

The NIH CATALYST

A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

NATIONAL INSTITUTES OF HEALTH ■ OFFICE OF THE DIRECTOR ■ VOLUME 6, ISSUE 4 ■ JULY-AUGUST 1998

NIH Holds Historic Seminar THE FALL AND RISE OF RESEARCH ETHICS

by Fran Pollner

The year 1998 marks the 60th anniversary of a series of events that took place in Austria that, among other disastrous consequences, turned a university that had been a beacon of medical and scientific scholarship into an arm of Nazi propaganda and genocide. In March of 1938, more than half of the medical faculty senior staff of the University of Vienna—the Jews and other “undesirables”—were expelled, concomitant with the annexation of Austria into the Third Reich.



Fran Pollner

Wolfgang Schütz

Ten years ago, on the 50th anniversary of the annexation and the expulsion, there was silence in Austria, Wolfgang Schütz, dean of the medical faculty of the University of Vienna, told

an NIH audience earlier this year. But today, he said, his country, his university, and the medical profession are bent on remembering. They are investigating the university's history between 1938 and 1945 and beyond, and the university calendar is dotted with commemorative assemblies.

“We are constantly evoking the memory of all these events because the medical profession must ever be vigilant to the challenges they represent. It is incumbent upon the medical profession to recognize its role in the Holocaust,” Schütz avowed at an NIH symposium on “Medical Research Ethics at the End of the 20th Century: What Have We Learned?”

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THE BIG PICTURE: HOW TOP RESEARCHERS WOULD SPEND MORE MONEY

by Celia Hooper

The most recent meeting of the Advisory Council to the Director (ACD) of NIH, June 4, featured a discussion best described as “whither NIH research in an era of increased funding?”

Although no one knows how fast the NIH budget will grow, NIH director Harold Varmus thought it would be useful to consider how additional funds could best be used.

One group of 30 leading biomedical investigators assembled informally on a crisp, sunny Sunday morning in mid-February to address the question at the Watergate apartment of Bruce Alberts, head of the National Academy of Sciences. The folks came—on their own dime—from as far away as California, and were invited by Alberts and Eric Lander, director of the Whitehead/MIT Center for Genome Research in Cambridge, Mass., because they were deemed to be individuals who could see the big picture and not just argue for their own particular institution or discipline. Alberts' furniture was moved aside to make room for chairs for everyone.

Site-Specific Targeting

The brainstorming session, led by Lander, also an ACD member, focused on four broad areas and then filled in specifics. The broad areas included which particular research topics were ripe for added support, what funding mechanisms should be used to provide the support, training issues, and what additional infrastructure was needed to support the growth of research.

Lander summarized the conclusions of the crowded crew for the ACD. Particular research areas that would and should be growing included genomic infrastructure, cell circuitry and molecular medi-



cine, the development of disease models, cancer research, neuroscience, world health, bioengineering, and genetic engineering, including stem cell research. For genomic infrastructure, he said, a key fact of life will be that the scale of incoming information will zoom as the numbers of genes sequenced rise by orders of magnitude. NIH could ex-

pect in the not-too-distant future to see an entire mammal genome sequenced each year.

As the newly sequenced genes emerge, they will yield up for study vast numbers of proteins for which scientists will want to identify functions. This desire will mean a second, postgenomic, echo boom in research determining the complete molecular circuitry of the cell. Lander said that this research should be tightly coupled to molecular medicine, supported with lots of what NIGMS Director Marvin Cassman called “glue” grants to provide money just to bring different types of scientists together on projects. Essential to determining cir-

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FOSTERING COLLABORATION AND TEAMWORK AT NIH



Michael Gottesman

NIH has traditionally been known as an institution that is able to assemble multidisciplinary teams of researchers to solve difficult biomedical research problems—an excellent recent example is the diverse multi-institute group that identified *MEN-1*, the multiple endocrine neoplasia gene. In the years ahead, collaborative, interactive groups of scientists will become increasingly critical in areas such as vaccine development, imaging research, huge sequencing and mapping projects, and combinatorial analysis and screening of thousands of potential new drugs. At NIH, for example, our efforts to develop vaccines against AIDS and other diseases inherently require the cooperative efforts of virologists, immunologists, molecular biologists, molecular modelers, chemists, pharmacologists, and clinicians. These scientists, in turn, need the back-up of talented support staff.

But almost like entropy, tugging away at efforts to assemble ordered, cooperative teams, are mitigating forces deeply ingrained in the culture of science: esteem of individual achievement and the pride and creativity that flow from independent scientific efforts. The system of investigator-initiated independent research has historically led to astounding levels of scientific achievement and motivated scientists to the highest levels of performance. The Intramural Research Program has encouraged independent scientific effort with the creation of a tenure track, a stringent tenuring process, and clearer demarcation of the privileges and responsibilities of the tenured independent investigator.

The competing forces of individual achievement and team effort come to their most agonizing conflict for the tenure-track scientist. Is it ever advisable to collaborate with a powerful and successful senior scientist? What about joining a creative, productive, star-studded team that is on its way to a major scientific breakthrough?

The tenure process at NIH now entails the review of an individual scientist's accomplishments by an NIH-wide panel—the Central Tenure Committee. This group of senior NIH scientists looks at recommendations from the leadership of the candidate's institute, evaluations from institute promotion and tenure committees, Board of Scientific Counselors' reviews of the scientist's work, letters from outside scientists, publications, mentoring

skills, and future plans.

For the scientists who make it through the tenure track to come before the Central Tenure Committee, the most difficult question—and a leading cause for denial of tenure at NIH—is the question of intellectual independence.

For the tenure-track scientist who is inclined by personality or circumstances to collaborate with a more senior investigator or to join a larger team to solve an important biological problem, I offer the following advice: Work cooperatively, but carve a distinctive niche within the project that is clearly defined as your territory. Make sure that you are developing an area of expertise that is distinctly your own and is recognized by your scientific colleagues at NIH and elsewhere. It is acceptable to collaborate with your supervisor, but not on every paper, and not always as a junior author. Present your work at major meetings. Make yourself visible and known personally to the outside experts in your field who will someday be asked to comment on your work.

For my senior colleagues who are mentoring brilliant early-career scientists, I offer this advice: Do everything you can to be sure that you encourage independence of thought and action so that your junior colleague can occupy a unique niche in any joint projects. Give your junior colleagues every opportunity to present their work and be sure to credit them appropriately in every presentation you give.

In the years ahead, NIH and other academic institutions will increasingly need to build new teams and larger collaborative groups. This endeavor will not be easy. We will need to work with our Boards of Scientific Counselors so that they appreciate that intellectual independence can flourish in a collaboration among partners of unequal

position. We will have to find ways to cultivate a new breed of research leader who can assemble and motivate dynamic, productive groups. We will have to find new ways to encourage the formation of teams, to keep them integrated and functioning efficiently, and then to honor their success. I welcome your advice on how we can best accomplish these goals.

—Michael Gottesman
Deputy Director for Intramural Research

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INHERENT CONFLICT OF INTEREST IN PEER REVIEW: WHERE NIH GUIDELINES LEAVE OFF

by James L. Fozard, NIA, John J. O'Shea, NIAMS, and Joan P. Schwartz,
NINDS (for the Committee on Scientific Conduct and Ethics)

Reviewing grant proposals and manuscripts submitted to scientific journals is an integral part of the working life of scientists—an activity that increases with seniority and stature in their fields. Objectivity and impartiality of judgment are the ethical prerequisites for the scientist engaged in peer review, just as important as his or her scientific knowledge and acumen. These ethical prerequisites require a peer reviewer to avoid conflicts of interest.

The NIH guidelines for study section members explicitly enjoin a reviewer from participating in the review of grant proposals by professional collaborators, rivals, or organizations in which she or he has a financial interest. Moreover, the *NIH Guidelines for the Conduct of Research in the Intramural Research Program* state that the material to be reviewed must be held confidential and not be used for the reviewer's personal gain until it has been made public. Finally, the review should be based on the quality of data and logic presented, not on personal knowledge that is not available to the author or public. Most journals and granting agencies have similar guidelines and requirements.

A Hypothetical Case

However instructive they may be, there are gaps in existing guidelines on how to avoid conflicts of interest. A fictitious case study on Peer Review, used in NHGRI intramural ethics training and soon to be presented in other intramural programs, illustrates some aspects of conflict of interest that aren't covered explicitly by the guidelines (for further discussion, see this Web site:

<http://www.nhgri.nih.gov/About_NHGRI/Dir/Ethics/Seminars_and_courses/index.html>).

Don, a full professor and respected scientist, participated in an NIH study section. Among the grants he reviewed was one by a scientist working in the same field. His review of this grant led Don to recognize—after the study section meeting—that his approach to research on a similar problem required major changes. Specifically, he realized that his postdoctoral fellow's research project was headed toward a dead end. In addition, Don was involved in a company doing similar research.

