project costs will be borne largely by ICDs, although OAM will provide approximately $15,000 per fellow per year.

Over the course of three years, alternative medicine postdoctoral fellows will be required to complete two or three research projects: one systematic review or meta-analysis plus clinical or basic science projects. Developing or coordinating two clinical investigations as well as teaching and giving lectures on their research projects flesh out the fellows' duties.

The fellows will spend their first six months at NIH in the classroom, where they will be introduced to a variety of research methods and alternative-medicine practices through lectures, seminars, and teaching labs given by research scientists and practitioners of alternative medicine. The didactic sampling is only part of what Jonas terms a "liberal arts research education" designed not only to familiarize the postdocs with alternative-medicine terms but also to provide a sound underpinning for a successful research career by training the fellows in protocol development, statistical analysis, grant writing, critical appraisal of scientific literature, lab and clinical measurement techniques, and research design.

The second half of the first year will focus on developing and structuring individual projects with the help of senior scientists. Year two will involve getting approval for and conducting research projects under the supervision of senior staff mentors and OAM. The final year is devoted to managing clinical investigations, giving lectures on alternative-medicine topics, and writing manuscripts. Any institute, center, or division that has a research effort that could benefit from having a postdoc interested in alternative medicine is encouraged to contact OAM (phone: 402-2466; e-mail: jonas@helix.nih.gov).

Pat Mail, a public health analyst at NIAAA, says she sees potential applica-



Public Inquiries Received by OAM.

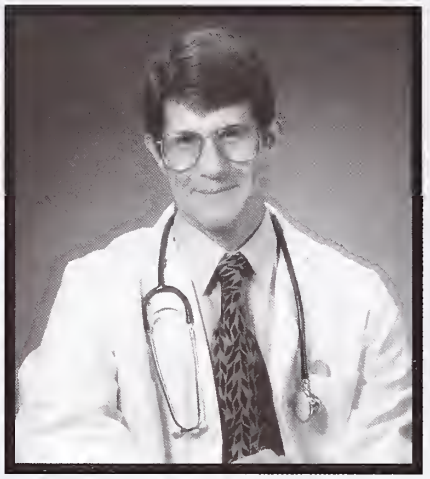
tions for alternative-medicine research at her institution. "In addition to the 'traditional' therapeutic approaches to prevention and treatment of alcohol misuse, there are a number of approaches utilized by people in different cultures that might be beneficially explored," Mail says. "One example comes to mind: the adaptation of Western-style group process by American Indians in their alcohol-treatment programs. This adaptation is often referred to as 'Talking Circles,' which describes both the structure and the process of these therapeutic groups. ... In an increasingly multicultural society, our research should reflect reality, and alternative medicine is the umbrella under which cross-cultural solutions might be explored."

Acknowledging that "good science" often has not been applied to alternative treatment strategies in the past, Jonas says he hopes that OAM's new focus on rigorous preliminary screening and selective funding of both intramural fellows and extramural research grant proposals will lead to a more solid foundation of knowledge about such therapies. "Good science is the way to separate the pearls from the mud," he says.

In this era of limited resources for biomedical research, some may question the expense of sifting through a ton of alternative-medicine mud when mining more traditional veins of research may yield far greater therapeutic returns. However, Jonas is quick to point out that alternative medicine is an area of great interest to both Congress and the U.S. public, with one in three Americans reporting they have used some sort of alternative therapy.

Jonas emphasizes that the intramural research program represents just a small fraction of OAM's activities. One of its biggest efforts is a phone-in clearinghouse to provide the public with descriptive information about alternative therapies and related research. The toll-free line (1 800 531-1794) averages 1,200 calls per month, with the greatest number of inquiries related to alternative therapies for cancer and acquired immune deficiency syndrome (see figures, page 5). Since its inception, OAM also has awarded 42 grants totaling $1.26 million to individual extramural researchers and, along with NIDR, NICHD, NCI, and the Office of Research on Women's Health, has awarded 10 three-year grants totalling $9.7 million to set up alternative-medicine research centers at extramural institutions.

"It is the optimal goal of the Office of Alternative Medicine to foster both rigor and realism in complementary alternative medicine research," Jonas says. "It is our vision to bring together the *best* of healing and the *best* of science." ■



Wayne Jonas

OAM at a Glance

Contact: Director Wayne Jonas
Phone: 402-2466
Location: Building 31, Room 5B-37
Resources: Provides support for selected postdocs interested in alternative medicine and matches them with appropriate investigators at NIH and outside institutions. Awards extramural grants for alternative-medicine research projects. Handles public inquiries about alternative therapies.

A Short History of OAM

The office was founded in 1992 at the direction of Congress under legislation sponsored by Sen. Tom Harkin (D-Iowa). Its congressional mandate is to investigate and evaluate alternative treatments, disseminate information to the public, and support research training in alternative-medicine practices. OAM received $2 million in 1992 and 1993, $3.5 million in 1994, and $5.4 million in 1995. It has used that money to fund extramural grants, establish a popular public clearinghouse, and sponsor a technology-assessment conference.

OAM's first director, Joseph Jacobs, vacated the position after two years. He was replaced in July 1995 by Wayne Jonas, former director of Medical Research Fellowships at Walter Reed Army Institute of Research in Washington, D.C.. Upon his arrival, Jonas reorganized the office and began developing a plan for the intramural training of postdocs. Since Jonas assumed directorship, the office has more than doubled its staff, from four to 10.

HIV Funds Deadline

NIH's Intramural AIDS Targeted Antiviral Program (IATAP) has set Aug. 23 as the deadline for funding proposals for fiscal 1997 and 1998. For more information on how to apply for the funds, contact Janet Smith (402-3444; fax: 402-3443; e-mail: js43d@nih.gov).

