FOSTERING COMMUNICATION AND COLLABORATION

The NIH CATALYST

A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

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FROM KHARAGPUR TO BETHESDA

by Susan Chacko, Ph.D., NIDDK

It's rare for foreign scientists at NIH to feel the sort of cultural isolation that might be experienced if they had left their homelands for, say, a small town in the Midwest. After all, just walk into the Building 10 cafeteria, and you're almost in the United Nations. You are surrounded by a huge variety of accents and languages, many of which you can vaguely identify only by continent. In the lab, your colleagues are as likely to be Chinese, Indian, or Hungarian as American.

This atmosphere of ethnic diversity extends beyond the Bethesda campus into the Washington metropolitan area where foreign-language videos, music, and literature are readily available. Because there's no better comfort than home food (or some facsimile thereof!) in moments of extreme cultural alienation, it helps to be surrounded by the ethnic restaurants of Bethesda and its neighbors. You can also watch foreign films at the Kennedy Center and attend cultural performances by your countrymen. As in most places in America, news from home is often sparse, but CNN and electronic newsgroups on the Internet are improving things considerably. In addition, competition among the long-distance phone companies keeps on driving down

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LAND OF MILK AND HONEY? NIH THROUGH THE EYES OF FOREIGN SCIENTISTS

by Rebecca Kolberg

Next time you hit one of NIH's inevitable administrative glitches, imagine trying to conduct cutting-edge biomedical research on a lab budget of only a few hundred dollars a month. Or figuring out how to earn a Ph.D. in molecular biology in a land where there are no molecular biology departments. Or pursuing a research career in an economic climate in which accomplished biologists aren't even paid enough to rent a decent apartment. Or attempting to fine-tune experimental designs and put data into perspective without easy access to other leading minds in the field.

Foreign Scientists in NIH Visiting Program
Top 20 Nations in FY 1994

Japan	291	Israel	62
China	232	Australia	43
Italy	135	Argentina	42
Russia	100	Poland	40
South Korea	99	Spain	36
India	95	Hungary	34
France	92	Taiwan	29
United Kingdom	78	Brazil	25
Germany	77	Greece	21
Canada	66	Czech Republic	20

For many of the approximately 2,000 foreign scientists in NIH's intramural research program, it may not take much imagining. Although American researchers are often tempted to see NIH's glass as half empty, grousing about the cramped quarters, funding pressures, and cumbersome ordering systems, most foreign scientists view NIH's glass as half full, if not overflowing, when compared with labs in their homelands. Almost to the person, foreign scientists interviewed by *The NIH Catalyst* say they were struck by the abundance of resources they found awaiting them at what many consider the leading biomedical research institution in the United States, if not the world.

"When I came to the United States, I was moved to awe," says Yun-Bo Shi, a tenure-track NICHD scientist who trained at several U.S. institutions after arriving from China in 1983. "The facilities were so much better than they were back at home." NHLBI's Sue Goo Rhee, who came to NHLBI as a postdoc in 1973 and now is chief of NHLBI's Laboratory of Cell Signaling, says he was accustomed to building his own apparatus for distillation experiments in his native Korea.

Recent arrivals continue to be impressed. Sasha Zivkovic, a postdoc who came to NIDR in the spring of 1995 from Croatia, says, "The number one difference is resources. We were working with such a small amount of money—several hundred dollars a month for experiments. It's almost magic if you can get experiments to work with that." Even scientists from

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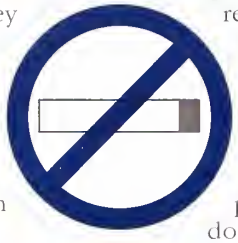
Catalytic Reactions

"From the Deputy Director for Intramural Research" column will return next issue. Below are comments we received for topics raised in the September–October issue, along with some general reactions.

On smoking at NIH

Instead of asking that smokers be punished even more than they are already, Gerry Dienel might hold his breath for the short time needed to traverse the deadly nicotinic zone outside the doors of NIH buildings. The don't-inhale reflex thus acquired might save his life in the event of a lab accident.



—Charles McCutchen, NIDDK

Just to add to Gerry Dienel's comments—it is worth concern that employees in Building 37 (ironically, NCI) sit on the steps overlooking the day-care center for their "smoke breaks." The area adjacent to the children's playground should be a no-smoking zone.

—Kimberly Duncan, NCI

Gerry Dienel recommends that NIH establish programs to help break people of the smoking habit. The Office of Human Resources Management, through its Division of Workforce Development, does offer a course called "Break the Smoking Habit," presented by SmokeEnders. An institute can pay for this course for an employee who is interested in stopping smoking. Dienel also recommends that NIH offer reduced health and life insurance rates for nonsmokers. The U.S. Office of Personnel Management manages the health and life insurance programs for all government employees. The NIH cannot negotiate its own rates/programs for its employees.

—Marvene Horwitz, OD

On safety and security at NIH

I realize that NIH must respond to the recent Building 37 incident quickly and responsibly. I also realize that many lab workers take the privilege to use isotopes for granted. However, the new rule requiring all rooms that are posted for radioactivity use be locked whenever unattended has made a safe situation unsafe. Here is an example. Consider the situation in which a postdoc working in one room, alone, has a sequencing gel that needs to be dried on a gel drier in a second room. After preparing the gel to be dried he now has to carry the wet gel—this takes two hands—to the second room. But when he leaves his room, he has to lock it (with his third hand?) and potentially unlock the room with the drier (removing his key from his pocket with his potentially contaminated third hand). Upon returning to his own room, he now has to reach into his pocket again to open his room! To expose this gel to film, he now has to juggle a box of film and a large cassette (or several) and close the door (with that third hand again) and again reach into his pocket for his key to open the door to the lab with the darkroom. A formerly simple situation has become very unwieldy.

A much more dangerous situation at NIH is the lack of adequate safety precautions for the numerous hazardous chemicals and carcinogens. While we are all required to take radiation-safety courses and refresher courses, there is not a similar requirement for chemical hazards. You can detect exposure and spills of radioactive compounds relatively easily—not so with many very dangerous chemicals.

—Anonymous

On Dec. 1, the Nuclear Regulatory Commission approved a modification to NIH security policy that will make lab life a little easier. The modification allows researchers to leave posted rooms unlocked provided that no radioactive materials are in use and no radioactive waste or unsecured radioactive materials are present in the room. Concerning your second point, all NIH staff who work with hazardous chemicals or blood-borne pathogens are, in fact, required by law to take safety training in these areas. Courses are offered monthly. To obtain dates and an application form for the next courses, contact the Occupational Safety and Health Branch (phone: 496-3353; fax: 402-0313).

—Michael Gottesman, DDIR

On NCI's new leadership

Many members of NCI's professional staff have really picked up on Klausner's quote in this [September–October] issue: "It is no secret that it [the NCI] has not been a place where people have uniformly loved to work ... . It tended to be an institution run by fiat and fear." Although Klausner did not dwell on the details of this statement, the Oct. 20 edition of the *Cancer Letter* did. This report summarizes numerous investigations into the conduct of the very top managers of the "Old NCI," including pre-trial deposition of same [in connection with NIH's treatment of Principal Investigator Bernard Fisher after revelations of fraudulent data in the NSABP Breast Cancer Trials]. ... Klausner's "fiat and fear" quote indicates that he understands that, to greater and lesser degrees, the entire management of the "Old NCI" has been given (and in many instances have taken) the "fiat and fear" management style as their premier institutional administrative model. What steps is Klausner taking to guarantee to the professional staff of the "New NCI" that the old "fiat and fear" formula for research excellence and integrity failure will not creep back into our institutional culture?

—Henry Stevenson-Perez, NCI

On postdoc concerns

The want ads in recent issues of *Science* say a lot about the extramural community's perception of postdoctoral positions at NIH. There, emblazoned in black and white across the top of an entire page, is "Post-Doctoral Opportunities at the National Institutes of Health." NIH has tremendous resources and there is a glut of Ph.D.s. So why does NIH need to advertise for postdocs? Ten years ago, an NIH ad for postdocs was unheard of. Most new Ph.D.s wanted to work at NIH, but now, they don't. What's happened? The answer is quite simple. ... Postdocs are flocking to institutions that can get them into the best jobs as soon as possible, and NIH ain't one of them. Many senior NIH officials state that the new tenure-track policy scares postdocs away. Forget the new tenure-track policy—it means little to postdocs. Most fellows know that it is extremely rare to land a tenure-track position at the institution where you were a postdoc, so any tenure-track-policy changes are irrelevant. The negatives to being a fellow at NIH are as follows:

1) It is becoming increasingly difficult to land a tenure-track position in academia with five or fewer years of postdoctoral experience. It is necessary to develop some sort of name recognition within a field and, generally, five years is far too short a period to develop such recognition. The current policy of limiting fellows to five years, with a few exceptions, basically throws the fellows out the door before they are

competitive for the best jobs in the extramural environment.