What should Don do? What should any of us do who have experienced any of the issues mentioned in the hypothetical case? In a very lively discussion of the case held by members of the NIH Committee on Scientific Conduct and Ethics, it became clear that the case re-

flected what we characterized as the **inherent conflict of interest created by the peer review system**. Reviewers are selected because of their expertise in a specific area of science. They should agree to serve because they want to be good citizens, but in reality they also benefit from hearing about good science and innovative ideas. If there were absolutely nothing to gain from serving on a study section or reviewing manuscripts for a journal, and it was purely an act of altruism, it would undoubtedly be much more difficult to get scientists to agree to serve as reviewers.

From the outset, then, being a reviewer involves a balancing act: achieving the proper balance between applying the expertise that brought you to the study section in the first place and maintaining complete objectivity in evaluating research related to your own. Obviously, a direct competitor would be ruled out as a reviewer, but where is that fine line to be drawn?

Don's case involved a **delayed recognition of conflict of interest**—the relevance to our own work of something we review is recognized only after the formal review process has been completed. One might react as follows: "On the basis of what I learned, I should change procedures, or do a different control in order to get the result I expect" or "This person's plan makes me more confident about what is going on in my lab."

One consequence of recognizing a conflict of interest after the fact may be the **problem of competition among ethical goals created by the delayed knowledge** gained by the reviewer. Again, one might ask, "Is it more important to maintain strict confidentiality or to give a hint to my postdoc that will improve or redirect his project?" Everyone agrees that providing proper guidance to fellows is an essential function of a mentor. If a mentor has information that substantially affects the success of a postdoc's research, how should his/her mentoring responsibilities be weighed relative to obligations to maintain confidentiality?

Furthermore, this knowledge could save precious resources in the laboratory or institute, and we as NIH scientists have an obligation to U.S. taxpayers. If we learn that we are bound to fail with a given approach, is it appropriate to waste a fellow's time and government money on it? Is there a greater standard of confidentiality when the issue involves a for-profit organization, because information generated in NIH labs must be made equally available to all?



Fran Pollner

John O'Shea, Joan P. Schwartz, and
James Fozard

Strategies to Avoid Inherent Conflicts of Interest

So what should we do with confidential information that we know can help us in our work? Committee members unanimously agreed that one cannot use this knowledge to help friends or to hurt competitors—or use the confidential information to give oneself or one's lab an unfair advantage. Most importantly, credit needs to be given to the person from whom the information came.

Several possible approaches came up in the discussion by the Committee. First, there is a time element to be considered. If the grant has been funded or the paper is published, credit can be given openly. Frequently these days, abstracts of papers, or abstracts from grant applications, are published on a Web site; some abstracts appear before the publication. Such information is no longer confidential, and citing it is perfectly reasonable. However, could one invite the individual to present a seminar, since he or she is likely to be a scientific colleague? If he/she voluntarily divulged the information in question, it would no longer be confidential and you could use it and credit the scientist. Or does that make use of the confidential information you have obtained, in a more subtle way? Alternatively, could one guide the postdoc without breaking confidentiality, by suggesting that ambiguous studies be rerun with additional controls, or that certain papers be reread and reconsidered? Finally, it was unanimously agreed that the wall of confidentiality was even higher when a for-profit organization was involved.

In all ethical dilemmas, such as the ones that may arise in peer review, we should deal openly with the issues. This means discussing the general problem, without violating confidentiality, with colleagues, supervisors, editors, the NIH Ombuds, etc. We should not assume that we can be objective when the stakes are high, and our own success or failure is involved; we need to turn to our colleagues for a reality check. ■

RESEARCH ETHICS

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The symposium was sponsored by NIH, the United States Holocaust Memorial Museum, the New York Academy of Medicine, and the Austrian Embassy. The NIH coordinating committee included Robert Nussenblatt, NEI scientific director; Pablo Gejman, head of molecular investigation in the NIMH Clinical Neurogenetics Branch; Michael Gottesman, deputy director for intramural research; Ezekiel Emanuel, director of the Department of Clinical Bioethics; and Alan Sandler, head of the Office of Human Subjects Research who coordinates the institutional review boards (IRB) for NIH clinical protocols.

The symposium addressed the complexity of German and Austrian physicians in the Third Reich's "ethnic cleansing" crusade and the postwar efforts by a horrified world citizenry to establish codes of ethics to prevent future medical atrocities—including, on an international level, the Nuremberg and Helsinki codes; nationally in the United States, the IRB network and commissions for the protection of human subjects of biomedical research; and, on the NIH campus, the Clinical Bioethics Department and Ethical Grand Rounds.

"Our intent," Nussenblatt said later in an interview, "was not to dwell on the past but to use the historical framework to show why controls are necessary, to reflect on the philosophy of medicine, the ethical focus—especially important now with the rejuvenation of clinical research on campus. We wanted a positive message—to reconfirm clinical research in an ethical context."

The symposium was nearly two years in the organizing. The seeds were planted when Nussenblatt and Gejman attended a lecture series at the Holocaust Museum on Nazi medicine and there met Karl Holubar, a professor of dermatology and head of the Institute for the History of Medicine at the University of Vienna—and one of the driving forces behind the university's investigation into the activities of its medical community during the Holocaust.

Another impetus for the meeting—and an issue NIH had to address—was that the NIH library houses the *Pernkopf Atlas*, a meticulously detailed, vividly drawn tome of human anatomy for decades viewed as a masterwork of medical art and now the subject of intensive

investigation at its place of origin, the University of Vienna. Eduard Pernkopf, an anatomy professor at the university, was a dedicated Austrian Nazi who became dean of the medical faculty in 1938 and rector of the university in 1943. The suspicion is that the subjects for his depictions were shipped to him from prisons and concentration camps.

After much discussion, Nussenblatt said, it was decided that the *Pernkopf Atlas* would remain available in the NIH library, with a proviso accompanying the computer reference and the work itself regarding Pernkopf's history and the questionable source of his drawings. A similar information sheet accompanies copies of the atlas at the University of Vienna, pending the outcome of the investigation, to be released later this year.



Fran Pollner
Teresa Magone

But when Teresa Magone, now a visiting fellow at the NEI Clinical Branch, had her anatomy training during her first two years of medical school at the University of Vienna Medical Faculty in the early 1990s, the unadorned *Pernkopf Atlas* was the text. "I am shocked that I could go through school and not be informed of this," she said during the symposium question-and-answer period. It was only after she came to NIH in 1995, where she interned for three months in the Clinical Center's bioethics program and attended the Holocaust Museum lecture series, that she learned "the whole Pernkopf story" from Nussenblatt, she said in an interview.

Responding to Magone during the NIH symposium, Schütz assured her that the



Fran Pollner

Looking back and forward: (top row, left to right): Michael Gottesman, NIH; Wolfgang Schütz, University of Vienna; Robert Proctor, Penn State University; Michael Wunder, Protestant Foundation of Alstrersdorf, Germany; Karl Holubar, University of Vienna; Robert Nussenblatt, NIH; (bottom row, left to right): Barbara Mishkin, Hogan and Hartson; James Childress, National Bioethics Advisory Commission; William Seidelman, University of Toronto; Pablo Gejman, NIH

Pernkopf inquiry is "only the beginning of a more detailed investigation." He and other speakers—Austrian, German, and American—were unflinching in their discussions of potential and actual perversions of medical ethics.

Schütz faulted the Austrian medical hierarchy for the fact that "after the Reich collapse, most of those with a Nazi past remained in office. Pernkopf finished his notorious atlas and co-authored a work on euthanasia of retarded children and adults. . . . A progression of past Nazis held their places in Vienna's universities."

But his nation and his profession have slowly come to grips with the past: In the 1980s, he said, an IRB-equivalent system was developed in his country, and courses in medical ethics and the history of medicine emerged. In 1991, the country as a whole took responsibility for its support of the annexation, and in 1997 the Pernkopf Commission was officially constituted to investigate the connection between the atlas and the death camps.

Jeremiah Barondess, president of the New York Academy of Medicine and

Science: Then and Now

Twin studies at Auschwitz, said William Seidelman, professor of family and community medicine at the University of Toronto, were peer reviewed and approved at the Kaiser Wilhelm Institute. (A twin study example: One twin was injected with typhoid and the other killed when the first one died; their organs were then compared.)

Tracking the fall of what had been the "finest" medical community in the world, Seidelman asked his colleagues: "Are we less susceptible to seduction? Are we guileless in fighting for grants? Are we ever contemptuous or intolerant of patients who are incontinent, unwashed, insane, incurable?"

Among issues to ponder today, he advised, are the relationship of the physician to the state, the inherent conflict between individual and population health, the role of the physician in determining which genetic characteristics are desirable and undesirable, the selection of patients for therapy and the denial of therapy, physician-assisted suicide and euthanasia, science as a vehicle for social change, and the individual physician conscience in the face of institutional brutality. ■

professor emeritus of clinical medicine at Cornell Medical College in New York, pointed to the Tuskegee syphilis study as an example of "problematic research in this country, too." He observed that the United States had also had its proponents of eugenics and involuntary sterilization.