INTERINSTITUTE INTEREST GROUP DIRECTORY

Major Interest Groups/Faculties

Cell Biology Interest Group
Meeting time: Varies, meetings restricted to NIH scientists
Meeting place: Building 18T, Room 101
Contact: Jennifer Lippincott-Schwartz, NICHD
Phone: 402-1010; 402-1009
E-mail: jlippin@helix.nih.gov
ListServ: subscribe to CELBIO-L

Clinical Research
Meeting time, place: Varies
Contact: Cliff Lane, NIAID
Phone: 496-7196
E-mail: cl17d@nih.gov

Genetics Interest Group
Meeting time: Last Tuesday, 4:00–5:30 p.m.
Meeting place: Building 49, Conference Room A and B
Contact: Robert Nussbaum, NCHGR
Phone: 402-2146
E-mail: rlnuss@nchgr.nih.gov
Listserver: subscribe to MAJORDOMO@NCHGR.NIH.GOV post to GIG@NCHGR.NIH.GOV

Immunology
Meeting time: Wednesdays, 4:15 p.m. (see NIH Calendar of Events)
Meeting place: Building 10, Lipsett Auditorium
Contact: Pierre Henkart, NCI
Phone: 496-1554
E-mail: henkartp@dc10a.nci.nih.gov
Listserver: subscribe to IMMUNI-L at Listserv@LIST.NIH.GOV

Molecular Biology/Biochemistry Interest Group
Meeting time, place: Varies
Contact: Reed Wickner, NIDDK
Phone: 496-3452
E-mail: wickner@helix.nih.gov

Neurobiology
Meeting time: Not available
Meeting place: Building 49, Conference Room
Contact: Ron McKay, NINDS
Phone: 496-6574
E-mail: mckay@codon.nih.gov
Listserv: JLS@LSR.NEI.NIH.GOV

Structural Biology Interest Group
Meeting time, place: Announced by e-mail and regular mail
Contact: Alasdair Steven, NIAMS
Phone: 402-3418 Fax: 402-3417
E-mail: steven@calvin.niams.nih.gov
To register for e-mail announcements:
E-mail: cch@discus.niams.nih.gov

Other Interest Groups

[Groups in brackets are just getting started. Umbrella groups are affiliated major faculties, or other coordinating or oversight groups]

Alzheimer's Interest Group
Meeting time: First or second Thursday
Contact: Gerald Ehrenstein, NINDS
Phone: 496-3206
E-mail: gerry@helix.nih.gov

Antisense Interest Group
Umbrella Group: Clinical Research
Meeting time: Last Thursday, 4:00 p.m
Meeting place: Building 10, Room 4B36
Contact : Yoon Cho-Chung, NCI
Phone: 496-4020
E-mail: yc12b@nih.gov

Apoptosis Interest Group (AIG)
Meeting time: Once a month on Monday, 4:00 p.m.
Meeting place: Building 30, Conference Room 117
Contact: Yves Pommier, NCI
Phone: 496-5944
E-mail: pommiery@dc37a.nci.nih.gov

Behavioral and Social Sciences Interest Group
Meeting time: Monthly
Meeting place: See Calendar of Events
Contact 1: Jaylan Turkkan, NIDA
Phone: 443-1263
E-mail: jaylan@nih.gov
Contact 2: Ron Abeles, NIA
Phone: 594-5943
E-mail: abelesr@gw.nia.nih.gov

BSSR Methodology and Measurement Interest Group
Umbrella Group: Behavioral and Social Sciences
Meeting time: First or second Tuesday, 8:30 a.m.
Meeting place: Building 45, Room 3AS10
Contact: Jared Jobe, NIA
Phone: 496-3137
E-mail: Jared_Jobe@nih.gov

Bioinstrumentation Interest Group
Meeting time: First Tuesday, 2:00 p.m.
Meeting place: Building 13, Room 3W54
Contact: Steve Leighton, NCRR
Phone: 435-1948
E-mail: leighton@helix.nih.gov

Birth Defects and Teratology Group
Meeting time, place: Varies
Contact 1: Kenneth Warren, NIAAA
Phone: 443-4375
Contact 2: James Hanson, NICHD
Phone: 496-5099

Breast Biology Interest Group
Meeting time: Fourth Monday, 4:00 p.m.
Meeting place: Building 10, Room 13S235B
Contact: JoAnne Zujewski, NCI
E-mail: zujewski@nih.gov

[Carcinogenesis Interest Group
Contact: Umberto Saffioti]

Cell and Molecular Neuroscience Interest Group
Umbrella group: Neurobiology
Meeting time, place: Varies
Contact: Ron McKay, NINDS
Phone: 496-6574
E-mail: mckay@codon.nih.gov

Cell Cycle Interest Group
Umbrella group: Cell Biology
Meeting time: First Wednesday, 2:30 p.m.
Meeting place: Building 37, Room 6B23
Contact: Patrick M. O'Connor, NCI
Phone: 435-2848
E-mail: oconnorp@dc37a.nci.nih.gov

Cellular and Molecular Biotherapy Interest Group
Meeting time: Quarterly half-day symposia
Contact 1: John R. Ortaldo, NCI-FCRF
Phone: 301 846-1323; Fax: 301 846-1673
E-mail: ortaldo@ncifcrf.gov
Contact 2: Jack Greiner, NCI
Fax: 496-2756
E-mail: greinerj@ltiblp.nci.nih.gov

Chaos and Biocomplexity Interest Group
Meeting time: Once a month on Thursday, 4:00 p.m.
Meeting place: Building 10, Rose Room
Contact: Julio Licinio, NIMH
Phone: 496-6885
E-mail: licinio@codon.nih.gov
Listserv: subscribe to BCMPLXTY

Cytokine Interest Group
Meeting time, place: Varies
Contact 1: Howard Young, NCI
Phone: 301 846-5700
Contact 2: Alan Sher, NIAID
Phone: 496-3535

Developmental Biology Interest Group
Umbrella group: Cell Biology
Meeting time, place: Varies (see NIH Calendar of Events)
Contact 1: Igor Dawid, NICHD
Phone: 496-4448
E-mail: idawid@nih.gov
Contact 2: Joram Piatigorsky, NEI
Phone: 496-9467
E-mail: joram@helix.nih.gov

DNA Repair Group
Umbrella group: Molecular Biology
Meeting time: Third Tuesday, 12:30 p.m.
Meeting/Videoconference Locations: Natcher Bldg., Room H; GRC (Baltimore), Room 1E03; FCRDC Building 549, Conference Room A
Contact 1: Kenneth Kraemer, NCI
Phone: 496-9033
E-mail: kraemerk@nih.gov

Drosophila Interest Group
Umbrella group: Developmental Biology
Meeting time: Third Tuesday, 1:15–2:30 p.m.
Meeting place: Building 6B, Room 4B429
Contact: Sue Haynes, NICHD
Phone: 496-7879
E-mail: sh4i@nih.gov

Drug Discovery
Meeting time: Once a month on Thursday, 3:00–4:30 p.m.
Meeting place: Building 37, Room 6B25
Contact: John Weinstein, NCI
Phone: 496-9571
E-mail: weinstein@dtpax2.ncifcrf.gov

Economics Interest Group
Umbrella Group: Behavioral and Social Sciences
Meeting time: Second Tuesday or announced
Meeting place: Announced
Contact 1: James A. Schuttinga, OD
Phone: 496-1454
E-mail: schuttij@od1tm1.od.nih.gov
Contact 2: Agnes Rupp, NIMH
E-mail: ar24f@nih.gov