2) The current tight funding levels make grant-writing skills extremely important. A mentor who is very successful at obtaining funding can be an invaluable resource for a fellow writing his or her first grant. ... Most senior NIH scientists have had very little experience applying for NIH grants, and courses on grantsmanship do not substitute for actually going through the ordeal a few times before you are on your own.

3) Because of the tight funding situation, many universities are requiring their departments to hire only new faculty who already have grants. ... Thus, an NIH fellow has fewer job opportunities than an extramural postdoc.

These three problems make NIH a very unattractive place to do a fellowship... . Any intelligent grad student considering postdoc positions will take these factors into account and consider NIH a less than optimal place to obtain postdoctoral training. And any mentor who has his or her graduate students' best interests in mind will steer them away from NIH.

What solutions can I offer? The first step would be to establish an NIH equivalent of academia's research track by setting up renewable, limited-term contracts. After five years of postdoc work, a talented young scientist could be offered a five-year contract ... . At the end of the five years, the scientist would be reviewed by a group of intramural and extramural scientists, and if his or her work has been of sufficient quality, the contract can be renewed. This procedure could be repeated indefinitely, until the scientist lands a more stable position or until his or her work begins to falter. This process would allow young scientists to develop some name recognition and to demonstrate that they are capable of doing independent research.

Second, NIH needs to set up a system for NIH fellows to apply for grants through NIH. It is important that the application process and the review process be identical to what extramural scientists endure. This is to ensure that the funded intramural applications are indeed competitive with funded extramural applications. To preserve harmony with the extramural community, successful intramural applicants' grants could be funded from intramural funds. Given the current low level of funding, this should not cost the intramural program very much. Successfully funded intramural scientists could then use the money to obtain academic positions. If NIH would establish such mechanisms, it could again attract the best young scientists in the country.

—Robert Caudle, NIDR

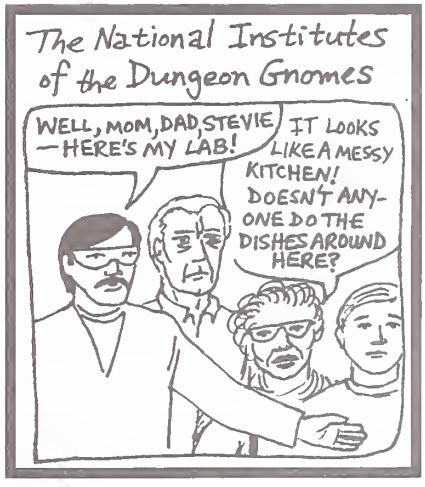
I applaud the creativity shown in the ideas that you suggest to improve the career prospects of NIH postdoctoral fellows, but must take exception to some of the conclusions you reach in your letter. NIH continues to attract the world's best postdocs; two of the four winners of the 1995 Pfizer awards for best thesis research are fellows at NIH. We have a vast excess of applications over postdoc positions available. The reason we advertise is to be sure that the opportunities at NIH are known to all qualified individuals. The best tenure-track positions in academia go to scientists with less than five years of postdoctoral experience and no independent research support; too many years in one institution without a long-term commitment increases, rather than decreases the difficulty of finding a good job, hence, our five-year limit on NIH postdoctoral experience.

—Michael Gottesman, DDIR

On the Dent cartoon

I am absolutely appalled by the cartoon and its implications. I can assure you that the M.D. researchers in my section in Building 37 do not have more or qualitatively "better" space than the Ph.D. researchers. If you examined the space allotment in Building 10, where there is a higher density of M.D. researchers than Ph.D.s, there does not appear to be an excess of space. Rather than emphasizing the potential bases for divisions between different segments of the NIH community and potential sources of combustion, I would prefer *The Catalyst* to catalyze synthetic reactions.

—Edward Sausville, NCI



I found the cartoon to be pretty sexist in nature. The last thing I expected to see circulated among NIH intramural scientists—who have been accused of sexist attitudes in the past—is a cartoon in which a woman visits a laboratory and says, "It looks like a messy kitchen! Doesn't anyone do the dishes around here?" I mean, *really*.

—Jaylan Turkkan, NIDA

Since I first saw it, I have been annoyed by what I perceive as the whiny tone and essential lack of humor in the comic strip about postdocs. I know how badly Ph.D. postdocs are treated at this and other institutions from having a spouse who was one and having spent several years in graduate school myself. However, the strip dealing with issues of space has finally caused me to set finger to keyboard. If Dent thinks Ph.D.s have less space than M.D.s, he is grossly mistaken. Clinical fellows are routinely packed into what are essentially library carrels or less. I am an M.D. with tenure who has been here for going on seven years. I have a quarter of a module to call my own. It makes meeting with visitors, frankly, embarassing. (Of course, the sweaty bike clothes and piles of food don't help either.) It appears to me that it is administrators who have more (and nicer) space than anyone, relative to rank, but would any of us trade places?

Ph.D. postdocs have plenty to complain about; that's not at issue. Rather, I suggest that discontent be expressed in more constructive and less divisive terms. If Dent wishes to question the difference in status between M.D.s and Ph.D.s in society at large, let him do so. I think there would be much sympathy from M.D.s (many of whom are also Ph.D.s) at this institution, but let's not fight each other over what are, after all, pretty meager spoils.

—Eric Wassermann, NINDS ■

ETHICS IN PEER REVIEW: A SCENARIO TO CONSIDER

In the spirit of Valentine's Day, this is the story of Dr. Red and Dr. White. Red's paper was submitted to *Journal V*. *Journal V* sent it to White, who reviewed it carefully, shared it with members of his lab, identified a problem, suggested that appropriate changes be made before the paper was accepted, and asked to see the revisions. At the time of the review, White's group was in the very early stages of research that was similar to Red's. White subsequently submitted a paper to *Journal L* with results essentially identical to Red's. White's paper did not cite Red's publication in *Journal V*.

It is increasingly evident that there is little love lost between researchers over scenarios like this one. Ethics in the peer-review process is an increasingly critical—and volatile—element in the culture of science. In this column, the NIH Committee on Scientific Conduct and Ethics would like to ask intramural scientists to debate our Valentine's Day scenario and consider the following questions. Should White have reviewed Red's paper, or returned it immediately, based on conflict of interest? Should White have shared Red's paper with his lab? Should White have cited Red's paper? As a reviewer, what would you have done? What action should Red take now, if any?

Send us your best responses (e-mail: catalyst @od1em1.od.nih.gov). We will publish representative and informative responses in a future column. Readers are also encouraged to suggest topics for future Ethics Forums. ■

A HUNT FOR HISTORY: LOCATING NIH'S "LOST" ARTIFACTS

by Victoria A. Harden, Ph.D., NIH Historian

After more than a century of existence, NIH almost certainly has many objects of historic importance. The problem is that no one knows exactly how many such objects exist—or precisely where they are. A new inventory being conducted by the NIH Alumni Association should provide a unique chance to register NIH's historic artifacts and protect them for future generations.

Under a contract with the NIH Historian's Office, the alumni group is launching a six-month effort to identify and label artifacts of historic importance to NIH. Because a major part of that effort involves locating objects relating to the intramural program, all investigators and support staff are asked to be on the lookout for potential historic items within their institutes and to alert the Alumni Association to them.

Over the past few years, the NIH historian and other staff of NIH's DeWitt Stetten, Jr., Museum of Medical Research, a museum without walls that has exhibits in the Clinical Center, Building 1, and Building 31, has grown aware of the apparent loss of several historic artifacts. In May 1994, the museum was granted authority to identify, label, and protect objects of historic importance. Subsequently, a contract was awarded to the Alumni Association to inventory and label existing historic objects throughout NIH.

The goal of the project is *not* to disturb or move the historic objects, but simply to identify and label them. The labels will alert anyone who may be considering discarding such objects that they are of historic importance and should be sent to the Stetten Museum rather than thrown away. Objects that anyone wishes to donate now will be reviewed by the museum's Collections Committee for possible acquisition.

The range of objects and memorabilia to be identified is broad. Examples include building cornerstones, memorial plaques, sculptures, busts, portraits, gifts to NIH or an institute, awards to NIH or an institute, photographs in which individuals and the date of photo are indentified, time capsules and their contents, historic clothing worn in labs, other historic laboratory fixtures or equipment, blueprints of building floor plans, and architectural models. No personal property of NIH personnel will be included unless voluntarily offered and appropriate, such as high-level awards for work done at NIH.

In general, scientific instruments are not included in this project. Any instruments with possible historic value should be offered directly to the Stetten Museum. Documents—letters, memos, laboratory data, notebooks, and the like—are also not included because they are the subject of a separate intramural records study being conducted in conjunction with the National Archives and Records Administration.