Barondess advised his audience to recognize that the majority of German physicians embraced National Socialism and responded with alacrity to the state's call to help "prevent the disabled from overwhelming the abled. . . . [They] performed selections in concentration camps, experimented on the nonconsenting and nonwilling, and reported their results in medical journals on race hygiene." He asked U.S. physicians to consider the implications of any differences now in treatment in this country among different races and classes. He cautioned that yet another hierarchy based on genotype lies waiting in the wings.

Robert Proctor, professor of the history of science at Penn State University, in University Park, Penna., cautioned against "demonizing" Nazi physicians, lest "we forfeit our ability to understand how this can happen."

With a series of cartoons and posters published in Germany in the 1930s, Proctor illustrated the advanced understanding and public policy of the German public health establishment with regard to cancer prevention and the dangers of cigarettes, alcohol, and environmental carcinogens. Smoking was banned in factories and damned as a major cause of lung cancer and angina. Asbestos was targeted as the culprit in mesothelioma and lung cancer.

Posters warned pregnant women not to drink alcohol or smoke; the world's first brochure on the need for breast self-exam appeared in Germany in 1936; other posters admonished Germans to eat whole-grain bread and to pay as much attention to their colons as their cars and get themselves screened for cancer once a year. There were also numerous depictions of Jews and other non-Aryans as diseased races. "The ordered, hygienic state [was the] ethic of Nazi medical practice," Proctor said. ■

Symposium proceedings will be published in the *Journal of Clinical Ethics*. A videotape of the symposium is on-line at <<http://www2.cc.nih.gov/nih/symposium/>>. There is a link to the required software—RealPlayer 5—at the site.

Ethics Grand Rounds at NIH

Ethics Grand Rounds are now a feature of clinical research at NIH. Four to six times a year, the ethical questions and decisions arising from an actual Clinical Center case will be open for public view and review, according to Ezekiel Emanuel, director of the Department of Clinical Bioethics.

The whole idea of Ethics Grand Rounds is "not to criticize or point fingers or be ethics police, but to engage in serious discussion about real cases," Emanuel said in opening remarks at an Ethics Grand Rounds held in May to review a case emanating from the NIMH geriatric psychiatry branch involving informed consent from a cognitively impaired research subject to participate in an Alzheimer's disease study. The issues that arose were whether the woman herself was competent to give consent or to designate a proxy and whether the chosen individual was acceptable as a proxy. Decisions had been made with the help of an NIH bioethics consultant. At Grand Rounds, the facts of the case and rationale for decisionmaking were presented; an independent review was offered by invited discussant Paul Applebaum, director of the law and psychiatry program at the University of Massachusetts Medical School in Worcester.

The issue of informed consent involving mentally impaired patients was also on the agenda at the last meeting of the NIH Advisory Committee to the Director (ACD). NIMH director Steve Hyman summarized recommendations that emerged from a workshop to devise additional IRB safeguards to protect vulnerable individuals involved in human research. Among them were ensuring that at least one IRB member be qualified to represent the subjects of the research under review, that patient advocates be voting members of the IRB, and that an individual's capacity to consent be based on appreciation of the risks and benefits—an understanding that risks and benefits are not abstractions but actual possibilities in that person's life. The consensus at the workshop and at the ACD meeting: It would be in everyone's worst interest *not* to study such disorders as Alzheimer's disease, manic-depression, and alcoholism as a result of unachievability of perfection in informed-consent criteria. ■

"It was an introspective day for NIH. It gave us the opportunity to understand what a duty and honor it is to be a physician."



Fran Pollner

Robert Nussenblatt

"We are balancing the inherently moral content of what we do as clinical researchers at NIH with the autonomy and rights of the patients."



Fran Pollner

Michael Gottesman



Fran Pollner

Amends: Karl Holubar (left), director of the Institute for the History of Medicine at the University of Vienna, apologizes for his country's past to Czech physician and researcher Tomas Radil, professor of psychiatry at Charles University, Prague, who as a boy survived Auschwitz. The dialogue unfolded as the NIH symposium ended, with Radil requesting: "I want someone to tell me and the tens of thousands of us who are still here: 'We are sorry.' No one has yet." Holubar came forth and responded: "We do repent. We are sorry"—upon which Radil observed: "Yes, those who are sorry are always those who did nothing wrong."

SWIMMING WITH THE SHARKS: A MAVERICK FORMER NIH SCIENTIST'S LIFE IN THE CORPORATE WATERS

by Doug Loftus

Ten years ago, Michael Zasloff left NIH to move a scientific discovery into an arena where it could more readily be transformed into a clinically relevant entity. To do this, he had to transform himself as well, from chief of NICHD's human genetics branch to a corporate entrepreneur. He founded Magainin Pharmaceuticals, Inc., engraving the name he'd given his discovery into the title of his company. Zasloff was at NIH recently to deliver the 11th Annual Paul Erlich Lecture, at which he discussed his ongoing research and Magainin's efforts to develop novel therapeutics for the treatment of infection and cancer.

In 1987, while still at NICHD, Zasloff was the sole author of a PNAS paper in which he described a novel class of antimicrobial peptides isolated from the skin of *Xenopus laevis* frogs; he named the peptides "magainins" (from the Hebrew word for "shield"). His search for these compounds began after he noted that frogs with surgical wounds from an unrelated study healed without local inflammation or infection, despite the fact that they'd been placed in a microbe-laden laboratory aquarium after surgery. The discovery process, says Zasloff, was "something I was executing almost as a hobby—as something exciting to me."

His deep affection for benchwork has not been eclipsed by managerial obligations. "I continue to [spend about] 30–40 percent of my day at the lab bench. I still work with my hands," he says, despite the demands of his roles directing the Magainin Research Institute, an internal division of the company, and as executive vice president of the company proper, based in a Philadelphia suburb.

Since the time of his initial discovery, Zasloff and other groups have identified scores of antimicrobial peptides and proteins produced by various amphibians, insects, and mammals, including humans. In humans, antimicrobial polypeptides are produced by granulocytes in the blood and by epithelial cells



Michael Zasloff

at mucosal surfaces, including the gut, airway, and urogenital tract.

Zasloff says that, in general, the microbicidal action of these substances stems from their ability to form membrane-spanning pores that lead to the destruction of the microorganism. Magainins, for example, are short (23-amino-acid) peptides with the ability to bind to the negatively charged membranes found on a variety of bacteria, fungi, and viruses. As shown in

the figure below, upon binding, these peptides assume an amphiphilic α -helical structure with one face of the helix charged and the other exposing hydrophobic residues. At a critical local concentration of peptide, the helices self-assemble to form channels that permeabilize the membrane and lyse the pathogen. These substances also show remarkable selectivity for microbial membranes, typically affecting the host's cellular membranes only at very high concentrations.

The human antimicrobial polypeptides, termed "defensins," are thought to possess similar pore-forming capabilities, although "no one has seen a defensin pore," according to Zasloff. He believes these molecules provide a

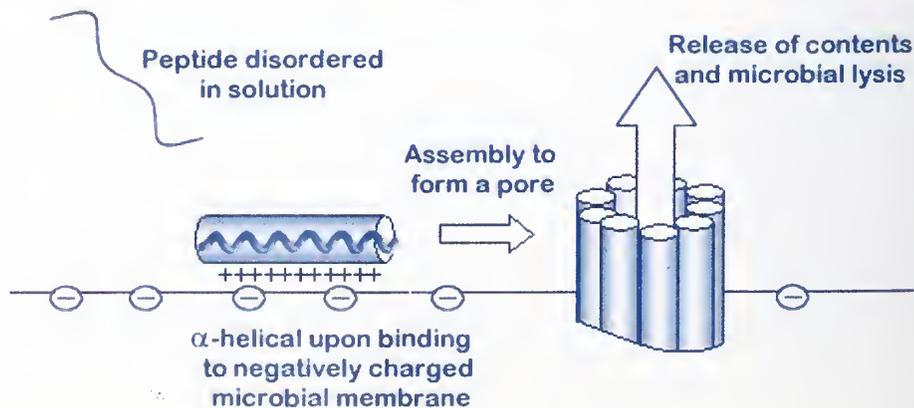
primitive but important first line of defense for sensitive tissues exposed to microbes in our environment. "What's most exciting," he says, "is that when I look at your cornea, I think I understand now why you don't have chronic inflammation, or why your mouth or tongue or sweat glands are not being ravaged by chronic inflammatory processes."

At the time of his discovery, Zasloff recognized the possible therapeutic potential of magainins and wanted to take an active role in guiding his findings through their logical course of development. "I wanted very badly to make these [ideas] real; I wasn't satisfied with putting a few papers out—that was [the easy thing] to do," he says.