Epidemiology and Clinical Trials Interest Group
Meeting time: Monthly
Meeting place: See Calendar of Events
Contact 1: Martina Vogel, OD
Phone: 496-6614
E-mail: MartinaV@nih.gov
Contact 2: Dick Havlik, NIA
Phone: 496-1178
E-mail: HavlikR@gw.nia.nih.gov
Listserv:subscribe to Epidem-L at listserv@list.nih.gov

Extracellular Matrix Interest Group
Meeting time, place: Varies
Contact 1: W. Stetler-Stevenson, NCI
Phone: 496-2687
E-mail: stetler1@helix.nih.gov
Contact 2: Larry Wahl
E-mail: wahl@yoda.nidr.nih.gov

Fluorescence Interest Group
Meeting time: Fridays, 4:00 p.m.
Meeting place: Building 10, Room 5D21
Contact: Jay Knutson, NHLBI
Phone: 496-2557
E-mail: jaysan@helix.nih.gov

Gene Therapy Interest Group
Meeting time: Second and fourth Tuesdays, 12:00–1:00 p.m.
Meeting place: Lipsett Auditorium
Contact: R. Michael Blaese, NCHGR
Phone: 496-5396
E-mail: mblaese@nchgr.nih.gov

Glia Club
Meeting time: Bimonthly on second Wednesday, 4:00–5:30 p.m.
Meeting place: Building 36, Room 1B
Contact 1: Vittorio Gallo, NICHD
Phone: 402-4776
E-mail: vgallo@helix.nih.gov
Contact 2: Joan Schwartz, NINDS
Phone: 496-4049
E-mail: jps@helix.nih.gov

Glycobiology Interest Group
Meeting time: Once a month on Thursday, 3:00–5:00 p.m.
Meeting place: Building 30, Room 117
Contact: Diana Blithe, NICHD
Phone: 496-6437
E-mail: blithed@cc1.nichd.nih.gov
Listserver: subscribe to GLYCO-L@LIST.NIH.GOV

Hard Tissue Disorders Interest Group
Umbrella group: Clinical Research
Meeting time: First Wednesday, 12:00 p.m.
Meeting place: Varies
Contact: Pamela Robey, NIDR
Phone: 496-4563
E-mail: probey@yoda.nidr.nih.gov

Image Processing
Meeting time, place: Varies
Contact: Bonnie Douglas, DCRT
Phone: 496-2847
E-mail: douglasb@magic.dcrt.nih.gov

Integrative Neuroscience Interest Group
Umbrella group: Neurobiology
Meeting time: Alternate Thursdays, 4:00 p.m.
Meeting Place: Building 49, Conference Room
Contact: James Olds, NINDS
Phone: 402-6079
E-mail: olds@bernard.ninds.nih.gov
Listserv: subscribe to JLS@LSR.NEI.NIH.GOV

Lambda Lunch (Bacterial and Phage Genetics)
Meeting time: Thursdays, 11:00 a.m.–12:30 p.m.
Meeting place: Building 36, Room 1B13
Contact: Susan Gottesman, NCI
Phone: 496-3524
E-mail: susang@helix.nih.gov
Anonymous FTP site: FTP.CU.NIH.GOV directory "LAMBDA_LUNCH"

Lymphoma and Leukemia Interest Group
Meeting time: Second Monday, 2:00 p.m.
Meeting place: Building 10, Room 9S-235
Contact: Ivan Horak, NCI
Phone: 594-1127
E-mail: idhorak@helix.nih.gov

Mass Spectrometry
Umbrella group: Structural Biology
Meeting time: First and third Thursdays, 10:30 a.m.
Meeting place: Building 10, Room 7C101
Contact: Lewis Pannell, NIDDK
Phone: 402-2196
E-mail: pannell@nih.gov

[Molecular Modeling Interest Group
Meeting time: To be decided
Meeting place: Building 12, Room B51
Contact: Robert Pearlstein, DCRT
Phone: 402-3043
E-mail: staff@cmm.dcrt.nih.gov]

Motility Interest Group
Meeting time: First Monday (except July and August)
Meeting place: Building 10, Bunim Room
Contact: Leepo Yu, NIAMS
Phone: 496-5415
E-mail: lcyu@helix.nih.gov

Mouse Club
Umbrella group: Developmental Biology
Meeting time: Once a month on Tuesday, 4:00–5:30 p.m.
Meeting place: Building 31, Room 2A-52
Contact: Heiner Westphal, NICHD
Phone: 402-0545
E-mail: hw@helix.nih.gov

Nerve Growth Factor (NGF) Club
Meeting time: First Tuesday (see NIH Calendar of Events)
Meeting place: Building 49
Contact: Gordon Guroff, NICHD
Phone: 496-4751
E-mail: gordong@helix.nih.gov

Nerve-Muscle Interest Group
Meeting time: Every other Wednesday, 8:30 a.m.–9:30 a.m.
Meeting place: Building 36, Room 1B07
Contact: Matt Daniels, NHLBI
Phone: 496-2898
E-mail: mdaniels@codon.nih.gov

Neuroimmune Interactions Interest Group
Meeting time: Once a month on Tuesday, 4:00 p.m.
Meeting place: Building 10, Room 11S-235
Contact: Esther Sternberg, NIMH
Phone: 402-2773
E-mail: ems@codon.nih.gov

Nucleic Acid Biochemistry Interest Group
Umbrella group: Molecular Biology
Meeting time: Third Friday
Meeting place: Building 5, Room 127
Contact: Janet Yancey-Wrona, NIDDK
Phone: 496-2038
E-mail: janety@bdg10.niddk.nih.gov

Pigment Cell Research Interest Group
Meeting time: Third Monday, 3:00 p.m.–4:30 p.m.
Meeting place: Building 37, Room 6B23
Contact: Vincent Hearing, NCI
Phone: 496-1564
E-mail: hearingv@dc37a.nci.nih.gov

Postdoctoral Structural Biology Interest Group
Meeting time: Once a month on Tuesday, 3:00–5:00 p.m.
Meeting place: Building 31, no room given
Contact: Teresa Strzelecka, NIDDK
Phone: 496-2815
E-mail: strzel@speck.niddk.nih.gov

[Prostate Cancer Interest Group
Contact: W. Marston Linehan, NCI
Phone: 496-6353]

Protein Folding
Meeting time: Thursdays, 4:00 p.m.
Meeting place: Building 12A, Room 3026
Contact: Joe Bryngelson, NCI/DCRT
Phone: 496-1135
E-mail: jdb@helix.nih.gov