To facilitate the new effort to inventory historic objects, NIH Deputy Director Ruth Kirschstein has asked each institute, center, and division (ICD) director to appoint a contact person for the Alumni Association. The alumni group, in turn, has organized volunteers to take responsibility for each ICD. These volunteers will locate objects through discussions with a variety of institute personnel—both current and retired—and through physical inspection of facilities. Because many objects may be in storage or even located off-campus, staff should direct alumni representatives to the locations of important items. At the end of the project, a list of the historic objects will be generated, maintained, and updated by the NIH Historian's Office.

Questions about the project should be directed to Richard Seggel, chair of the NIH Alumni Association's historical committee (phone: 301 424-6449). ■

THE INTEREST GROUP GAZETTE

From Alzheimer's disease to zebra fish, NIH's interinstitute interest groups are continuing to extend their reach into nearly all realms of biomedical research. In the past few months, at least six new groups have sprung up to meet the seemingly boundless interests of the intramural research community.

Founded by a group of staff scientists at NCI in Frederick, the **Cellular and Molecular Biotherapy Interest Group** held an initial organizational meeting on Dec. 13. The group discussed ways of exploiting novel clinical findings at the basic research level, as well as ways of translating basic biological observations into clinical trials. The group plans to hold periodic seminars featuring intra- and extramural speakers, as well as an intramural retreat to foster the exchange of information about cellular and molecular biotherapy. For more information, contact John Ortaldo (fax: 301 846-1673; e-mail: ortaldo@nci.fcrf.gov). Please include your e-mail address and/or fax number.

Organizers of the **Alzheimer's Interest Group** held an initial meeting on Dec. 7 to discuss the scope of their scientific interests in Alzheimer's disease as well as the format, frequency, time, and location of future meetings. The interest group will meet on the first Thursday of each month (or the second Thursday if there are scheduling problems) at 9:00–10:00 a.m. in Bldg. 36, Rm. 1B13. The hour-long meeting will consist of original scientific presentations, discussions based on journal articles, and/or a general discussion on a specific topic. For more information, contact Gerald Ehrenstein at NINDS (fax: 496-8765; e-mail: gerry@helix.nih.gov). Volunteers interested in giving presentations and suggesting topics are asked to respond by e-mail.

Another newcomer, the **Breast Biology Interest Group (BBIG)**, kicked off its meeting schedule on Oct. 23 with presentations on cell-cycle regulation of BRCA1 by NCI's Jean Gudas and on molecular characterization of human premalignant lesions by NCI's Pat Steeg. The group, formed by NCI researchers to foster increased collaboration and cooperation among the many Washington-area scientists and clinicians interested in breast carcinogenesis, plans to meet on the fourth Monday of each month at 3 p.m. in Bldg. 10, Rm. 13S235B. Please note that the number posted outside the room is mistakenly labeled 13"F"235B. For more information, contact Steeg (phone: 496-9753; e-mail: steeg@helix.nih.gov), JoAnne Zujewski (phone: 402-0985; e-mail: ajueski@nih.gov), or Ken Cowan (phone: 496-4916; e-mail: khc@helix.nih.gov).

Jaylan Turkkan of NIDA's Office of Behavioral and Social Sciences Research, in conjunction with the Health and Behavior Coordinating Committee, held a meeting on Dec. 15 to form the new **Behavioral and Social Sciences Interest Group.** Attendees discussed how the interest group can help coordinate research efforts not only within the intramural program, but also in the extramural program. For more information, contact Turkkan (phone: 443-1263; e-mail: jaylan@helix.nih.gov).

A newly formed **Cytokine Interest Group** is open to NIH staff whose research involves cytokines, lymphokines, chemokines, interferons, and growth factors. The group will sponsor four microsymposia per year, three on the Bethesda campus, and one in Frederick. The first symposium, focusing on TGF-ß, will be held on the Bethesda campus on Feb. 20 in the Natcher Building's auditorium, and a second symposium, focusing on chemokines, is scheduled for the spring and will be held in Frederick. A database of group members, including information about their research areas, is being generated and will be made available to the NIH community. NIMH's Mark Doherty and Roel de Rijh are also heading efforts to build a home page for the interest group on the World Wide Web—a page that should be accessible sometime in January. To join the group or get more information, contact Howard Young at NCI (e-mail: youngh@ncifcrf.gov) or Alan Sher at NIAID (e-mail: asher@box-a.nih.gov).

The **Human Retrovirus Interest Group** will meet on the third Wednesday of every month from noon to 1 p.m. in the Natcher Bldg., Conference Rm. B. Discussions will focus mainly on events in the nuclei of infected host cells, such as integration, transcription, and splicing. For more information, contact Fatah Kashanchi at NCI (phone: 496-0987; fax: 496-4951; e-mail: kanshancf@dce41.nci.nih.gov). ■

—Lorna Heartley

PIPETS AND PATENTS

The impact of recent developments in patenting and licensing on molecular biology research will be addressed at a workshop at the National Academy of Sciences in Washington, D.C., on Feb. 15–16.

Organizers of "Intellectual Property and Research Tools in Molecular Biology" are particularly interested in getting the opinions of rank-and-file researchers because much of the action in this controversial realm has been dominated by the legal and commercial worlds. As a starting point for discussion, the workshop will consider a group of case studies, including the controversy over the patents for the polymerase chain reaction (PCR) and expressed-sequence tags (ESTs). There will also be comments from scientific and technology-transfer leaders.

The workshop is co-sponsored by NIH, the National Research Council, the Institute of Medicine, the Academy-Industry Program of the National Academy of Sciences, and the National Academy of Engineering. If you wish to attend or want more information, contact Jeff Peck (phone: 202 334-2483; e-mail: jpeck@nas.edu). ■

SAY "HI" TO THE SCIENCE GUY

Bill Nye the Science Guy, who hosts a popular children's television program on PBS, will be meeting with NIH's own science guys, gals, and kids on March 26 at 6:30 p.m. in Natcher Auditorium. As part of his ongoing effort to get the American public more excited about the scientific process, Nye has expressed interest in doing more TV segments on the biomedical sciences. "If we don't have a scientifically literate society, this is a formula for disaster," Nye says. Before the March 26 program, Irene Eckstrand, director of the Office of Science Education, hopes to introduce Nye to some intramural scientists and show him some interesting research projects on NIH's Bethesda campus. For more information on Nye's talk, which is open to the public, contact the Office of Science Education (phone: 402-2469). ■

GCG-Lite: A Web Interface to the GCG Sequence Analysis Package

The past year has seen the coming of age of the electronic information era with the exponential rise in the popularity and functionality of the World Wide Web. Although accompanied by considerably less fanfare, the ability of the Web to provide a universal interface to many computational tasks has ignited a revolution in scientific computing. One area that has been affected dramatically by this revolution is the field of DNA- and protein-sequence analysis.

Taking advantage of this newfound power to connect many types of computers across many types of computing platforms, I have recently developed a Web interface to give NIH researchers better access to what many regard as the industry standard for sequence-analysis software, Genetics Computer Group Inc.'s GCG Wisconsin Sequence Analysis Package. This interface, called GCG-Lite, provides intramural scientists with rapid, easy access to a powerful set of computational tools running on centrally maintained, high-performance computers.

Pre-Web Options

In the "pre-Web" world, a scientist had two main choices when it came to sequence analysis: local computing or central computing. Both options had pros and cons. The local computing approach typically involved evaluating, purchasing, installing, and running a sequence-analysis package on local, desktop computers, typically a personal computer (PC) or Macintosh computer. The main attractions of the local computing option were the relative ease of use of such programs. However, these benefits were often offset by the limited computational power available on desktop computers, combined with the need to continually maintain and update the software and associated databases. Additionally, because of significant costs and restrictive licensing, such software has generally been accessible only through a subset of computers available to research staff, resulting in bottlenecks and competition for the "analysis computer." The second approach—the central computing option—has traditionally presented a less user-friendly environment than the desktop computing model, requiring operational knowledge of a telecommunication package, the UNIX operating environment, and the GCG software itself. However, this model *has* proven adequate in addressing the needs of many in the NIH sequence-analysis community. The attractiveness of central management of software and databases, the functionality of the software, and the computational power of a large UNIX-based machine have generally offset the hurdles presented by the user interface. In fact, during the past year, more than 650 intramural researchers have used the GCG sequence-analysis software running on the DCRT-maintained, UNIX-based Helix system. The local and central computing options are not mutually exclusive, however, and many NIH labs have opted for some combination of both.

Best of Both Worlds

With the introduction of the Web interface to sequence-analysis software, biomedical scientists may now more easily avail themselves of the "best of both worlds." A brief tour of the Internet, starting at the Web page found at the uniform resource locator (URL) http://molbio.info.nih.gov/molbio/ leads to a wide array of sequence-analysis tools, including NIH's own GCG-Lite.