In those days, however, the Office of Technology Transfer (OTT) was still part of the Office of General Counsel and functioned in a narrower capacity than it does today—formal opportunities for negotiating technology transfers or cooperative research (such as the CRADA) were limited or nonexistent. Zasloff left NIH and founded Magainin Pharmaceuticals, initially assuming an advisory role while maintaining a faculty position at the University of Pennsylvania School of Medicine in Philadelphia and serving as chief of the Division of Human Genetics and Molecular Biology at the Children's Hospital of Philadelphia. In 1992, he joined the company full-time.

Today, Zasloff's "hobby" has been transformed by Magainin Pharmaceuticals into a topical cream that contains magainin-like peptides. The preparation, carrying the commercial name "Cytalex," has successfully undergone Phase III

Pore Formation by Magainin Peptides





clinical testing for the treatment of diabetic foot ulcers. It could reach the market in a year or so, according to Zasloff, and he expects that the product will have additional applications.

The company Zasloff founded, like Zasloff himself, has grown beyond his 10-year-old discovery, and a visit to the Magainin, Inc., Web site these days will find it enlivened not with the African clawed frog, but a shark. That's because in 1992, Zasloff, again at the bench, working with a graduate student, isolated the compound "squalamine" from the dogfish shark. Squalamine is an aminosterol, and one of its principal biological activities is inhibition of angiogenesis, a feature that could make this substance useful as an antitumor drug. But it's still in its infancy as a product for Magainin; Phase I trials of this compound have begun only recently.

Angiogenesis inhibitors blasted their way to public and investment-house visibility just four days before Zasloff's May 7 visit to NIH when Gina Kolata wrote a gushing front-page story in the *New York Times* extolling their praises as a potential cancer cure—despite the fact that there are very limited data to support their effectiveness against human tumors. EntreMed, Inc., based in Rockville, is the licensee of two antiangiogenesis compounds developed by Judah Folkman of Boston's Children's Hospital, and the company saw its stock prices rise dramatically in response to press coverage of its announcement to begin Phase I trials.

Although Magainin, Inc., could gain from such hyperbole—the company incurred a \$14.4 million loss in 1997—Zasloff makes no secret of his disdain for "hype" and his uncertainty regarding the future of angiogenesis inhibitors as anticancer therapeutics. "The problem is, you want people to support you—you want your stock to be favored by people," he says, but "the bottom line is, if something works, it works; if it doesn't work, it doesn't. With squalamine, we're doing something new—I hope that the observations we made in animals extend to man, [but] we don't know enough. It's an experiment, and you don't know how [it's] going to end—that's what's so tough,

actually." Referring to the media stir, he adds that it has been "irresponsible—totally irresponsible. It hurts us in the scientific community, and makes scientific leaders look like fools." He is equally troubled by the effect of such reporting on emotionally vulnerable cancer patients. "I just think it was terrible—it's going to make what we do less credible, frankly."

Speaking of sharks, it's difficult to ignore the metaphorical significance of the creature in the corporate world—witness, for example, entrepreneur Harvey Mackay's 1988 field guide for would-be business tycoons, *Swim With The Sharks Without Being Eaten Alive*. Zasloff says that he prefers to maintain his distance from the commercial concerns of Magainin. "I live in sort of these two worlds—in one, as somebody who's exploring why animals don't get infected [under certain conditions], and what's so special about the shark, or sea urchin, or hagfish; and, in the other, as this guy who's also making drugs. "But," he adds, "I feel very strongly about my principles—I really have tried to maintain those principles that have kept me as a working scientist, through this phase of my career. That's why I'm not the CEO—because he has a different agenda. . . . I can talk about the discovery process and the biology I see in it. I can hype the *science*, because I'm excited about it, but I can't hype the *product*. Although I'm proud of [Cytotex], it still is funny for me to show [the logo], because I feel like I'm advertising."

Nevertheless, the success of Magainin remains closely tied to Zasloff's research efforts, and vice versa. Zasloff finds the responsibilities somewhere between terrifying and exhilarating. "I feel like I'm in an airplane, a jet, and I have very limited guidance equipment, and the jet is going over terrain that is uncharted, and I'm a couple of feet off the ground and I'm going a bit too fast," he says, laughing. But he also notes, "I love what I'm doing. I'm happy now. I've somehow been able, I hope, to take my own personal NIH experience and mature with it, if you will. I have an opportunity now to take ideas and make them real—into entities that can be used for the treatment of disease, which is just wonderful. That's ultimately why I came to NIH. That's why we're all here." ■

Tech Transfer Today

The Federal Technology Transfer Act (FTTA) of 1986 was designed to ensure that discoveries made in federal research laboratories would be efficiently and routinely made available to commercial interests for further development. At NIH, the Office of Technology Transfer (OTT), a division of the Office of the Director, is charged with carrying out the FTTA mandate. Headed by Maria Freire, the OTT has overseen a nearly threefold growth in the transfer of NIH technologies to the private sector in the last five years. In 1997, 119 patents were issued for NIH discoveries, and findings entered the commercial domain through 208 granted licenses and 153 Cooperative Research and Development Agreements (CRADAs). NIH royalties for last year totaled more than \$35 million.

Although NIH inventors receive royalty payments if their findings translate into a commercial success, instances in which a researcher can "run with" a discovery are, according to OTT's Ted Roumel, "rather rare." For a researcher to launch a commercial venture based on findings made in an NIH lab, NIH would have to waive licensing rights back to the inventor. Such instances are likely to arise only when there is a lack of any commercial interest in the technology—making a foray into the entrepreneurial realm decidedly less appealing to an inventor.

Given the current technology-hungry climate of the biotechnology industry and an OTT now eager to feed it, Michael Zasloff's experience is perhaps unlikely to be reproduced by any of today's NIH researchers. But for those who desire to see their ideas turned into reality, the possibilities for doing so are greater now than they ever were. If your results lead you to wonder "what if?" speak to your Institute's Technology Development Coordinator (see <<http://www.nih.gov/od/ott/tdc.htm>> for listings) about how to proceed. You might see your findings made real without ever leaving campus, while keeping the "sharks" at a safe distance—unless, of course, like Michael Zasloff, you happen to be using them in your research. ■

—D.L.

INTERINSTITUTE INTEREST GROUP DIRECTORY

MAJOR INTEREST GROUPS

Cell Biology Interest Group

Meeting time: Varies, meetings restricted to NIH scientists

Meeting place: Building 18T, Room 101

Contact: Jennifer Lippincott-Schwartz

Phone: 402-1010; 402-1009

E-mail: <jlippin@helix.nih.gov>

Listserv: subscribe to CELBIO-L

Clinical Research Interest Group

Meeting time and place: Varies

Contact 1: Cliff Lane

Phone: 496-7196

E-mail: <clane@atlas.niaid.nih.gov>

Contact 2: Harry Keiser

Phone: 496-1518

E-mail: <keiserh@fido.nhlbi.nih.gov>

Genetics Interest Group

Meeting time: Usually second Tuesday, 4:00 pm

Meeting place: Building 49, Conference Room A and B

Contact 1: Lynn Hudson

Phone: 496-9660

E-mail: <hudson@helix.nih.gov>

Contact 2: Beverly Mock

Phone: 496-2360

Listserv: subscribe to

MAJORDOMO@NCHGR.NIH.GOV

post to GIG@NCHGR.NIH.GOV

Immunology Interest Group

Meeting time: Each Wednesday (except summer), 4:15 pm

Meeting place: Building 10, Lipsett Auditorium

Contact: David Margulies

Phone: 496-6429

E-mail: <dhm@helix.nih.gov>

Listserv: subscribe to IMMUNI-L at

Listserv@LIST.NIH.GOV

Molecular Biology/Biochemistry Interest Group

Meeting time: Yearly to consider speakers

Meeting place: Building 8, Room 122

Contact: Reed Wickner

Phone: 496-3452

E-mail: <wickner@helix.nih.gov>

Neurobiology Interest Group

Meeting time: To be announced

Meeting place: Building 36, Room 1B13

Contact 1: Chip Gerfen

Phone: 496-4341

E-mail: <gerfen@helix.nih.gov>

Contact 2: Chris McBain

Phone: 402-4778

Listserv: JLS@LSR.NEI.NIH.GOV

Structural Biology Interest Group

Meeting time and place: Announced to

members by e-mail and regular mail

Contact: Adrian Parsegian

Phone: 496-6561

E-mail: <aparsegi@helix.nih.gov>

Contact 2: Marius Clore

Phone: 496-0782

To register for e-mail announcements:

E-mail <cch@discus.niams.nih.gov>



OTHER INTEREST GROUPS

AIDS Interest Group

Meeting time and place: Varies

Contact: Fulvia Veronese

Phone: 496-3677

E-mail: <fv10X@nih.gov>

Listserv: subscribe to AIDSINTG-L

Alzheimer's Interest Group

Meeting time: First Thursday (except summer), 9:00 am

Meeting place: Building 36, Room 1B13

Contact: Gerald Ehrenstein

Phone: 496-3206

E-mail: <gerry@helix.nih.gov>

Apoptosis Interest Group

Meeting time: First Monday, 4:00 pm

Meeting place: Building 30, Conference Room 117

Contact: Yves Pommier

Phone: 496-5944

E-mail: <pommier@nih.gov>

Behavioral and Social Sciences Interest Group

Meeting time: Varies

Meeting place: See NIH Calendar of Events

Contact 1: Jaylan Turkan

Phone: 443-1263

E-mail: <jaylan@nih.gov>

Contact 2: Ronald Abeles

Phone: 594-5943

E-mail: <rabeles@box-r.nih.gov>

BSSR Methodology and Measurement Interest Group

Meeting time: Quarterly, 8:30 am

Meeting place: Gateway, Room 525

Contact: Jared Jobe

Phone: 496-3137

E-mail: <Jared_Jobe@nih.gov>



Bioethics Interest Group

Meeting time: First Monday (except August), 3:00 pm

Meeting place: Natcher, Room D

Contact: Miriam Keltly

Phone: 496-9322

E-mail: <mk46u@nih.gov>

Bioinstrumentation Interest Group

Meeting time: First Tuesday, 2:00 pm

Meeting place: Building 13, Room 3W54

Contact: Paul Smith

Phone: 435-1945

E-mail: <pdsmith@helix.nih.gov>

Biophysics Interest Group

Meeting time: Varies

Meeting place: Varies, mostly Building 10, Bunim Room

Contact: Peter Basser

Phone: 435-1949

E-mail: <pjbasser@helix.nih.gov>

Birth Defects and Teratology Interest Group

Meeting time: Varies

Meeting place: Natcher, NIEHS

Contact 1: Kenneth Warren

Phone: 593-4375

E-mail: <kwarren@willco.niaaa.nih.gov>

Contact 2: Harold Slavkin

Phone: 496-3571

Breast Biology Interest Group

Meeting time and place: Varies

Contact 1: JoAnne Zujewski

Phone: 402-0985

E-mail: <zujewski@nih.gov>

Contact 2: Patricia Steeg

Phone: 496-9753

Calcium Interest Group

Meeting time: Usually Tuesday, 3:00 pm

Meeting place: Building 49, Room 1A50

Contact 1: Arthur Sherman

Phone: 496-4325

E-mail: <asherma@nih.gov>

Contact 2: Indu Ambudkar

Phone: 496-1478

Listserv: Subscribe to CALCIUM-L

Cell Motility Interest Group

Meeting time: First Monday (except July and August), 4:00 p.m.

Meeting place: Building 10, Bunim Room (9S235)

Contact: Jim Sellers

Phone: 496-6887

E-mail: <jsellers@helix.nih.gov>

Chemistry Interest Group

Meeting time: Monthly seminars
 Meeting place: Varies
 Contact 1: John Schwab
 Phone: 594-1338
 E-mail: <schwabj@nigms.nih.gov>
 Contact 2: Kenneth Kirk
 Phone: 496-2619

Chromatin and Chromosomes Interest Group

Meeting time: Every other Thursday, 11:00 am
 Meeting place: Building 32T, Conference Room
 Contact: David Clark
 Phone: 496-6966
 E-mail: <djclark@helix.nih.gov>

Clinical Pharmacology Interest Group

Meeting time: Quarterly, 7:00 pm
 Meeting place: Varies
 Contact 1: William D. Figg
 Phone: 402-3622
 Contact 2: Art Atkinson

Cornea Interest Group

Meeting time: First Monday, 8:30 am
 Meeting place: Building 6, Room 412
 Contact: Christina Sax
 Phone: 402-4342
 E-mail: <sax@helix.nih.gov>

Cytokine Interest Group

Meeting time: Quarterly symposia
 Meeting place: Varies
 Contact 1: Sharon Wahl
 Phone: 496-9218
 E-mail: smwahl@yoda.nidr.nih.gov
 Contact 2: electronic, Marco Schito
 E-mail: <mschito@atlas.niaid.nih.gov>

Developmental Biology Interest Group

Meeting time and place: Varies
 Contact 1: Igor Dawid
 Phone: 496-4448
 E-mail: <idawid@nih.gov>
 Contact 2: Joram Patigorsky
 Phone: 496-9467

DNA Repair Interest Group

Meeting time: Third Tuesday, 12:30 pm
 Meeting/Videoconference Locations:
 Natcher Building Room H; GRC (Baltimore) Room 1E03; FCRDC Building 549, Conference Room A; NIEHS (Research Triangle Park, NC) Building 101, Room B200
 Contact 1: Kenneth Kraemer
 Phone: 496-9033
 E-mail: <kraemer@nih.gov>
 Contact 2: Vilhelm Bohr
 Phone 410-558-8162

Domestic Violence Research Interest Group

Meeting time and place: To be announced
 Contact: John C. Umhau
 Phone: 496-7515
 E-mail: <umhau@nih.gov>

Drosophila Interest Group

Meeting time: Third Tuesday, 1:15 pm
 Meeting place: Building 6B, Room 4B429
 Contact: Sue Haynes
 Phone: 496-7879
 E-mail: <sh4i@nih.gov>

Drug Discovery Interest Group

Meeting time: Usually one Thursday a month, 3:00 pm
 Meeting place: Building 37, Room 6B25
 Contact: John Weinstein
 Phone: 496-9571
 E-mail: <weinstein@dtpx2.ncifcrf.gov>

Economics Interest Group

Meeting time and place: Varies
 Contact 1: James A. Schuttinga
 Phone: 496-2229
 E-mail: <js4lz@nih.gov>
 Contact 2: Agnes Rupp
 E-mail: <ar24f@nih.gov>

Endocrinology Interest Group

Meeting time and place: Varies
 Contact 1: George Chrousos
 Phone: 496-4686
 E-mail: <George_Chrousos@nih.gov>
 Contact 2: Phil Gold
 Phone: 496-1945

Epidemiology and Clinical Trials Interest Group

Meeting time and place: Varies
 Contact 1: Bob Hoover
 Phone: 496-1691
 E-mail: <rh62m@nih.gov>
 Contact 2: Martina Vogel-Taylor
 Phone: 496-6614
 ListServ: subscribe to Epidem-L at listserv@list.nih.gov

Extracellular Matrix Interest Group

Meeting time: Second Friday, 11:00 am
 Meeting place: Natcher or Building 30
 Contact 1: William Stetler-Stevenson
 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: typically second and fourth Friday, 4:00 pm
 Meeting place: Building 10, usually Room 5N264
 Contact: Jay Knutson
 Phone: 496-2557
 E-mail: <jaysan@helix.nih.gov>
 Contact 2: Dan Sackett
 Phone: 496-4033

Gene Therapy Interest Group

Meeting time: Second and fourth Thursday, 2:00 pm
 Meeting place: Building 10, Lipsett Auditorium
 Contact 1: Richard Morgan
 Phone: 402-1833
 E-mail: <rmorgan@nhgri.nih.gov>
 Contact 2: Fabio Candotti
 Phone: 402-1833

Genomics and Bioinformatics Interest Group

Meeting time: Usually one Thursday a month, 3:00 pm
 Meeting place: Building 37, Room 6B25
 Contact: John Weinstein, NCI
 Phone: 496-9571
 E-mail: <weinstein@dtpx2.ncifcrf.gov>]

Glia Club

Meeting time: Bimonthly, second Tuesday, 4:00 pm
 Meeting place: Building 36, Room 1B13
 Contact 1: Vittorio Gallo
 Phone: 402-4776
 E-mail: <vgallo@helix.nih.gov>
 Contact 2: Joan Schwartz
 Phone: 496-4049

Glycobiology Interest Group

Meeting time and place: Varies
 Contact: Diana Blithed
 Phone: 496-1661
 E-mail: <blithed@exchange.nih.gov>
 ListServ: Subscribe to GLYCO-L@LIST.NIH.GOV

GTP Binding Proteins Interest Group

Meeting time: Second Friday, 2:00 pm
 Meeting place: FAES Social & Academic Center
 Contact: R. Victor Rebois
 Phone: 496-2007
 E-mail: <rebois@box-r.nih.gov>

Hard Tissue Disorders Interest Group

Meeting time: Day varies, 9:30 am
 Meeting place: Building 30, Room 106
 Contact: Pamela Robey
 Phone: 496-4563
 E-mail: <probey@yoda.nidr.nih.gov>
 Contact 2: Michael Collins
 Phone: 496-4913

INTERINSTITUTE INTEREST GROUP DIRECTORY



Head and Neck Biology Interest Group

Meeting time: bimonthly, second Monday, 3:30 pm
 Meeting place: Building 10, Room 9C401
 Contact: Frank G. Ondrey
 Phone: 435-2072
 E-mail: <fondrey@pop.nidcd.nih.gov>