Protein Trafficking Interest Group
Umbrella group: Cell Biology
Meeting time: Second Tuesday, 3:30-5:00 p.m.
Meeting place: Building 10, Room 9S-235 (Bunim Room)
Contact: Harris Bernstein, NIDDK
Phone: 402-4770
E-mail: harris_bernstein@nih.gov

Human Retrovirus Interest Group
Meeting time: Third Wednesday, noon-1:00 p.m.
Meeting place: Natcher Conference Center, Room B
Contact: Fatah Kashanchi, NCI
Phone: 496-0987
E-mail: kanshancf@dce41.nci.nih.gov

RNA Club
Umbrella group: Molecular Biology
Meeting time: First Tuesday, 4:00-6:00 p.m.
Meeting place: Building 41, Room C509
Contact 1: Carl Baker, NCI
Phone: 496-2078
E-mail: ccb@helix.nih.gov
Contact 2: Susan Haynes, NICHD
Phone: 496-7879
E-mail: sh4i@nih.gov

Signal Transduction Interest Group
Meeting time, place: Not available
Contact 1: John Northup, NIMH
Phone: 496-9167
E-mail: JKNGTP@helix
Contact 2: Jim Battey, NIDCD
Phone: 402-2829
E-mail: jbattey@pop.nidcd.nih.gov

Social Structure & Demographic Issues in Health Interest Group
Umbrella group: Behavioral and Social Sciences
Meeting time, place: To be announced.
Contact 1: Laura E. Montgomery, NCHS/CDC
Phone: 436-3650 x 177
E-mail: lem3@nch07a.em.cdc.gov
Contact 2: Julie Reid, NHLBI
Phone: 435-0410
E-mail: Julie_Reid@nih.gov

Transcription Factors
Meeting time: First Thursday (except July-Sept.), 2:15 p.m.
Meeting place: Building 49, First Floor Conference Room
Contact 1: Stoney Simons, NIDDK
Phone: 496-6796
E-mail: steroids@helix.nih.gov
Contact 2: U. Siebenlist, NIAID
Phone 496-7662
E-mail: us3n@nih.gov
Listserv: subscribe to TFACTORS

Virology Interest Group
Meeting time: Third or fourth Thursday, 3:30 p.m.
Meeting place: Building 4, Room 433
Contact: Edward Berger, NIAID
Phone: 402-2481
Listserv: contact CBuckler@nih.gov

Washington Area Yeast Club
Umbrella group: Molecular Biology
Meeting time: Second Wednesday, 5:15–7:15 p.m.
Meeting place: Building 6B, Room 4A-05
Contact 1: Reed Wickner, NIDDK
Phone: 496-3452
E-mail: wickner@helix.nih.gov
Contact 2: Alan Hinnebusch, NICHD
Phone: 496-4480
E-mail: ah8j@nih.gov

WorldWideWeb Interest Group
Meeting time: Second Tuesday, 2:30 p.m.
Meeting place: Bldg. 10, Lipsett Auditorium
Contact : Dale Graham, DCRT
Phone: 402-1805
E-mail: degraham@helix.nih.gov

Xenopus/Zebrafish Interest Group
Umbrella group: Developmental Biology
Meeting time: Last Friday (except summer), 4:00 p.m.
Meeting place: Building 6B, Room 429
Contact: Tom Sargent, NICHD
Phone: 496-0369
E-mail: tsargent@nih.gov

X-ray Crystallography
Umbrella group: Structural Biology
Meeting time: Sporadically announced to members via e-mail
Meeting place: Building 5, Room 231
Contact 1: James Hurley, NIDDK
Phone: 402-4703
E-mail: hurley@tove.niddk.nih.gov

Youth and Family Interest Group
Umbrella group: Behavioral and Social Sciences
Meeting time: Third Tuesday; time to be set
Meeting place: Building 31, 6A23
Contact: Carmen Moten, NEI
Phone: 496-4308
E-mail: cpm@b31.nei.nih.gov

To make additions or changes, contact The NIH Catalyst (fax: 402-4303; e-mail: catalyst@od1em1.od.nih.gov). ■

Wanted: Grad-School Director

If shaping a curriculum interests you as much as designing an experiment, the Foundation for Advanced Education in the Sciences (FAES) may have the perfect job for you. FAES is seeking a scientist to serve as the new director for its Graduate School at NIH, a 37-year-old education program that has an enrollment of more than 2,500 students and offers nearly 100 courses. The part-time position is being vacated by NIDDK's Louis Cohen, who is stepping down after leading the school for the past 35 years. FAES says the new director must be a scientist who is familiar with NIH and its science-education needs, but he or she does not need to be employed by NIH. Among the director's responsibilities will be developing a new curriculum for the school, including courses that use a modern molecular biology teaching lab. For more information on the directorship, contact Lois Kochanski at FAES (phone: 496-7975; e-mail: KochanskiL@FAES.OD.NIH.Gov). ■

RECENTLY TENURED

Sanford Dawsey *joined NCI's Division of Cancer Prevention and Control in 1987 and is currently an investigator in the division's Cancer Prevention Studies Branch. Dawsey received his M.D. from Stanford Medical School in Palo Alto, Calif., in 1976.*

My major research interest is the prevention and control of esophageal cancer—a cancer that kills 10,000 Americans annually and is the fourth most common cause of cancer death among African American men. Less than 10% of patients with esophageal cancer survive for five years after diagnosis, largely because most of these tumors do not produce symptoms until it is too late for surgery and nonsurgical treatments are usually not curative. In this setting, we will probably need to develop successful primary-prevention and/or early-detection strategies to significantly reduce esophageal cancer mortality.

Ralph Isenburg

Sanford Dawsey

At NCI, I have participated in two large nutritional-intervention clinical trials in Linxian, China, a region with extraordinarily high rates of esophageal and gastric cardia cancer. During these trials, my collaborators and I performed several studies that were relevant to an early-detection approach to squamous esophageal cancer. We carried out two prospective follow-up studies that documented the predictive value of esophageal cytology, another follow-up study that showed that high-grade squamous dysplasia is the only important near-term histologic precursor of squamous esophageal cancer, and two endoscopic studies that demonstrated that this histologic precursor lesion is usually associated with visible mucosal abnormalities that can be biopsed.

Our discovery that squamous dysplasia can usually be identified through an endoscope has important implications for research and clinical practice. In research, endoscopic biopsies should be an accurate gold standard for validating less-invasive diagnostic techniques such as esophageal cytology, and endoscopic protocols should be able to evaluate future intervention studies that use squamous dysplasia as an intermediate endpoint. In the clinic, endoscopic biopsies should be able to confirm and localize screening-detected abnormalities, primary endoscopic screening may be feasible in certain high-risk groups, and focal endoscopic therapy may be possible for controlling precursor and early invasive disease.