Before delving into the details of GCG-Lite, let's briefly review the features of the complete GCG Wisconsin Sequence Analysis Package. Consisting of more than 120 individual analysis programs, the full GCG software package is typically operated from the command-line on a central system or via the X-Windows graphical interface. Additionally, each GCG analysis program comes with an extensive array of optional command parameters that, although very powerful in the hand of an expert, are daunting to the less-experienced user.

To create a Web interface to a subset of GCG's impressive suite of sequence analysis programs [see box], I wrote a collection of programs and hypertext markup-language (HTML) forms, dubbed GCG-Lite. The new interface can be reached by using a Web browser program to access the NIH Home Page, which is located at the URL http:///www.nih.gov/ and then sequentially clicking on the links to Scientific Resources and Molecular Biology. For a more direct route

What Can GCG-Lite Do?

GCG-Lite

- Text-word database searches for DNA and protein sequences
- Restriction-enzyme-site identification
- DNA-to-protein translation
- PCR-primer prediction
- Protein-to-DNA backtranslation
- Protein-isoelectric point (pI) prediction
- Identification of protein motifs within a protein sequence
- Protein-structure prediction
- Prediction of protease-digestion patterns
- Graphical dot-plot comparison of two DNA or protein sequences
- Local or global homology comparison of two DNA or protein sequences ■

by Peter FitzGerald, Ph.D., DCRT
(e-mail: pcf@helix.nih.gov)

to GCG-Lite, go straight to the following URL: http://molbio.info.molbio/gcglite/

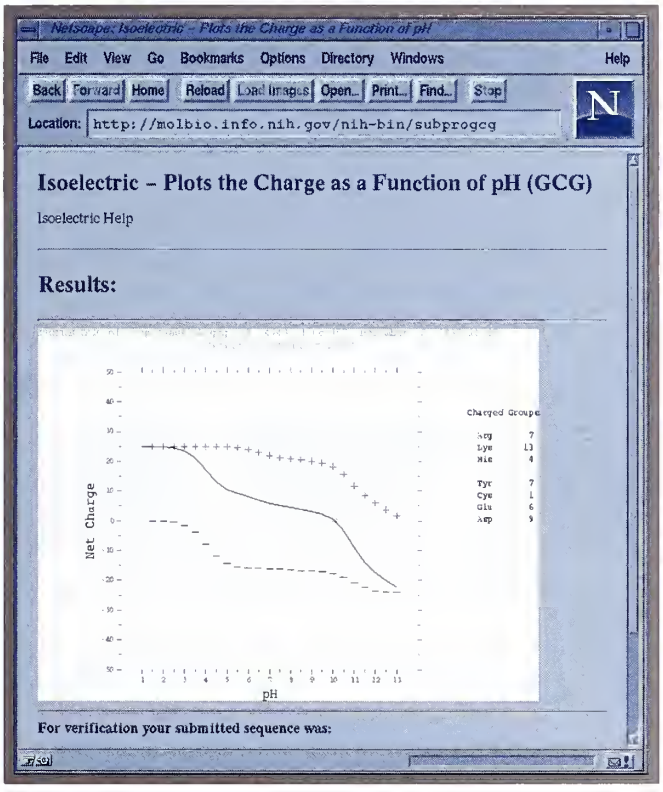
Advantages

Perhaps the foremost of GCG-Lite's features is the ease of access by NIH researchers. As a Web-based application, GCG-Lite provides a uniform interface to anyone with network access, regardless of the type of computer they use, be it Mac, PC, or UNIX work station. In developing GCG-Lite, I took into account the way NIH researchers have used the full GCG package on the Helix system over the past few years. For example, feedback from the scientific community prompted the creation of both novice and expert modes for all analyses. In the novice mode, the user simply provides a sequence, selects an analysis function, and launches the analysis. In the expert mode, the user has more control over certain parameters that may affect the analysis. By incorporating the sequence-format translator, "readseq," developed by D.G. Gilbert of Indiana University in Bloomington, GCG-Lite is capable of accepting a wide variety of input sequence formats. Additionally, because sequence input and formatting is inherently an error-prone procedure, all GCG-Lite output includes a copy of the sequence analyzed, thus providing a check of data integrity.

Analysis functions that display data as graphs have been notoriously difficult for researchers to use effectively through the regular GCG command-line interface. In contrast, GCG-Lite takes advantage of the multimedia-handling capabilities of Web browsers to support the output of graphs in both GIF and Postscript formats.

Limitations

GCG-Lite does not provide access to the complete set of GCG programs. Thus, scientists who require access to many of the less popular but powerful features of GCG are still best served by the full GCG package. In addition, it should be remembered that GCG-Lite's functionality is largely determined by the operation of the Web browser—and few of today's browsing programs operate correctly in *every* situation. That means researchers can only expect GCG-Lite to function as well as the Web browser they are using.



An example of graphical output from GCG-Lite showing the predicted change in charge of a protein sequence as a function of pH.

To Use...

GCG-Lite's set of sequence-analysis tools should be particularly attractive to researchers who have not learned to use the full GCG software on the NIH Helix computer or those who seldom use sequence-analysis programs and are thus likely to forget the appropriate syntax necessary for using GCG on Helix. In addition, all intramural scientists involved in DNA- and protein-sequence analysis should be attracted to GCG-Lite because of its ease of use, especially the way it enables a researcher to readily view the results of altered program parameters and to produce graphs.

...Or Not to Use?

Among the researchers who are the least likely to find GCG-Lite useful are those who are already familiar with the command-line interface of the full GCG software, who are comfortable in the UNIX operating environment, or who require access to the GCG analysis modules not incorporated into GCG-Lite. Furthermore, scientists who rely on the data-management and -integrity features provided by the full GCG software operating on Helix should be aware that GCG-Lite does not provide those features because it is purely an interface to analysis functions.

Unlike many Web applications, GCG-Lite is not generally accessible to the greater Internet community. To comply with GCG software-licensing restrictions and internal DCRT policy, access to GCG-Lite is restricted to computer users on the NIH network. In the future, access to this software may be further restricted to researchers with Helix accounts.

Looking Ahead

Future enhancements to GCG-Lite will include the incorporation of additional GCG analysis modules and the expansion of the analysis functions to include software outside the GCG suite. And that's not all. With the predicted improvements in the functionality of Web browsers and extensions to the basic Web protocol, it's reasonable to expect that in the near future, biomedical researchers may be doing most—if not all—of their data analysis via World Wide Web interfaces such as GCG-Lite. ■

Metastasis Model in a Bottle

Fruit flies have served as an invaluable model for deconstructing the genetics of development. The power of fly genetics was recently recognized by the award of the Nobel Prize in physiology or medicine to Edward Lewis, Christiane Nusslein-Volhard, and Eric Wieschaus for work that identified *Drosophila* genes required to establish the body plan of the fly. Many of the genes that were identified in flies by these groups have vertebrate homologs that are also required for development. Could fruit flies be as powerful in helping us understand cancer as they have been in development? In this Hot Methods Clinic, we report on new models that extend the power of *Drosophila* genetics to the field of cancer progression and metastasis.

Current methods for studying metastasis, tumorigenesis, and tumor suppression in vivo generally rely on rodent models. For example, studies of metastasis typically require injection of tumor cells into nude mice, a delicate animal system that requires a large investment of time and upkeep. Comparatively little use has been made of *Drosophila*, one of the best-defined animal models. Although much smaller than more traditional models for metastasis, fruit flies also have tumors, including tumors that metastasize when transplanted from a larval donor into an adult host. By studying metastasis in *Drosophila*, it is possible to do experiments in a few bottles that would otherwise consume substantial resources with rodents. Furthermore, one can take advantage of a large body of genetic techniques and knowledge about *Drosophila* that make it possible to generate mutants, clone genes, and express transgenes with relative ease.

Recent studies in the field of *Drosophila* tumorigenesis and metastasis have shown that this genetic system can provide an excellent means for studying metastasis, as well as tumorigenesis and tumor suppressors. Mutations in single genes in *Drosophila* can cause tumorous overgrowth of the larval brain and imaginal discs—groups of cells in the larva that will give rise to adult structures. The overgrowth is accompanied by the loss of capacity of the brain and imaginal disc cells to differentiate. These tumors are not metastatic in the larva, but when transplanted into adult hosts, they cause large primary tumors which can metastasize and invade host organs. Aided by the introduction of a *lacZ* reporter gene into various tumor mutant backgrounds, we have studied the tumors which form after transplantation. The reporter gene is used to identify the tumor cells after transplantation since none of the adult host cells contain the *lacZ* reporter. Using the reporter gene to follow tumor cells after transplantation, we have been able to study the metastasis of tumorous brain tissue and imaginal discs from several *Drosophila* mutants. Tumors can also form in other tissues of *Drosophila* such as the gonads and hematopoietic organs. Overall, more than 50 tumor suppressor genes have been identified in *Drosophila* (1). Although many of these genes have not been extensively characterized, they open exciting new avenues of research.