Head and Neck Cancer Interest Group

Meeting time: To be announced
 Meeting place: Building 30, Room 211
 Contact: Wendy Weinberg
 Phone: 594-5270
 E-mail: <wwinberg@yoda.nidr.nih.gov>
 Contact 2: Adrian Senderowicz
 Phone: 496-4119

Human Development Across the Lifespan Interest Group

Meeting time and place: Varies
 Contact: Kim Roberts
 Phone: 496-0420
 E-mail: <roberts@ssed.nichd.nih.gov>
 Contact 2: Kimberly Kendziora
 Phone: 496-4407

Image Processing Interest Group

Meeting time and place: Varies
 Contact 1: Bennes Trus
 Phone: 496-2250
 E-mail: <trus@helix.nih.gov>
 Contact 2: Calvin Johnson
 Phone: 402-3045

Integrative Neuroscience Interest Group

Meeting time: Alternate Thursdays, 3:30 pm
 Meeting Place: Building 49, first floor Conference Room
 Contact 1: Michael Goldberg
 Phone: 496-9375
 E-mail: <meg@lsr.nei.nih.gov>
 Contact 2: Robert Wurtz
 Phone: 496-9375
 ListServ: subscribe to JLS@LSR.NEI.NIH.GOV

In Vivo NMR Interest Group

Meeting time: Varies
 Meeting place: Building 10, Room B1N256
 Contact: Jeff Duyn
 Phone: 402-1981
 E-mail: <jhd@helix.nih.gov>
 Website: <http://mri.info.nih.gov>

Java Interest Group

Meeting Time: Second Thursday, 11:30 pm
 Meeting place: Building 12B, second floor Conference Room
 Contact: Ronald Taylor
 Phone: 496-4051
 E-mail: <rtaylor@helix.nih.gov>

Lambda Lunch (Bacterial and Phage Genetics)

Meeting time: Each Thursday, 11:00 am
 Meeting place: Building 36, Room 1B13
 Contact: Susan Gottesman
 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: Third Thursday, 4:00 pm
 Meeting place: Building 10, Room 13S235A
 Contact 1: Larry Kwak
 Phone: 301-846-1607
 E-mail: <kwak@mail.ncifcrf.gov>
 Contact 2: Charles Zacharchuk
 Phone: 496-4514

Mass Spectrometry Interest Group

Meeting time: First and third Thursday, 11:00 am
 Meeting place: Building 10, Room 7C101
 Contact 1: Lewis Pannell
 Phone: 402-2196
 E-mail: <L_Pannell@nih.gov>
 Contact 2: Jack Simpson
 Phone: 496-7544

Microtubule Interest Group

Meeting time: Every other Friday, 4:00 pm
 Meeting place: Building 10, Room 9S235 (Bunim Room)
 Contact: Dan Sackett
 Phone: 496-4033
 E-mail: dsackett@helix.nih.gov

Mitochondria Interest Group

Meeting time: First Monday, 3:00 pm
 Meeting place: Natcher, Room J/H; NIEHS; GRC
 Contact: Steve Zullo
 Phone: 435-3576
 E-mail: <zullo@helix.nih.gov>

Molecular Modeling Interest Group

Meeting time: See <http://cmm.info.nih.gov/MMIGnet/events>
 Meeting place: Building 12A, conference rooms
 Contact: Peter Steinbach
 Phone: 496-1100
 E-mail: <steinbac@helix.nih.gov>

Molecular Psychiatry Interest Group

Meeting time: Monthly, Thursday (with summer break), 4:00 pm
 Meeting place: Varies
 Contact: Julio Licinio
 Phone: 496-6885
 E-mail: <licinio@nih.gov>

Mouse Club

Meeting time: First Tuesday, 4:00 pm
 Meeting place: Building 31, Room 2A52, or Building 6A, Room 405
 Contact: Heiner Westphal
 Phone: 402-0545
 E-mail: <hw@helix.nih.gov>

Multisensory Interest Group

Meeting time: Alternate Thursdays, 4:00 pm
 Meeting place: Building 15K, ground-floor conference room
 Contact 1: Peter Grossenbacher
 Phone: 496-7672
 E-mail: <Peter_Grossenbacher@nih.gov>
 Contact 2: Scott Adams
 Phone: 496-7874
 URL: <http://www.nih.gov/sigs/mig/>

Nerve Growth Factor (NGF) Club

Meeting time: First Tuesday, 2:00 pm
 Meeting place: Building 49, Room 1A59 (lecture) and Room 5A46 (discussion)
 Contact: Gordon Guroff
 Phone: 496-4751
 E-mail: <gordong@helix.nih.gov>

Nerve-Muscle Interest Group

Meeting time: Alternate Wednesdays, 8:45 am
 Meeting place: Building 36, Room 1B07
 Contact 1: Matt Daniels
 Phone: 496-2898
 E-mail: <mdaniels@codon.nih.gov>
 Contact 2: Zuhang Sheng
 Phone: 435-4596

Neuroimmune Interactions Interest Group

Meeting time: Usually one Tuesday a month, 4:00 pm
 Meeting place: Building 10, Room 11S235
 Contact: Esther Sternberg
 Phone: 402-2773
 E-mail: <ems@codon.nih.gov>

Pain Interest Group

Meeting time: Second Monday, 3:00 pm
 Meeting place: Building 49, Conference Room A
 Contact: M. A. Ruda
 Phone: 402-4980
 E-mail: <ruda@yoda.nidr.nih.gov>
 ListServ: subscribe to: PAINGROUP-L@LIST.NIH.GOV

PET Interest Group

Meeting time: Each Friday, 2:00 pm
 Meeting place: Building 10, Room 1C520.
 Contact: Peter Herscovitch
 Phone: 402-4297
 E-mail: <herscovitch@nih.gov>

Pigment Cell Research Interest Group

Meeting time: Third Monday, 3:00 pm
 Meeting place: Building 49, Conference Room A
 Contact: Vincent Hearing
 Phone: 496-1564
 E-mail: <hearingv@nih.gov>

Prostate Cancer Interest Group

Meeting time: Usually one Tuesday a month, 4:30 pm
 Meeting place: Building 10, 2 East Conference Room
 Contact 1: Marston Linehan
 Phone: 496-6353
 E-mail: <wml@nih.gov>
 Contact 2: Michael Emmert-Buck
 Phone: 496-2912

Protein Folding Journal Club

Meeting time: Each Thursday (usually October-June), 4:00 pm
 Meeting place: Building 12A, Room 3026
 Contact: Joe Bryngelson
 Phone: 496-1135
 E-mail: <jdb@helix.nih.gov>

Protein Trafficking Interest Group

Meeting time: Second Tuesday, 3:30 pm
 Meeting place: Building 10, Room 9S235
 Contact 1: Harris Bernstein
 Phone: 402-4770
 E-mail: <harris_bernstein@nih.gov>
 Contact 2: Peng Loh
 Phone: 496-3239

Reactive Oxygen Species Interest Group

Meeting time: Second Friday (Sept.-May), 4:00 pm
 Meeting place: Building 49, Conference 1A-B
 Contact: C. C. "Mike" Chiueh
 Phone: 402-2369
 E-mail: <chiueh@helix.nih.gov>

RNA Club

Meeting time: First Tuesday (except August), 4:00 pm
 Meeting place: Building 41, Room C509
 Contact 1: Carl Baker
 Phone: 496-2078
 E-mail: <ccb@helix.nih.gov>
 Contact 2: Susan Haynes
 Phone: 496-7879

Signal Transduction Interest Group

Meeting time: Second and fourth Friday, 4:30 pm
 Meeting place: 5 Research Court, Conference
 Contact 1: John Northup
 Phone: 496-9167
 E-mail: <drjohn@codon.nih.gov>
 Contact 2: James Battey
 Phone: 402-0900

Social Structure & Demographic Issues in Health Interest Group

Meeting time and place: Varies
 Contact 1: Laura E. Montgomery
 Phone: 436-3650, ext 177
 E-mail: <lem3@cdc.gov>

Therapeutic Oligonucleotides Interest Group

Meeting time: Last Thursday, 4:00 pm
 Meeting place: Building 30, Room 117
 Contact : Yoon Cho-Chung,
 Phone: 496-4020
 E-mail: <chochung@helix.nih.gov>

Transcription Factors Interest Group

Meeting time: First Thursday (except July-Sept.), 2:15 pm
 Meeting place: Building 49, Conference Room B
 Contact 1: Stoney Simons,
 Phone: 496-6796
 E-mail: <steroids@helix.nih.gov>
 Contact 2: Uli Siebenlist
 Phone 496-7662
 Listserv: subscribe to TFACTORS