Building upon these results, I have recently begun a series of studies to evaluate and possibly improve some techniques that may be useful in a practical early-detection program for squamous esophageal cancer. One study is aimed at evaluating the sensitivity and specificity of the currently available esophageal cytologic samplers and at developing improved models of these samplers. Another study focuses on whether mucosal staining can improve endoscopic localization of squamous dysplasia and cancer, thereby optimizing the visualization of such lesions for focal therapy. A third study is designed to evaluate how accurately endoscopic ultrasonography can stage early squamous cancers so that focal therapy will not be attempted on tumors that are already too advanced. A fourth study is aimed at assessing the safety, acceptability, and preliminary efficacy of several methods of focal endoscopic therapy, including endoscopic mucosal resection and thermal coagulation.

I am also currently involved in etiologic studies of the roles of human papillomavirus and certain fungal toxins in the development of squamous esophageal cancer, and other studies of the role of *Helicobacter pylori* in the development of gastric cardia cancer. In addition, I am participating in a group of new genetic studies of esophageal and gastric cancers in high-risk Chinese populations. We are hopeful that our etiologic and genetic studies will contribute to the development of additional promising strategies for the prevention and control of esophageal cancer.

Ralph Isenburg

Vittorio Gallo

Vittorio Gallo *received his Ph.D. from the University of Rome in 1979. He joined NICHD's Laboratory of Cellular and Molecular Neurophysiology in 1992 as head of the Unit on Neurobiology, and he is currently chief of the lab's Section on the Molecular Neurobiology of Glia.*

My lab's recent research has centered on glial cells of the mammalian brain. Glial cells do not directly participate in synaptic transmission, and their precise role in the developing and adult brain is yet to be defined. Using oligodendroglial progenitor (O-2A) cells purified from the embryonic rat cerebral cortex as a model system, we are trying to understand the regulation and physiological role of neurotransmitter receptors in glia during development.

In the embryonic mammalian brain, oligodendroglial cells divide, migrate, and differentiate later than neurons. This observation has given rise to the hypothesis that neurotransmitters released by neurons may play an important role in the development of the oligodendroglial lineage—a hypothesis that we are testing by focusing on the main excitatory neurotransmitter of the mammalian brain, glutamate, and its receptors.

Our previous work, which demonstrated that O-2A cells express glutamate-receptor (GluR) genes and genes that encode functional glutamate-gated channels, led to two important findings. First, we characterized two subtypes of GluRs with distinct molecular composition and function in cells of the oligodendrocyte lineage. Second, we identified a set of genes that are induced by GluR-activation in a calcium-dependent fashion in O-2A progenitors. In more recent experiments, we demonstrated that activation of GluRs in O-2A cells reversibly inhibits their proliferation and prevents lineage progression through the indirect blockage of delayed-rectifier potassium channels. Our future work will focus on the molecular analysis of intracellular events crucial to glial-cell development that are triggered by GluR activation.

My lab is also using glial cells to study how GluR genes are regulated in the mammalian brain. Our specific goal is to determine whether the DNA regulatory elements and transcription factors that regulate GluR gene transcription in glia and in neurons are the same. We have cloned the entire rat gene encoding the GluR subunit KA2. This gene, named *GRIK5*, is abundantly expressed in both glia and neurons. *GRIK5* spans approximately 70 kilobases of genomic DNA and comprises 20 exons. We identified multiple transcription-start sites in its 5' flanking region, and also found that *GRIK5* displays features of a housekeeping gene. Our analysis in rat neural cells and in nonneural rat and human cells, as well as in transgenic mice, demonstrated that a region of *GRIK5's* 5'-flanking sequence restricts tissue-specific expression of this GluR gene in vitro and in vivo. Now, we are working on characterizing the mechanisms of transcriptional regulation of *GRIK5* during

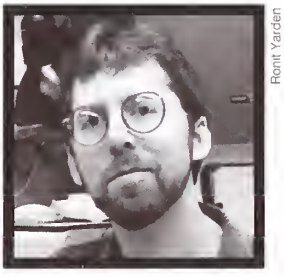
development and identifying the DNA-binding sites involved.

Finally, I am also collaborating with Mark Mayer and Chris McBain of NICHD's Laboratory of Cellular and Molecular Neurophysiology on projects to determine whether GluRs can be regulated at the transcriptional level by growth factors that are known to modulate glial development and to define the precise role of other membrane ion channels in glial development.

Eric Green *received his M.D.-Ph.D. from Washington University in St. Louis in 1987. In 1994, he joined NCHGR, where he is now head of the Physical Mapping Section and acting chief of the Genome Technology Branch.*

The major focus of my research program over the past five years has been to establish the genetic architecture of one human chromosome by constructing a complete physical map of its DNA and then determining the DNA sequence.

My lab's efforts have centered on chromosome 7, which spans an estimated 170 million base pairs (bp) and accounts for roughly 5% of the human genome. Our mapping approach uses yeast artificial chromosomes (YACs) as the cloned DNA fragments and sequence-tagged sites (STSs) as the landmarks for establishing the overlapping relationships among the YACs. STSs are short stretches of DNA that can be specifically detected using the polymerase chain reaction (PCR). We have developed and implemented strategies for generating STSs specific to chromosome 7 and for identifying YACs containing each of these STSs. This has involved performing an average of 1,000 to 2,000 PCR assays per day for nearly three years.



Ronit Yarden

Eric Green

We reached a major milestone recently when we completed construction of one of the most detailed maps of a human chromosome to date—a physical map of chromosome 7 that provides YAC coverage across the chromosome as well as a mapped STS every 80,000 bp. This achievement reflects the development of more than 2,000 STSs unique to chromosome 7, the mapping of each of these STSs to individual YACs, the rigorous integration of our physical map with the genetic and cytogenetic maps, and the mapping of hundreds of gene sequences. These results also provide support for an experimental paradigm, termed YAC-based STS-content mapping, that we proposed in 1991 for building a physical map of the human genome.

As a result of our mapping efforts, chromosome 7 is among the first targets for large-scale DNA sequencing within the Human Genome Project. In collaboration with the genome centers at Washington University in St. Louis and the University of Washington in Seattle, we have begun genomic sequencing of chromosome 7. While the notion of sequencing an entire human chromosome may seem daunting, remember that only five years ago the idea of making a complete physical map of a human chromosome was equally intimidating. On the basis of preliminary data and previous experience, we expect that our collective efforts will yield a first-pass sequence of chromosome 7 within three to four years.