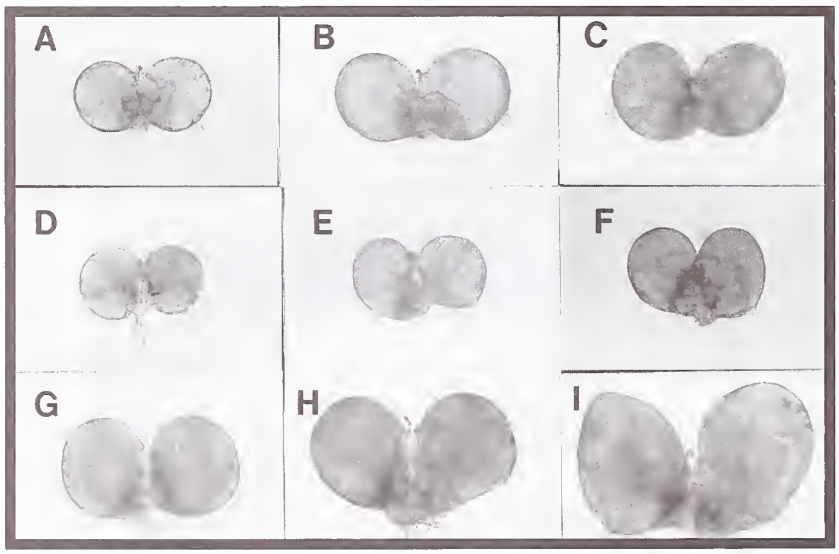


Figure 1. Developmental profile of* lethal giant larvae *brains compared with wild type. *The brains of* lethal giant larvae *mutants overgrow during the extended larval period. The brain lobes were dissected from the ventral ganglion of wild-type (Canton S) and* lethal giant larvae *(lgl) mutant larvae that were grown at 20 °C.* Lethal giant larvae *mutants are hemizygous ($lgl^{l4}/Df(2L)net^{62}$). A) Canton S brain, 5 days of development; B) Canton S brain, 6 days of development; C) Canton S brain, 7 days of development—metamorphosis begins after this point in these wild-type larvae; D) lgl mutant brain, 5 days of development; E) lgl mutant brain, 6 days of development; F) lgl mutant brain, 7 days of development; G) lgl mutant brain, 8 days of development; H) lgl brain, 9 days of development; I) lgl mutant brain, 10 days of development—lgl larvae typically die between day 12–15, without undergoing metamorphosis. All the brains were photographed at the same magnification.*

The Method and How it Works

The general approach of our lab and that of Allen Shearn at Johns Hopkins University in Baltimore is to use *Drosophila* to investigate factors involved in metastasis, as exemplified by our work on the *lethal giant larvae* mutant. Loss of function of the *Drosophila* gene *lethal giant larvae*, which is located on the second chromosome, leads to tumors of the imaginal discs and brain, and death at the late larval stage. The *lethal giant larvae* mutants have an extended larval period during which cells in the brain and discs continue to proliferate and become tumorous. When this brain or imaginal disc tissue is transplanted into adult hosts —for example, by injecting the tissue into a fly's abdomen—it can grow as a primary tumor and metastasize to adult structures.

In 1995, Mechler and colleagues cloned the *lethal giant larvae* gene, and several investigators are now beginning to elucidate its function (2). Recent biochemical studies have shown that the Lethal Giant Larvae (LGL) protein is part of a large complex and that a major component of this complex is nonmuscle myosin (3), suggesting that the LGL protein may be involved with the cytoskeleton. Immunostaining has localized the LGL protein to the cell surface at regions of cell junctions. These results hint that the LGL protein may be part of the signal pathway from the cell surface via the cytoskeleton.

For marking and following the *lethal giant larvae* mutant cells, we used a construct consisting of the *lacZ* gene under the control of the *armadillo* promoter and inserted onto the X chromosome so it can easily be crossed into the *lethal giant larvae* genetic background. Using this marked *lethal giant larvae* line, we transplanted brain tissue into adult hosts. In

by Elisa Woodhouse, Ph.D., NCI,
and Lance A. Liotta, M.D., Ph.D., NCI

addition to the growth of primary tumors in the abdomen near the site of injection, cells metastasized to other regions of the adult hosts. Sometimes these invasive secondary tumors were very small and would have been impossible to identify had they not been marked to differentiate them from the host cells.

This work opens the door to questions about factors involved in metastasis. For example, research we have done with these *Drosophila* tumors on differential expression of specific proteins in the tumor cells have indicated that there are similarities between human tumor cells and *Drosophila* tumor cells in the differential expression of two proteins, Type IV collagenase (4) and Abnormal wing discs (Nm23 in humans) (5), two proteins implicated in the metastasis of human tumor cells. The panoply of drugs, proteins, and environmental factors that may play a role in metastasis and protection from metastasis have barely been tapped for study in fruit flies.

It is likely that by pursuing these genes—or many others in *Drosophila*—researchers will gain new insight into the basic biochemical mechanisms underlying the spread of cancer. The genetics of fruit flies, which are comparatively simple to analyze, provide a way to identify new tumor-suppressor genes or proteins that mediate the invasive phenotype. The fact that tumors can arise due to the loss of function of a single gene in *Drosophila* greatly simplifies the study of these tumors, because *Drosophila* lines that are heterozygous for tumor mutations can be maintained and crossed together to generate homozygous tumorous larvae that would die before reproducing as adults. It is also easy to generate mutations in these lines in addition to the tumor mutations to see whether changes in other genes enhance or suppress any of the properties exhibited by these tumor cells. Identification of genes in which mutations have this kind of effect could be very useful for understanding metastasis. This type of mutation can be generated by P-element-mediated-mutagenesis in which single P elements are mobilized in the genome and insert randomly, causing mutations. Single-P-element-mutagenesis can be done on a large scale and allows for the mutated genes to be cloned relatively easily. This type of genetic screen could lead to the identification of a completely new group of genes which mediate metastasis.

Although *Drosophila* can provide clues to the mechanisms of metastasis, the model has limitations due to fundamental differences between flies and humans. For example, the open circulatory system of the fly means that angiogenic factors that promote tumor growth in vertebrates will not be modeled in the fly. Also, the lack of a highly complex immune system in flies is likely to make *Drosophila* less relevant for probing immune factors affecting tumorigenesis and metastasis. However, despite these limitations, the many functional similarities between human and *Drosophila* malignant tumor cells and the ease of genetic manipulations suggest that *Drosophila* cancer may provide insight into the primordial conserved proteins, or their functional equivalents, necessary for cancer invasion in both *Drosophila* and in humans.

Figure 2. LacZ-*marked* lethal giant larvae *tumor cells injected into the abdomen of a ßgal^{n1} host produced a small primary tumor in the abdomen. Some of the cells from the primary tumor metastasized to the thorax, where they proliferated, forming a large secondary tumor that fills the thorax.*

Protocol

Researchers interested in obtaining *Drosophila* stocks should contact the Bloomington Stock Center (e-mail: matthewk@fly.bio.Indiana.edu). Information on basic techniques for working with *Drosophila* is contained in two books by Michael Ashburner (6,7).

1. *Drosophila melanogaster* strains are constructed that have a mutation that causes the formation of tumors (e.g., *lethal giant larvae* on the second chromosome) as well as a reporter gene that expresses ß-galactosidase in all cells (e.g., a construct consisting of the bacterial *lacZ* gene under the control of the *armadillo* promoter, which has been inserted onto the X chromosome).

2. Five to eight of these female *Drosophila* are mated and allowed to lay eggs in a vial for one day. Larvae are grown at constant temperature until a late stage of development when the brains are overgrown (11 days at 20 °C for *lethal giant larvae* mutants). The brains are dissected from the larvae in phosphate buffered saline solution (PBS).

3. The two dissected brain lobes from each larva are cut into quarters. Each quarter is then transplanted into an adult host. The tissue is injected into the abdomen of the host with a glass needle. The adult hosts should be from a *Drosophila* strain lacking endogenous production of ß-galactosidase (*ßgal^{n1}*). The lack of ß-galactosidase in the hosts simplifies interpretation of results since only tumor cells will produce ß-galactosidase.

4. After incubating the cells by growing the host flies for 10 days at 25 °C on standard cornmeal, molasses, and yeast medium, the hosts are dissected along the ventral midline and fixed in 3.7% formaldehyde in PBS for 10 min. After fixation, the hosts are washed for 5 min in PBS and then stained with 0.2% X-gal for several hours. After staining, the hosts are washed with PBS. Blue staining will identify distant metastases in the hosts. For detection of invasive tumor cells, the hosts can be sectioned and stained as described. ■

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LAND OF MILK AND HONEY?
continued from page 1.