Viral Hepatitis Interest Group

Meeting time: One Monday a month, 3:30 pm
 Meeting place: Building 10, Bunim Room (9S235)
 Contact: T. Jake Liang
 Phone: 496-1721
 E-mail: <jliang@nih.gov>

Virology Interest Group

Meeting time: Third or fourth Thursday, 3:30 pm
 Meeting place: Building 4, Room 433
 Contact 1: Jeffrey Cohen
 Phone: 496-5221
 Contact 2: Peter Collins
 Phone: 496-4205
 ListServ: Contact <CBuckler@nih.gov>

Washington Area Yeast Club

Meeting time: Second Wednesday, 5:15 pm
 Meeting place: Building 6B, Room 4A05
 Contact 1: Reed Wickner
 Phone: 496-3452
 E-mail: <wickner@helix.nih.gov>
 Contact 2: Alan Hinnebusch
 Phone: 496-4480
 E-mail: <ahinnebusch@nih.gov>

WorldWideWeb Interest Group

Meeting time: Second Tuesday, 2:30 pm
 Meeting place: Building 10, Lipsett Auditorium
 Contact: Dale Graham, DCRT
 Phone: 402-1805
 E-mail: <degraham@helix.nih.gov>

Xenopus/Zebrafish Interest Group

Meeting time: Last Friday (except summer), 4:00 pm
 Meeting place: Building 6B, Room 429
 Contact: Tom Sargent
 Phone: 496-0369
 E-mail: <tsargent@nih.gov>

X-ray Crystallography Interest Group

Meeting time: Quarterly, announced by e-mail, 2:00 pm
 Meeting place: Building 5, Room 127
 Contact 1: James Hurley
 Phone: 402-4703
 E-mail: <hurley@tove.niddk.nih.gov>
 Contact 2: Peter Sun
 Phone: 496-3792

To make additions or changes, contact Celia Hooper (fax: 435-2919; e-mail: <hooperc@nih.gov>).

IntraMall On-Line

The NIH IntraMall electronic shopping center is open for immediate use by all NIH staff who have registered for an IntraMall account. IntraMall provides streamlined, desktop, on-line catalogue shopping for scientific supplies and equipment that simplifies use of the IMPAC credit cards for payment. There are more than 60 vendors and more than 20 complete catalogues on-line today at <<http://intramall.nih.gov>>.

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NIH GRADUATE SCHOOL HEADS FOR A LIVELY FALL

In academic circles, the season of rebirth is the fall. The metaphor is especially true at the NIH campus this fall, where two new departments, 32 new courses, and an additional 20 instructors from the NIH fellows community promise to make the 1998–1999 academic year at the NIH Graduate School one of the most exciting in its 39-year history.

Shortly after my appointment earlier this year as director of the graduate school, which is run by the Foundation for Advanced Education in the Sciences (FAES), I put out a call for new course ideas and new instructors; the heartening and enthusiastic response I got from the NIH community has enabled us to revise and expand the curriculum to meet the directive of FAES president Ed Rall that the course offerings reflect the “revolutions occurring in biology” today.

The 184 courses that constitute the new curriculum encompass areas of current interest, new approaches and methodologies, cutting-edge basic and clinical research, introductory basic science courses, an MCAT review, and even a speed-reading class.

Among the new courses that capture contemporary currents are:

- An introduction to AIDS and HIV research that reviews the virology, biochemistry, and immunological aspects of the disease, vaccine and drug treatment and development, and design and implementation of methods to prevent HIV spread (Carl Dieffenbach, NIAID, coordinator).

- “Emerging Diseases” (spring; Catherine Laughlin, NIAID, instructor).

- “Nature’s Treasures: Exploring Natural Products Chemistry and Drug Development,” highlighting the premier natural products work here at NIH (Lewis Pannell, NIDDK, coordinator).

- “Biodiversity” (spring; Jamie Reaser, Smithsonian Institution, instructor).

But these are just the icing on the cake. The depth of expertise we have available around us has permitted the school to offer other new courses as well, including:

- “Neural-immune Interactions” (Esther Sternberg, NIMH).

- “Cytokines in the Immune, Inflammatory, and Hematopoietic Systems” (Scott Durum, NCI, and Joshua Farber, NIAID);

- “Calcium Signaling in Cells” (James T. Russell, NICHD).

- “The Structure and Function of the Nucleus” (Mary Dasso, NICHD).

- “Developmental Neurobiology” (Christine Brennan, NINDS).

- “Genetics in Complex Disease Research (Darrell Ellsworth, NHLBI).

- “Mitochondrial Genetics and Biogenesis (Steve Zullo, NIMH).

- “Survival Data Analysis and Categorical Data Analysis” (Timothy Chen, NCI).

- “Therapeutic Oligonucleotides and Antisense” (Y. S. Cho-Chung, NCI, and Serge Beauchage, CBER).

- “Clinical Significance of Molecular Markers of Carcinogenesis, Growth, and Differentiation (Nicholas J. Sarlis, NIDDK).

- Two neurophysiology courses that cover an introduction to the science and then move to pathologies such as Alzheimer’s and Parkinson’s (Wolfram Gottschalk, NINDS).

- Current topics in molecular genetics (Clair Francomano, NHGRI, and Robert Nussbaum, NHGRI).

This year, the FAES Graduate School will assist with CC director John Gallin’s now-indispensable “Core Course in Clinical Research,” which will be offered through the school as “Introduction to the Principles and Practice of Clinical Research.”

To support NIH’s growing interest in the imaging sciences, the FAES Graduate School has added a new Department of Imaging Sciences, headed by Nick Bryan (CC) and Robert Balaban (NHLBI). The fledgling department will offer three new courses in 1998–1999—“Magnetic Resonance Imaging” (Jeff Duyn, CC), “Positron Emission Tomography” (Peter Herscovitch, CC), and “Fundamentals of Light Microscopy and Electronic Imaging” (Kenneth Spring, NHLBI).

Calvin Johnson of NIH’s Center for Information Technology (CIT) is chairing a new Department of Computer Sciences, which will collaborate with the computer center to offer courses in 1998–1999 in “Fundamentals of Numerical Optimization,” “Numerical Methods and Computation,” “Artificial Neural Net-

by Paul Torrence, Ph.D., Director, and Chief, Biomedical Chemistry Section, NIDDK Laboratory of Medicinal Chemistry



Paul Torrence

Fran Pollner

works,” and “Design and Analysis of Algorithms.”

In another collaborative venture with the CIT computer center, Robert Phair, president of BioInformatics, a consulting firm in Rockville, will teach an intensive, hands-on course in “Integrative Bioinformatics.” Each student will build and test a computer model of the molecular or cellular system that he or she finds of greatest interest. The result will be a quantitative statement of a working hypothesis that can be tested against experimental data.

The basics have not been left behind, either. The introduc-

tory Biochemistry 300 course has been reinstated and restaffed, as has Biochem 433, “Current Methodology on Nucleic Acids Structure and Function.” And we are delighted to be able to continue offering “BIOTRAC” courses, now numbering 19 and including new offerings on mutation detection and analysis and the cell cycle, as well as familiar courses such as cell culture. Investigators considering venturing into new fields and the pre-IRTA community should find these courses invaluable.

For a catalog for the 1998–1999 academic year, call the FAES Graduate School at (301) 496-7976; it’s also available by mail: FAES, One Cloister Court, Bethesda, MD 20814-1460; interoffice: Building 60, Suite 230; or through the FAES Graduate School Web page: <http://faes.gradsch.htm>.

Registration deadline for the fall semester is August 31, by mail. Walk-in registration at FAES (Building 60) is September 1–8. Classes begin September 14. We urge everyone to register by September 8, because classes that do not meet enrollment quotas will be cancelled after that date.

Anyone interested in joining the faculty and offering a course should contact me at (301) 496-2653; e-mail: torrence@helix.nih.gov. ■

DUKE-NIH PROGRAM OFFERS NIH TRAINEES MASTER'S DEGREE IN CLINICAL RESEARCH

Formal clinical research training that culminates in a master's degree is now available to NIH trainees, thanks to an academic collaboration that begins in September between Duke University Medical Center (Durham, N.C.) and the Clinical Center.

"[This] experiment in long-distance learning is designed primarily for NIH clinical fellows and the medical students who participate in the NIH Clinical Research Training Program," says John Gallin, CC director and NIH associate director for clinical research. "They can now earn a master's degree while they're here."

The program requires 24 units of graded course work and a 12-unit research and thesis project. Successful completion earns a Master of Health Sciences in Clinical Research from Duke University School of Medicine.

"We're excited about the collaboration—this is our first step in making the program more widely available," says William Wilkinson, director of the Duke program. Launched in 1986, Duke's was one of the first clinical research training programs—and one of the few degree-conferring ones—in the United States. "We've had 11 years to refine and improve it," Wilkinson observes, adding that the need for clinical researchers, like the demands for evaluation of clinical practices and for clinical trials of new treatment modalities, has been growing.