The availability of an evolving genetic blueprint for 5% of the human genome is already providing spectacular opportunities to explore human biology. Our geographic map of chromosome 7 is now yielding serendipitous research opportunities that cut across biology. We are actively engaged in several projects to study the molecular basis of cancer susceptibility, cardiovascular disease, immune response, and neural development. In many of these projects, we are in pursuit of genes that cause human disease. In every case, our detailed maps, DNA-based reagents, and growing body of sequence data are enhancing our ability to study complex biological processes. These limited examples—which reflect only the tip of the future genetic iceberg—illustrate how the fruits of the genome project are creating a new era for biomedical research.

Ralph Isenburg

Arthur Sherman

Arthur Sherman *received his Ph.D. from New York University in 1986. Since then, he has worked in NIDDK's Mathematical Research Branch .*

Trained as an applied mathematician specializing in the analysis and development of methods for numerical solution of ordinary and partial differential equations, I came to NIDDK to work in the Mathematical Research Branch—a leading force in theoretical biology and computational neuroscience since the 1950s. I was particularly attracted by the group's reputation for fostering collaboration between theoreticians and experimental biologists.

I was assigned to model the electrical activity of pancreatic beta-cells in the islet of Langerhans using elaborated Hodgkin-Huxley equations that describe neural action potentials. Beta-cells exhibit rhythmic electrical activity, similar to that observed in many neurons, that plays an important role in insulin secretion. An as-yet-unidentified defect in beta-cell response to blood plasma glucose is thought to be central to the development of Type II diabetes.

Together with fellow theoreticians John Rinzel and Joel Keizer, I tested the hypothesis of two NIDDK experimentalists, Illani Atwater and Eduardo Rojas, that the bursting electrical rhythm of beta-cells is an emergent property of the gap-junction-coupled network of cells in the islet of Langerhans. Atwater and Rojas developed their "channel-sharing" hypothesis after they found that isolated beta-cells rarely displayed the bursting rhythm. We demonstrated that electrical coupling could not only synchronize the activity of inherently oscillatory units, but also play a role in generating oscillations.

More recently, Richard Bertram and I have worked with Atwater, Rojas, and others on parasympathetic regulation of beta-cell electrical activity. We proposed that the inositol-1,4,5-trisphosphate- and aceytylcholine-mediated release of calcium from the endoplasmic reticulum leads to depolarization via calcium-release activated current (CRAC) channels. Unexpectedly, our mathematical model revealed that the important first phase of insulin secretion following a glucose challenge might also be governed by CRAC, a prediction supported by follow-up experiments.

Bertram and I have also been collaborating with Elis Stanley of NINDS on mechanisms of synaptic release. We have developed a mathematical model of Stanley's hypothesis that facilitation by high-frequency stimulation is due to accumulation of calcium bound to release sites. We hope this work will help resolve long-standing controversies about synaptic facilitation and also shed light on endocrine secretion.

My long-term goals are to continue studying the mechanisms and dynamics

of insulin secretion, delving deeper into its regulation by metabolic and hormonal signals. The current flood of detailed biochemical information on vesicle exocytosis should also open up exciting opportunities for the mathematical modeling of this final step in secretion in both neural and endocrine cells.

Jack Taylor *received his M.D. from the University of Wisconsin in Madison in 1984 and his Ph.D. from the University of North Carolina in Chapel Hill in 1993. Taylor joined NIEHS's Epidemiology Branch as a senior staff fellow in 1988, and he is now a lead clinical investigator in that branch. In 1996 , he also became head of the Molecular and Genetic Epidemiology Group in NIEHS's Laboratory of Molecular Carcinogenesis.*

My research is directed toward understanding the interaction between genes and environmental exposures in human carcinogenesis. There are two main elements to this work: investigating the role of environmental exposure in critical-target gene mutation and investigating the role of genetic susceptibility and environmental exposure in cancer risk.

The research on critical-target genes addresses the hypothesis that different environmental exposures cause different patterns of mutation in genes that are important in carcinogenesis. My initial focus has been on mutational activation of oncogenes and deactivation of tumor-suppressor genes. Such patterns can be used to identify novel critical-target genes and to suggest mutational mechanisms by which an environmental agent causes cancer. If specific carcinogens produce characteristic patterns of gene mutation in tumors, detection of such patterns would be a powerful tool in studies of environmental risk and in prevention and early diagnosis.

Judith Stenger

Jack Taylor

Most of my work has been on lung and bladder cancer—two tumors that have strong environmental determinants. In a recent study done with Teddy Devereux at NIEHS and Geno Saccomanno at St. Mary's Hospital in Grand Junction, Colo., we showed that roughly one-third of large- and squamous-cell lung tumors from uranium miners had an identical mutation in the tumor-suppressor gene *p53*. This is one of only four known examples of an exposure-specific pattern of critical-target gene mutation in human tumors. It is a provocative result because alpha-particle radiation, although known to cause single base-pair mutations, might not be expected to produce such a highly specific DNA lesion.

My research on genetic susceptibility tests the hypothesis that commonly inherited allelic variants of selected candidate genes, in conjunction with environmental exposures, affect a person's risk of developing cancer. Working with genetically susceptible subgroups may allow us to identify the environmental exposures that cause disease and the true risks associated with exposure. It could also lead to programs for protecting susceptible populations and for targeted screening of high-risk groups.

We are studying inherited polymorphisms in selected genes that have potential links to bladder cancer risk: genes involved in carcinogen metabolism, proto-oncogenes, tumor-suppressor genes, and genes involved in DNA synthesis and repair. Doug Bell at NIEHS and I have looked at a polymorphism in the gene *GSTM1*, which is involved in detoxification of certain carcinogens. Interestingly, roughly half of the U.S. population has no working copy of this gene (homozygous null). We have found evidence of a gene-environment interaction on risk: people with the homozygous null *GSTM1* genotype have twice the risk of developing bladder cancer as people with at least one working copy of the gene—but only if they also are exposed to a carcinogen, such as cigarette smoke. Although the increased risk is fairly small, particularly compared with the risk posed by genes responsible for familial clusters of cancer, such a gene polymorphism can still be important to public health because both the polymorphism and the exposure are common. We calculate that 25% of bladder cancer may be attributable to the heritable defect in *GSTM1*.

My two research areas also overlap: critical-target genes are often polymorphic and their inherited allelic variants may affect susceptibility; conversely, the inherited variant alleles of susceptibility genes may ultimately affect the pattern of mutation in critical-target genes found within a tumor. By combining epidemiology and molecular biology, my long-term goal is to develop a more integrated view of how exposure, genetic susceptibility, and critical-target gene damage interact in lung and bladder cancers. ■

Research Festival Turns 10

NIH's intramural Research Festival marks its 10th anniversary this year. In honor of the occasion, festival director Henning Birkedal-Hansen wants to do something old and something new at the Sept. 16–20 event: revive VIP posters and begin a job fair for NIH postdocs.