Rebecca Kolberg

Yun-Bo Shi

more peaceful, prosperous nations find themselves amazed by the resources that the United States devotes to biomedical research. NICHD's Hiroshi Ohno, an M.D.-Ph.D. who came to NIH from Japan on a postdoc 18 months ago, says that due to the combined pressure of relatively low funding and high costs of reagents and equipment, Japanese labs often try to save money by buying reusable pipets and glassware—glassware that must be washed by the researchers themselves. "Here (in the United States), scientists use more disposable materials because they want to use their time to do experiments, not to wash glass," Ohno says. Jolanta Redowicz, who left Poland four years ago for a postdoc at NHLBI, says that due to tight funding, her lab at the Nencki Institute for Experimental Biology in Warsaw had to plan most of its experiments out in detail nearly one year in advance to ensure that they would receive the needed equipment and reagents in time. "I was shocked at how fast you could get reagents here," says Redowicz, adding that because of low pay, most Polish biologists with families either have a spouse working in a higher-paying field or moonlight doing things like selling eggs. "American scientists don't realize how good they have it."

Another aspect of NIH life that many foreign scientists find particularly appealing is a scientific culture that encourages open communication with senior researchers. "I'm not here for the machines—I'm here for the science," says Pierre Savagner, a Ph.D.-D.V.M. who has divided his research time between NIDR and France's Centre National de la Recherche Scientifique (CNRS). "I especially like that the communication is direct and easy. Traditionally, there's been more distance among French scientists, although that's been changing over the last 10 years."

Despite their enthusiasm for NIH resources and the American approach to scientific communication, most foreign scientists are quick to acknowledge that they've encountered a few cross-cultural bumps along the pathway to becoming productive NIH scientists, with language ranking at the top of the list. "One of my big problems is English. ... Many Japanese postdocs have a complex about their language," says Ohno, adding that communication is further complicated by the fact that while most Americans value straightforward expression of thoughts and feelings, Japanese are taught not to express personal thoughts or desires.

NHLBI Scientific Director Edward Korn, who has had numerous foreign scientists in his lab, beginning with a Turkish postdoc some 42 years ago, thinks many foreign scientists worry too much about their less-than-perfect English. "Language is a problem, but not an insurmountable problem," Korn says. "If someone does good science and organizes their data, tables, and figures in a logical way, it's relatively easy for an American

Just Wondering About J-1s?

The primary visa that allows foreign scientists to come to NIH for postdoctoral training is a three-year Exchange Visitor Program J-1 visa. As recently as 1994, the U.S. Information Agency (USIA) routinely granted extensions to visiting scientists to extend their J-1 visas to five years—or the maximum of six years—so that they could complete their training. Suddenly, in 1995, USIA pulled the rug out from under NIH's foreign training program and refused to grant most requests for J-1 extensions.

"This is unacceptable," says Deputy Director for Intramural Research Michael Gottesman. "We allow American citizens up to five years to complete a postdoc here. It is not reasonable to expect all of our foreign scholars to complete their training in three years." Gottesman and Associate Director for Intramural Affairs Philip Chen jumped into action last summer, meeting with USIA officials and, with encouragement from that agency, drafted a Memorandum of Understanding that would delegate to NIH the authority to extend NIH's foreign trainees J-1 visas to five years, or infrequently, to six years. The document was drafted and sent to USIA less than a week after the August meeting.

Unfortunately, in ensuing months, USIA continued to deny essentially all J-1 extension requests from NIH. On Dec. 13, Gottesman and Sylvia Funk—the Fogarty officer responsible for NIH's Exchange Visitor Program—again met with USIA officials and discussed steps that could be taken to alleviate the current situation. "We have not yet received the final word from USIA," reports Gottesman. "We hope to hear in early 1996."

On another front, Congress is expected to take up again in 1996 immigration legislation that may have multiple ramifications for NIH's ability to hire senior foreign scientists. Although an immigration-reform bill drafted by Sen. Alan Simpson, R-Wyo., appeared unlikely to clear Congress in 1995, as *The Catalyst* went to press, political observers expected a similar measure to be introduced this year. The 1995 bill would have required U.S. employers hiring new permanent foreign workers—including scientists—to pay a fee equivalent to 10% of the immigrant's annual wage and benefits into a training fund for U.S. workers. A similar piece of legislation introduced in the House in 1995 by Rep. Lamar Smith, R-Texas, would have also eliminated the "outstanding researchers" designation that exempts senior scientists from the requirement that employers prove that no U.S. workers are available for such jobs. The Senate bill would also make it easier for NIH to hire foreign scientists as nonimmigrant temporary workers on H-1B visas by requiring only that they be paid a salary that is competitive with similar research institutions, rather than one that is competitive with the private sector, as is currently required. ■

—C.H. and R.K.

mentor to help them turn it into a good paper. Besides, many American scientists don't write all that well, either." For those foreign scientists who would like help in fine-tuning their language skills, the Foundation for Advanced Education in the Sciences (FAES) offers courses on comprehending and speaking American English and writing a scientific manuscript (see box, page 13).

Edward Korn

Other difficulties confronting many foreign scientists include the intricacies of getting a family settled, figuring out pay and benefit policies, and trying to iron out visa problems. At NIH, the John E. Fogarty International Center (FIC) is the place where foreign scientists can turn to for help on many such matters (see box, page 13). "Our concern is to make the entry of all foreign scientists into NIH as smooth as possible. ... American scientists should be sensitive to the toll of making such a transition," says FIC Director Philip Schambra, who is no stranger to such transitions, thanks to a postdoc he did at the Institute for Radiobiology in Karlsruhe, Germany, in the early 1960s.

Before a foreign scientist arrives at NIH, he or she receives a packet of information from FIC that covers everything from specific details about their visa status to what to do in the event of a lab injury, along with a handbook that provides information on such mundane matters as banking, apartment hunting, transportation, child care, and even shopping malls. "If people want to be happy when they come here, they have to want to discover the place. If they are only coming to get papers, they will be very unhappy," says Savagner, who counts majestic trees among the benefits of living in Bethesda as opposed to his native Paris. Besides FIC, other organizations that help to equip foreign scientists and their families for such "exploration" include the NIH & NOAA Recreation and Welfare Association (R&W), the International Women's Group, and various nationality-based groups (see boxes, page 14, 15).

When people of different cultures share the same workplace, there is the potential for discrimination on the basis of those cultural differences, as was highlighted by the NIH Diversity Conference on Oct. 25–27. But none of the intramural scientists interviewed for this article reported encountering such discrimination at NIH. "I have found American scientists to be very nice. One reason is that I think they are used to having postdocs from the outside," Ohno says. "In the reverse situation—if American postdocs came to Japan—I think it would be more difficult than it is for me here." Bentzi Katz, who came to NIDR for a postdoc two years ago from Israel, finds NIH's international atmosphere a source of pleasure rather than friction. "I've learned not just about life here in the United States, but because of the wide variety of cultures and nationalities in the lab, I've learned a lot about life in Europe, Japan, around the world," Katz says. "Sure, we discuss science. But we also discuss politics and culture and current events."

Lorna Hearfiey

Pierre Savagner, left, Bentzi Katz, and Sasha Zivkovic

At a recent meeting, some members of The NIH Fellows Committee expressed concerns that foreign postdocs and clinical associates may be being held to tougher standards than their American counterparts. However, all of the foreign scientists that *The NIH Catalyst* talked with expressed the opinion that internal pressure rather than external coercion is what motivates some foreign scientists to spend long hours in the lab. Xufeng Wu, a native of Shanghai, China who got a Ph.D. at Johns Hopkins University in Baltimore before coming to NHLBI two years ago, says: "Some Chinese, especially those who come directly from China, think they have to work harder to compete with other scientists. ... Because they have a language barrier and can't express themselves well, the only way they have to express themselves is to work hard." NIDR's Katz also notes that many postdocs, including himself, are driven by the desire to return to their homelands as soon as possible.

"Everything takes longer for many foreign scientists," reflects NHLBI's Rhee. "Things that are simple for American scientists, like reading and sending e-mail, can take a lot longer for people who don't have good English. And when it comes to writing manuscripts, many foreign scientists really suffer." NICHD's Shi says that another reason that foreign scientists tend to work longer hours than U.S. researchers is that "other than work, they may have few things to do" because they are in a new environment with a different cultural background and are often not accompanied by family members. He observes that scientists who come with their families and who have been in the United States longer generally are less obsessive about their work because of their outside interests and social obligations.