Birkedal-Hansen, who is NIDR's scientific director, got the idea for the VIP posters from a scientist who gave a command poster presentation at the first Research Festival, NIDR's Abner Notkins. "People thought the VIP poster session was great," says Birkedal-Hansen. "It gave the postdocs a chance to talk to NIH's top scientists—who are world leaders in their fields." This year, the VIP posters will not be set off in their own session, but will be presented alongside posters from NIH postdocs and other scientists. Invited VIP presenters are expected to include institute directors, scientific directors, and maybe even Deputy Director for Intramural Research Michael Gottesman and NIH Director Harold Varmus.

At the Sept. 18 job fair, NIH's Office of Education and the Foundation for the Advancement of Education in the Sciences will arrange job interviews and meetings between NIH postdocs and representatives of biotechnology firms, many of whom will be on hand for the festival's tent show for biomedical suppliers on Sept. 19–20.

The 1996 Research Festival will open at 8 a.m. Sept. 16 at the Natcher Conference Center with a symposium on prion diseases. The symposium will be followed by a poster session from 11 a.m. to 1 p.m. About a dozen workshops will run simultaneously from 1:30 to 4:30 p.m., and a second poster session will follow from 4:30 to 6:30 p.m. The program for Sept. 17 will follow the same schedule, starting with a symposium on the genetics of complex disorders. A searchable program of events will be posted on the World Wide Web (http://mantis.dcrt.nih.gov/festival/). For more information, contact Gregory Roa at the NIH Visitor Information Center (phone: 496-1776; e-mail: gr25v@nih.gov). ■

—Celia Hooper

CHARGE CARD

continued from page 1.

Although such dollar figures are what grabs administrators' attention, Pepper says she was equally impressed by the amount of time saved by buying the IL-2 with her charge card rather than going through regular procurement channels. It took only three days to get a year's worth of IL-2 using the purchase card compared with a wait of two months or longer under the paper system. "I think the real value of the cards is in the time saved—time saved to do science," says Pepper, noting that if the lab needs a reagent immediately, she can use her card to place an order with a local supplier and get delivery by afternoon.

Ronit Yarden

Amy Pepper

NCHGR Scientific Director Jeff Trent is equally enthusiastic about the charge cards, calling them "the single most important reinvention authority [at NIH] to date." Although the IL-2 case may be the most dramatic example, Trent says there are many other smaller purchase-card success stories at NCHGR. He cites the purchases of a Plexiglas container for $4 at a local store compared with $40 through a traditional scientific supplier and of a computer service that was obtained in 24 hours compared with the two-week wait it would take if provided through NCRR's Biomedical Engineering and Instrumentation Program.

Along with the freedom to place orders by purchase card comes the responsibility to reconcile billing statements—checking shipping statements or invoices with the charges listed on the monthly statement prepared for NIH by the cards' issuer, Rocky Mountain BankCard System. While conceding that bill reconciliation is the hardest part of the process, Pepper says she can double-check her lab's $10,000 to $20,000 in monthly purchases in about 2 1/2 hours using a software program that she created for the chore. In the NIH-wide program, researchers won't have to resort to writing their own software for bill reconciliation because OPM, OFM, and DCRT are setting up a centralized automated system for documenting receipt of orders and reconciling purchase-card statements.

When the project is expanded to include all of NIH, OPM plans to impose a $5-per-order service charge. But many observers note that this is cheap compared with NIH's current procurement-services charges of anywhere from $15 to $100 per order for purchases under $25,000. The purchase rules are expected to follow those in place during the pilot. Most importantly, all federal procurement rules apply to purchases made with the cards. There is a single purchase limit of $2,500 per order unless a scientist undergoes three weeks of special procurement training. There are no limits on how many orders can be placed per month, and it is up to each ICD to set the dollar limits for each scientist's monthly purchases. For more information on the cards, contact Kemp (phone: 496-6071).

According to Pepper, some of the charge-card limitations might even work to a scientist's advantage. For example, when Pepper told a computer supplier that she could not buy a laptop for her lab because its $2,800 price exceeded her card limit, the supplier swiftly lowered the price to $2,500.

So what does Pepper's lab plan to do with the quarter-million dollars it saved using the charge card? "We are trying to figure out a way under reinvention to convert the money saved into space—that's one thing we never have enough of!" she says. ■

MAXIMUM CONTAINMENT LABORATORY

continued from page 1.

research units in the United States. The others are at the Centers for Disease Control and Prevention in Atlanta and at the U.S. Army Medical Research Institute for Infectious Disease in Fort Detrick, Md. NIH expects that both intramural and extramural researchers will use MCL and has set up the MCL Program Review Committee to examine proposals for scientific merit and safety concerns.

NIH's previous BL-4 facility, established in the mid-1970s for research involving recombinant DNA and cancer-causing viruses, later housed NIAID scientist Malcolm Martin's transgenic mouse containing the entire genome of the human immunodeficiency virus. But the old facility's design limited the types of benchwork that could be undertaken with pathogens requiring maximum levels of containment and could only handle animal projects involving small rodents. The new facility, with three interchangeable modules of lab and animal-care space, can accommodate animals ranging in size from mice to nonhuman primates.

According to Wilson, the emphasis on freedom of movement should make work safer for researchers in MCL. The old facility's cramped and inflexible glovebox design often led to researcher fatigue and made it difficult to maneuver sharp instruments during surgery and other procedures. Like BL-4, MCL will be limited to research on just one pathogen at any given time. However, the increased workspace of the new facility—about 2,000 square feet compared with the previous glovebox space of less than 500 square feet—should make it easier to simultaneously conduct a variety of studies involving the same pathogen than it has been in the past, Wilson says.

Mycobacterium tuberculosis will be the focus of the first research project in MCL: a series of NIAID studies aimed at creating a suitable animal model to use in testing therapeutic and vaccine interventions against multi-drug–resistant tuberculosis (MDR TB). Although *M. tuberculosis* itself is not a BL-4 pathogen, the MCL Program Review Committee agreed that maximum containment was indicated for such studies because the strains to be used in the studies are multi-drug resistant and because the inoculum will be delivered by aerosol—the route by which most TB infections are acquired.