Recently, with the heightened competition for tenure-track academic jobs in the United States, some members of the U.S. scientific and political communities have expressed concern that the growing numbers of foreign graduate students and postdocs who are coming to America for training may stay, taking jobs away from young U.S. scientists. But NHLBI's Rhee emphasizes that the need or desire for foreign scientists to stay—or even train—in the United States can change quickly, and the scientific opportunities in foreign nations can be increased by pioneers

trained at NIH. When he came to the United States from Korea in the late 1960s to get his Ph.D., Rhee says it was impossible to train for or conduct a biomedical research career in Korea due to economic conditions. Although things were beginning to improve in the late 1970s, Rhee chose a tenured position at NIH over top universities in Seoul because he realized that Korea could not provide the facilities he needed to do world-class research. However, when his first four Korean postdocs returned to their homeland in the early 1980s, they were able to build solid careers in biomedical research and set up labs in which Koreans could earn Ph.D.s before heading off to the U.S. for postdoc training. "My Korean postdocs now all want to return home because the opportunities are better for them there than here. There is no reason for them to stay," says Rhee, adding that, in time, a similar progression may occur in China and other nations where biomedical research is currently a low priority. Indeed, NHLBI's Redowicz reports that in the past couple of years, the biomedical research funding situation in Poland appears to be improving. American biotech industries are setting up operations in Poland and the government has also established a new NIH-style system of research grants with relatively high funding rates for good proposals submitted by scientists at leading research institutions.

Rebecca Kolberg

Jolanta Redowicz

Although NIH certainly has given a lot to foreign scientists and their homelands, America's hub for biomedical research has also received much in return. "Clearly, foreign scientists contribute substantially to NIH's scientific productivity, which is of use to the international scientific community," says NHLBI's Korn. "In addition, foreigners contribute a great deal to the intellectual and cultural environment in the lab. They widen our perspectives." ■

Tenure and Tenure Track: The Case of Foreign Scientists

Thanks to special authorities contained in the Public Health Service Act, NIH can hire the best available scientists for its tenure-track and tenured openings—even if those scientists happen to come from other countries. For example, two of the 26 people granted tenure by the Central Tenure Committee between June 1994 and October 1995 were foreign nationals. Furthermore, 33, or about 16%, of NIH's 201 tenure-track investigators are foreign nationals.

Gaining tenure or being placed on the tenure track does not instantly shift a foreign scientist into the same employment status as his or her American counterparts, however. Until tenured and tenure-track scientists become U.S. citizens—a process that usually takes at least five years after they become permanent residents and receive their green cards, they are still employed under the titles of "visiting associate" or "visiting scientist," rather than as General Schedule (GS) Civil Service employees, who must be U.S. citizens. That situation has created some confusion among scientists and administrators about the status and opportunities for pay increases for tenured and tenure-track foreign scientists. For information on specific cases, contact the Office of Intramural Research (phone: 496-4920). We asked Philip Chen and Richard Wyatt of that office to respond to the following commonly asked questions:

Q: Can a tenured or tenure-track foreign scientist be paid at the same level as a comparable tenured or tenure-track U.S. scientist?

A: Yes. However, pay rates are discretionary within the established ranges for visiting associates and visiting scientists, rather than being taken from a fixed pay table.

Q: Are there any restrictions on the GS level at which a tenured foreign scientist can be brought into the Civil Service system after he or she becomes a U.S. citizen? For example, can a tenured foreign scientist be brought in at GS-15 after gaining citizenship?

A: As you might suspect, Civil Service appointment standards are blind to one's past citizenship. Appointment at GS-15 is based on qualifications.

Q: What should tenured or tenure-track foreign scientists do if they feel they are not being fairly compensated?

A: Speak first to their supervisors, section heads, or laboratory or branch chiefs and—if necessary—to their scientific directors, who have the authority to set pay within certain ranges. Exceptional increases beyond set ranges may be granted by the Office of Intramural Research.

Q: Can a tenured or tenure-track foreign scientist be "promoted" before becoming a U.S. citizen?

A: Basically, yes, in that salary increases equivalent to a grade-level promotion for GS employees may be conferred, following a promotion-review process equivalent to that used for GS employees.

Q: What recognition can tenured or tenure-track foreign scientists be given in lieu of an official promotion?

A: They are certainly eligible for "exceptional" pay increases, if justified by circumstances, and for a wide variety of employee awards. Administrative responsibilities may be conducted on an "acting" basis, pending citizenship and a permanent Civil Service position.

Q: Are tenured or tenure-track foreign scientists offered insurance, retirement, and other benefits comparable to GS employees' benefits?

A: Yes. Because visiting associates and visiting scientists are employed by the federal government, they receive such benefits if their initial appointments are for more than 12 months. ■

NIH's CULTURAL LANDSCAPE
continued from page 1.

the rates for international calls to the friends and relatives you've left behind.

Anecdotal evidence indicates that the foreign-scientist population at NIH has been changing somewhat over time. Thirty years ago, almost all researchers came directly from their home countries to be postdocs or visiting associates at NIH. These days, it seems that more visiting fellows and foreigners with intramural research training awards (IRTAs) are coming, as I did, to NIH postdoc positions from Ph.D. programs in the United States. My move from Kharagpur, India, to Urbana, Ill., was a tremendous cultural shock, but moving from Urbana to Houston to Bethesda proved to be just a minor blip. In contrast, visiting fellows who come directly to NIH from a foreign country may encounter quite a few practical difficulties in their first few weeks.

Given the number of foreign scientists who arrive at NIH each year, it's surprising that the intramural program has no organized system to provide foreigners with some sort of accommodation for the first few days while they recover from jet lag, get all their paperwork processed, and find a place to live. Money can be another problem: many foreign scientists cannot afford to bring in the funds to cover the start-up expenses of rent, deposits, and buying furniture. As newcomers without credit histories, they cannot get short-term loans to tide them over until that first paycheck arrives. Most NIH supervisors are very helpful with practical problems, but it would be nice if new arrivals did not have to be completely dependent on such kindness. It's also surprising that a campus of such ethnic diversity has relatively few associations of foreign scientists compared with college campuses, where every ethnic group seems to have an association to assist newcomers.

Once here, many foreign scientists find themselves in a constant race with the visa clock. Some do want to stay in the United States, but even those who plan to return home are often faced with hard deadlines—and difficult scientific decisions—when their visas run out and bureaucratic red tape stands in the way of the needed renewals or extensions. Even a six-month visa extension could help a postdoc who needs to finish up an experiment or write a paper—a paper that might make a big difference in the job search back home. Federal legislation that would tighten some immigration regulations also makes foreign scientists nervous because they fear that if such initiatives pass, it could be a sign of even more restrictive measures to come [see box, page 10].

Once you become wrapped up in research and start exploring NIH's wealth of scientific opportunities, however, there's little time to worry about anything more than immediate challenges. The seminar listings on each week's "Yellow Sheet" are just one indicator of the high quality of science—and scientists—that are available to foreign researchers at NIH. The NIH Library is a step away, and anything you can't find there is probably two steps away at the National Library of Medicine. Researchers can use on-line databases, journals, reprints, fax machines, and telephones without the incessant funding concerns that preoccupy most labs abroad. There is still some room for improvement, though. Foreign scientists could use more opportunities to make oral presentations, especially because some may not have given many scientific talks in their homelands. Seminars in U.S. labs tend to be more informal and off-the-cuff than in many other nations, and this sort of public speaking takes practice, especially for those unfamiliar with the style.

After a period of adjustment, most scientists settle in at NIH and seem to do quite well in their research careers, whether they remain in the United States or return to their homelands. As for myself, I'm certain that the way my time in Bethesda has helped to polish my research skills—and my squash game—will prove valuable for years to come. ■

Foundation for Advanced Education In the Sciences

Purpose: This nonprofit organization operates many educational and cultural programs at NIH. Many of its services and activities are of interest to foreign scientists.

Membership: Open to NIH employees and other interested people.

Resources: Administers health-insurance plans for foreign scientists and their families, as well as for any NIH scientist who is not otherwise covered. Offers courses on English as a Second Language (ESOL), on writing scientific manuscripts, and, for English speakers, courses on other foreign languages, such as Chinese, French, and German.

Contact: Lois Kochanski, phone: 496-7975; fax: 402-0174. ■

FIC's International Services Branch

Contact: Sylvia Funk

Phone: 496-6166

Location: Bldg. 16A, Rm. 101

Resources: Provides foreign scientists with immigration documentation, a "Handbook for Visiting Foreign Scientists at NIH," and a housing list before arrival. Holds an orientation meeting with each foreign scientist to discuss his or her visa status and NIH policies and benefits. Maintains correct immigration documentation for foreign scientists. Provides new arrivals with a list of NIH scientists from their homelands. Arranges for foreign scientists to attend a seminar on their U.S. tax responsibilities. Offers assistance with any work- or immigration-related problem faced by foreign scientists. ■

Staff and Distaff

by Rebecca Kolberg

It's one thing to move halfway around the world to pursue your own career goals, but it's quite another to pull up stakes and leave your homeland for another person's aspirations. Yet, that is exactly what thousands of spouses and children have done over the years to help foreign scientists realize their dreams of training or working at one of the top biomedical research institutions in the world, NIH.