On the basis of past work describing the pathogenesis of TB in rabbits, NIAID's Mark Simpson, Thomas Kindt, and Richard G. Wyatt plan to explore the possibility of using rabbits as models for MDR TB. Among those assisting the NIAID team with the study will be the Division of Safety's Wilson, a microbiologist whose doctoral research was on the effect of vaccination on guinea pigs that were infected with *M. tuberculosis* through the aerosol route. Because the researchers want to familiarize themselves with the new facility and because the pathogenesis of MDR and non-MDR TB do not apparently differ, the initial study will be done with non-MDR TB. However, MDR strains will play an important role in future studies that will analyze interventions.

"The design of the old facility would not have permitted the study of rabbits. Technology has advanced since that facility opened, and the new facility will take advantage of that new technology," says Wyatt. "The Division of Safety did a superb job in designing the space."

Although researchers who use MCL will pay for supplies and animals used in their experiments, the Office of Research Services will cover the actual cost of running MCL. A major expense for researchers using MCL will likely be the labor costs involved in training people to work in the state-of-the-art facility. Wilson estimates that most staff will require at least a couple weeks of special safety training, including performing dry runs of their experiments, before receiving the go-ahead to begin their research with a BL-4 pathogen. ■

Maryland Young Scientists Awards

Robert A. Craigie

Robert A. Craigie, chief of the Molecular Virology section in NIDDK's Laboratory of Molecular Biology, is the 1996 winner of Maryland's Outstanding Young Scientist Award. Craigie recently received the honor for his outstanding contributions to the understanding of retroviral DNA integration—a critical step in the replication cycle of the human immunodeficiency virus (HIV) and other retroviruses—and for his contributions to work that determined the structure of the catalytic domain of HIV integrase. The $2,500 award, which recognizes cutting-edge scientists under the age of 40 who live and work in Maryland, is sponsored annually by the Maryland Academy of Sciences. Also cited this year was Alan Wolffe, chief of NICHD's Laboratory of Molecular Embryology. Wolffe was named one of Maryland's Distinguished Young Scientists for his work on the structure of nucleosomes and on how the architecture of chromatin regulates transcription-factor access to DNA. He is particularly interested in the role these nuclear components play in controlling gene expression during the various stages of embryonic development. ■

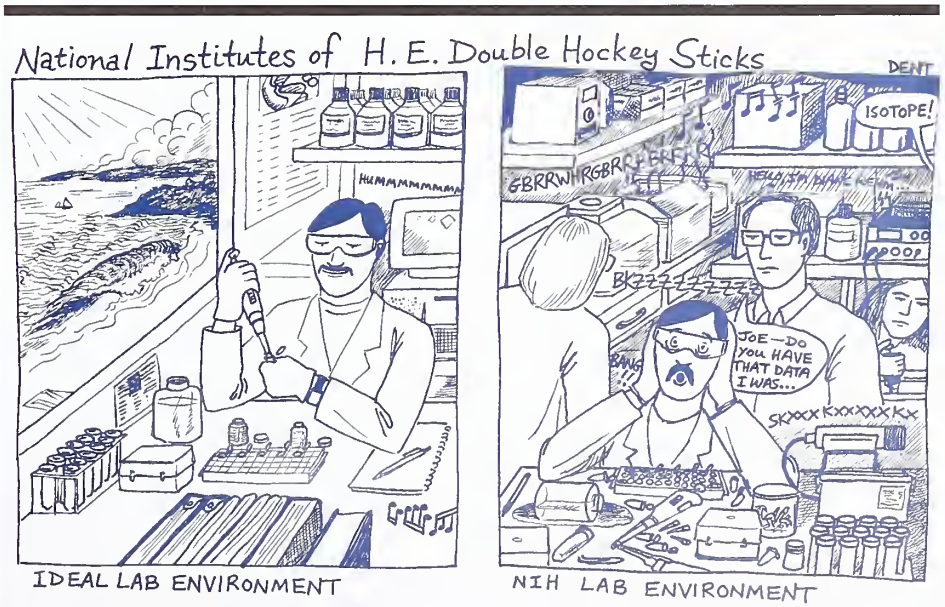
Alan Wolffe

Guess Who's Coming to FELLOW-L?

It's not quite "The David Letterman Show," but FELLOW-L, an electronic forum that provides announcements relevant to the postdoctoral community, recently started a lively new feature showcasing the views of invited "guests." In May, the first guest, NINDS's Joan P. Schwartz, who is co-chair of NIH's Committee on Scientific Conduct and Ethics, answered anonymous questions and comments on the subject of mentoring. The starting point for the discussion was Schwartz's article in the March-April 1996 issue of *The NIH Catalyst*. Schwartz's responses were posted on FELLOW-L and the ftp archive (ftp://helix.nih.gov/fellcom). Anyone with an interest in postdoc issues is welcome to subscribe to FELLOW-L. Postings on the list regularly include scientific questions, offers and requests for equipment, conference and seminar-related announcements, and discussions about jobs. To sign up, send an e-mail message that reads SUBSCRIBE FELLOW-L YOUR NAME to LISTSERV@ULIST.NIH.GOV ■

OHSR Home Page

Thanks to the power of the World Wide Web, it's now even easier for NIH scientists to get timely information on the regulations and ethical guidelines governing research involving human subjects. The Office of Human Subjects Research's (OHSR's) new home page on the Web offers intramural researchers ready access to a variety of resources, including electronic versions of its "Gray Booklet" that contains guidelines for human-subjects research and NIH's Multiple Project Assurance document. Also available at the site are a collection of 12 information sheets prepared by OHSR. To reach the OHSR site, go to the NIH home page on the Web and click on "Institutes and Offices" and then click on "Office of the Director." The page can also be accessed directly at the uniform resource locator (URL): http://www.nih.gov:80/od/ohsr/ ■



CATALYTIC REACTIONS

In this issue, we are asking for your reactions in four areas: charge cards, ethics report, Hot Methods Clinic, and parking. **Send your responses on these topics or your comments on other intramural research concerns to us via e-mail: catalyst@od1em1.od.nih.gov; fax: 402-4303; or mail: Building 1, Room 334.**

In Future Issues. . .

- Building 50, A Peek at the Plans
- Hot "Cold" Methods: Reducing Radioactivity
- Telemedicine's Ties To Clinical Research
- NIH's Chemistry With Chemists

1) What do you think of NIH's charge-card initiative? Do you plan to apply for a card? If so, in what situations do you think it will come in most handy?

2) What are your general reactions to the Commission on Research Integrity's report (see p. 4)? What specific things would you like to see added, deleted, or otherwise modified?

3) The Hot Methods Clinic will return in the next issue. What updates can you provide on previous Hot Methods? What techniques would you like to see covered in the future?

4) We are considering an article about on-campus parking. Have you experienced any problems lately? How could the parking system be improved to meet scientists' needs?

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