"It's the wives who make the most sacrifices," says Hiroshi Ohno of NICHD. "The husband wants to come here to study and do research. The kids usually find it easy to adapt and learn English. But sometimes the wives are not good at English and they have to go out [to U.S. stores, schools, doctors' offices] the most."

Lorna Hearlley

Such altruism is no longer the exclusive domain of women. Husbands of female foreign scientists also uproot themselves from jobs and familiar surroundings to help advance their wives' research careers. For example, Mariusz Redowicz is an engineer who stepped down as vice president of a small company in Poland to enable his wife to take a postdoc position in NHLBI's Laboratory of Cell Biology. "He did make a sacrifice for me," says Jolanta Redowicz, who followed the Fogarty International Center's suggestion that foreign scientists arrive at NIH several weeks before their families so they can find a place to live and settle into the lab without family pressures.

Even when their husbands come along, the major responsibility for figuring out how to run a household in America generally falls to female scientists, says Redowicz, who has 2-year-old and 6-year-old sons. "It was a hard struggle," she says, but she takes pride in her domestic accomplishments, such as getting the family's first credit card and renting a car for a vacation trip to Florida.

Easing such burdens—for both foreign wives and female scientists—is a major goal of the International Women's Group, one of the liveliest, and most practical, support groups for foreigners at NIH. "This group helped me survive my first month here," says Mona Albandar, who left her native Norway a year ago so her husband Jasim Albandar could work at NIDR. "I was feeling very lonely being so far away from my family. It was very nice to meet with other women who are all in the same situation." Jane Smith, a recent arrival from England along with her researcher husband Roger Smith, agrees; "This is the best thing to happen to me since I've been here. I look forward to it all week." Although one might think the transition from England to the United States would be a breeze given the common language, Smith finds that many Americans stare at her with a "blank expression" because they can't understand her accent.

At one of the group's weekly coffee hours at St. Luke's Episcopal Church just north of the Bethesda campus, women from Japan, Germany, Algeria, France, England, Sweden, Norway, France, Scotland, and the United States exchanged news while their children checked out the cookies and toys. "Morning coffee is a place where I have to speak English, and that's good for me," says Sophie Normant, who left her teaching job in France just a couple weeks earlier to join her husband Emmanuel Normant, a postdoc at NICHD. Her sentiments are seconded by Miya Ohtsuki, who came to the United Sates a year ago with her husband Toshiho Ohtsuki of NINDS: "I want a chance to speak English and a chance to meet persons from many different countries."

The gathering also gives women a chance to air their pet peeves about American life. "Driving! That's the hardest," says Ohtsuki, while Barbara Wichtroup-Otteken, whose husband Ahlent works at NIAID, could do without Maryland's hot, sticky summers and the inconvenient sprawl of American suburbs.

Some of the women who've put their professional lives on hold to come with their spouses to NIH are using the break in their careers to have a child. Catriona Yeudall, a dentist whose dentist husband Andrew Yeudall came to NIDR two years ago for a postdoc, says she's enjoyed having the time with the couple's 13-month-old son, Scott, and hopes to resume her career when she returns to Scotland. Others, once they get settled in, apply for green cards and start looking for work. Marie-Christine Fournier, who came to Bethesda 1 1/2 years ago from Quebec with her husband NICHD postdoc Stephen Lee, says her involvement in the International Women's Group was a driving force in her decision to go out and get a job as a lab technician at NICHD. "This group really helped me gain self-confidence in an English-speaking environment," she says. ■

International Women's Group

Purpose: To provide support, information, and entertainment to the group's 160 members, who include wives of foreign scientists and female foreign scientists.
Meetings: First Thursday of the month, 8 p.m. Coffee hour, every Wednesday, 10:30 a.m.–noon. Events held at St. Luke's Episcopal Church, on Grosvenor Lane off Old Georgetown Road.
Resources: Publishes a monthly newsletter and maintains a phone list to keep members in touch with each other. Activities include an international cooking club, a baby-sitting co-op, field trips to famous sites in the Washington area, and meetings to learn about international customs such as the Japanese tea ceremony. Provides individual assistance to members who are sick or in need of other help.
Contacts: Mirelle Lapeyre, phone: 301 424-2539; Marie-Christine Fournier, phone: 301 493-6249. ■

JUST ASK!

Lorna Heartley

Celia Hooper

The NIH Catalyst *is experimenting with a new column in which we will attempt to run down answers and solutions to your questions and problems that stand in the way of the efficient conduct of intramural research. Please don't ask us to analyze your data or get more money for your lab, but if you are having trouble tracking down collaborators or otherwise navigating the NIH bureaucracy, Just Ask! Send your questions to catalyst@od1em1.od.nih.gov*

Dear Just Ask:
All scientific papers from NIH have to be read by another NIH scientist before they are sent out to a journal. What's the purpose of this? The journals will peer review the paper, anyway, so why does it have to be pre-reviewed within NIH? Quite often, outside reviewers are more familiar with the subject matter than are other NIH scientists, and in any case, there's no requirement that the NIH reader be in the same field. Most readers seem to only superficially read the paper. And since they are not protected by the anonymity of journal peer review and since papers are traded back and forth between scientists, NIH reviewers would be highly unlikely to make critical comments!

—An anonymous scientist

Dear Anonymous:
We suspect that many senior investigators feel the same way you do. Aside from being a legal requirement for federal workers, publication clearance provides a very basic level of quality control, helps keep supervisors informed, and serves as a checkpoint for a few other procedures. The exact steps vary from one institute, center, or division (ICD) to the next, but the good news is that clearance does *not* have to slow down the publication process significantly.

Just Ask quizzed six scientific directors (SDs) or acting SDs on the review requirement. They agreed that local review is not a substitute for peer review,. but felt that local signoffs—whether by just the SD (the minimal NIH requirement) or by a colleague, a section chief, a lab or branch chief, the SD, *and* the institute director (the maximum requirement for any ICD)—can provide a coarse screen against embarrassing mistakes. For example, such reviews can weed out insulting or inflammatory language or ethical lapses you wouldn't even want journal peer reviewers to see. Beyond this, choosing an expert intramural reader may root out glaring experimental errors or serious omissions in citations, reducing revisions at later stages.

Signoff by supervisors also helps to keep them informed about ongoing work. This is good not only for the coordination of research programs, but also for the author the next time he or she starts thinking about a raise—or more space. Also, some SDs use the publication checkoff as an opportunity to be sure that scientists have followed the rules on authorship and have notified the Office of Tech Transfer of any potentially licensable discoveries, as well as to launch the needed paperwork to recover publication charges, to enter the *oeuvre* in the ICD's annual bibliography, and to give communications offices a heads-up if the subject is of wide public interest.

All of the SDs queried agree that clearance procedures should *not* substantially delay publications of a paper. Some institutes that require multiple signoffs formally or informally allow authors to complete the process after the paper has been submitted for publication. At institutes where the SD must sign off *before* submission, the turn-around time is short—from a few hours to a few days. NIAMS's Henry Metzger advises, "Scientists should work with their SDs if they think their institute's policies are too cumbersome." —C.H. ■

RECREATION AND WELFARE ASSOCIATION

Purpose: To promote and sponsor recreational, educational, and social and welfare activities for NIH and NOAA employees.

Membership: Open to all NIH and NOAA employees for a $5 annual fee.

Resources: Provides ticket service for entertainment and sports in the Washington area, frequently at a discount. Offers low-cost tours to other parts of the United States and nearby islands. Maintains lists of housing in the Bethesda area. Provides free notary service and discount privileges at some local stores.

Contact: Randy Schools, phone: 496-6061. ■

CATALYTIC REACTIONS

In this issue, we are asking for your reactions in four areas: staff scientists, Just Ask, Hot Methods Clinic, and alternative medicine. **Send your responses on these topics or 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. . .

- Defining the Role Of Staff Scientists
- Nerve Growth: Acclerators And Brakes
- Alternative Medicine Goes Intramural
- Wildlife in the Lab: What Are the Rules?

1) In our next issue, we plan to publish NIH's new policy defining the role of staff scientists, including facility heads. What have been your experiences working with or being a staff scientist at NIH? How would you like to see policy on these positions evolve?

2) In our new "Just Ask" column, we hope to dig out solutions to quandaries about how to get things done in the intramural research program. What questions or problems would you like to see addressed in future columns?

3) What suggestions or questions do you have about the *Drosophila* metastasis model featured in this issue's Hot Methods Clinic? What suggestions do you have for alternative techniques to avoid the use of radioisotopes?

4) We are working on an article about recent leadership changes at the Office of Alternative Medicine and its new intramural research initiative. How would you assess the general quality of research being done in the field? Do you think there is a role for alternative-medicine research in your institute, center, or division? Why or why not?

The NIH Catalyst is published bi-monthly for and by the intramural scientists at NIH. Address correspondence to Building 1, Room 334, NIH, Bethesda, MD 20892. Ph: (301) 402-1449; e-mail: catalyst@od1em1.od.nih.gov

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