Courses for the program will be videoconferenced to the CC from Duke University Medical Center. Some classes will also be held on-site at the CC by NIH faculty who will have adjunct appointments at

Duke. For additional information, contact William Wilkinson at <wilki016@mc.duke.edu> or call (919) 681-4561.

Courses

"Introduction to the Principles and Practice of Clinical Research." Overview of methodology; ethical, legal, scientific, regulatory, and biostatistical issues.

"Introduction to Statistical Methods." Statistical estimation and hypothesis testing; probability distributions; descriptive statistics; graphical displays; parametric and non-parametric tests for differences in central tendency; paired comparison and correlation; simple linear regressions; and one-way analysis of variance.

"Principles of Clinical Research." Formulating the research objective and research hypothesis; specifying the study population, the experimental unit, and response variables; study classification; and clinical epidemiology.

"Ethical Issues in Clinical Research." Underlying ethical principles relating to research conduct, subject selection, informed consent, compensation, confidentiality, regulatory requirements, termination of trials, conflict of interest, and scientific integrity.

"Statistical Analysis." Regression models, categorical data analysis, and survival analysis.

"Research Management." Budget development and financial management, project management, regulatory affairs, negotiations, conflict resolution, manuscript preparation, public relations, presentation skills, and dissemination of medical information.

"Clinical Research Seminar." Practical experience in developing and critiquing the methodological aspects of clinical research protocols and the literature.

The required courses are subject to change. Course electives will be announced later.

—Sara Byars

PRAT Programs: Now There Are Two

NIH is launching a new specialty program to recruit and train PRAT fellows in Clinical Pharmacology. The new program, organized by Arthur Atkinson of the Clinical Center, is designed to create a cadre of scientists with much-needed expertise in the clinical development, evaluation, and therapeutic use of small molecule- and biotechnology-based pharmacotherapy. The Clinical Pharmacology PRAT Fellows will devote most of their time to clinical and lab research, but will also receive didactic training in clinical research, principles of clinical pharmacology, and biostatistics. Each fellow will have a research preceptor; preceptor and applicant selection is by steering committee.

Candidates must be U.S. citizens or permanent residents and should have an M.D. degree with three years of residency training and board eligibility in a primary medical specialty. A good mathematics background is important. Applications are due in **October**; the program begins in July. Appointments are for two years, with a third year possible if warranted by the trainee's research. For more information, contact Arthur Atkinson [(301) 435-8791] or see the clinical pharmacology Web site: <<http://www.cc.nih.gov/OD/clinprat/>>.

The regular PRAT program continues to support fellows in other areas of pharmacological sciences. Applications are next due **January 5, 1999**. Individuals may now apply not only before coming to NIH or the FDA's CBER but also after, provided they began their postdoctoral work here within the 12 months preceding PRAT's application deadline. Applicants must be U.S. citizens or permanent residents and have received their doctorate or professional degree in basic or clinical science within the five years prior to applying. The Web site for the overall PRAT program is:

<http://www.nih.gov/nigms/about_nigms/prat.html>.



Ernie Branson

CLINICAL RESEARCH TRAINEES GO OUT IN STYLE

First Class: The first graduates of the Clinical Research Training Program (CRTP), sponsored by NIH and the National Foundation for Biomedical Research, posed for a group shot outside the Cloister, where they delivered their end-of-the-year scientific presentations on subjects ranging from "Pallister-Hall Syndrome: Combining Psychiatry and Genetics" to "Interferon Gamma Receptor Deficiency: Construction of a Retrovirus for Gene Therapy" and "Cytotoxic Activity of Anti-Tac(Fv)-PE38 toward Lymphocytes from Patients with Hairy Cell Leukemia." The nine were selected from a field of 78 applicants—all students who have completed their third year of medical or dental school. The program has expanded to 17 for the coming round: 15 new trainees and two students who are extending their CRTP stay into the optional second year. (Back row, left to right: Eric Eskioğlu, University of Kansas (Kansas City); Uri Lopatin, University of Medicine and Dentistry of New Jersey-Newark; Amin Azzam, Medical College of Virginia (Richmond), Cliff Davis (UCLA), Jill Anderson, University of Nebraska (Omaha); front row, left to right: Eric Brown, UCLA; Arthur Li, UCSF; Jonathan Samuels, Cornell University Medical School (New York); David Robbins, Mount Sinai School of Medicine (New York))

THE BIG PICTURE

continued from page 1

cuitry, as well as making the link to disease, will be animal models. Lander said the group also predicted that cancer research would be one of the areas capitalizing on the strides in molecular medicine, as would neuroscience, which is now driven by both neurogenetic discoveries and powerful new imaging breakthroughs.

Some of the increased funding should be directed to Third World diseases, Lander said, because these have been neglected in the past, and understanding the diseases could benefit all countries. Bioengineering similarly has been neglected because many NIH study sections simply didn't see "building tools" as an appealing way to spend money. Research on stem cells and genetic engineering techniques is another booming area that could benefit from additional funds.

In an interview, Alberts recalled that as the morning wore on, various participants in the Sunday gathering would get up to make sandwiches for themselves from the deli offerings he had laid out. Sunlight danced on the Potomac River, visible from Alberts' apartment, but the gatherers were not distracted from their task. A key point emerging from the discussion of funding mechanisms, Alberts said, was a surprising negative: that money should *not* just be poured into funding more RO1 grants. "We need to do something more creative," he said.

Tending to Talent

Lander told the ACD that as the Sunday gathering addressed mechanisms for supporting science, they suggested funding should be used to "keep bright people in the system." This might require some long-range rethinking of optimal numbers and sizes of grants, perhaps leading to loosening up the currently narrow range of grant sizes. At present, Lander said, grants cluster tightly around an average size of \$160,000, with support for 1.7 full-time scientists. In remarks tinged with shades of the existing NIH intramural program, Lander said that focusing instead on providing long-term support of a particular scientist would make it easier for him or her to switch fields as interests changed and would smooth out funding peaks and troughs that can squeeze productivity or even create "cliffs" that spell the end of scientists' careers.

In the broad area of training, the Sunday session cited training medical researchers as a priority for increased funding. Participants also felt that the level of support provided by NIH biomedical training grants should be reexamined: It does not appear to compare favorably with other fields, and more attention

should be devoted to attracting minority scientists to biomedical research.

Building up infrastructure to support growth in biomedical research would also be important, Lander said. The Sunday assembly concluded that large, shared instrumentation was "grossly undercapitalized." Major shared facilities should be considered in the areas of combinatorial drug screening, advanced light sources for molecular structure, brain imaging, and computing. With respect to light sources, Lander said new X-ray synchrotron beam lines are needed for crystallography, with appropriate staffing and technical assistance to allow researchers at the proposed center to solve one molecular structure per day. Additionally, funds should be applied to the renovation or reconstruction of transgenic mouse facilities and perhaps a single, nationally shared clinical-trials facility.

Fair Sharing

Alberts said one of the things he found most surprising was the willingness of the mavens assembled in his apartment to accept the concept of creating shared core facilities, which inevitably would require some central, top-down planning. Alberts observed that this goes strongly against the common grain: Scientists have typically expressed a preference for the bottom-up, investigator-initiated approach of the RO1 and against top-down mandates such as the War on Cancer.

Lander's discussion of shared facilities drew strong reactions from ACD members. Marc Kirschner, chairman of the Cell Biology Department at Harvard Medical School in Boston urged that the integrative approach—bringing together teams of scientists—should be a fundamental theme. Two areas, physiology and pharmacology, appear destined to undergo profound changes in the immediate future, thanks to the creation of transgenic mice and the vast numbers of genes that are now being sequenced, Kirschner said. Proportional to the increase in sequenced genes, he predicted, would be a huge number of chemical reagents that scientists would want to create and study through high-throughput screening. This would place demands on bioinformatics comparable to those emerging from gene discovery and would also necessitate the development of powerful chemistry research tools, protein-profiling systems, and mass-spectrometry approaches. These would require teams of scientists,



including chemists, engineers, and computer scientists, as well as molecular biologists, pharmacologists, and clinical investigators who could then apply discoveries to the detection, treatment, and prevention of specific diseases.

Kirschner's vision of such integrative science facilities sounded familiar to ACD member Philip Needleman, senior vice president of the Monsanto Company in St. Louis. Needleman esti-

imated that if, to date, there had been 500 proteins identified as possible targets for therapeutic intervention, then in the years ahead there could be 100,000. In industry, he said, discovery of a juicy therapeutic target would result in a company tasking dozens of pharmacologists, chemists, and molecular biologists to the project. This sort of approach would not likely be possible for academia, he observed, and if the government were to head in this direction, it should work on diseases companies wouldn't pursue due to inherent lack of profit potential.

All-Stars Approach

ACD member Shirley Tilghman, professor of molecular biology at Princeton (N.J.) University, suggested that academic scientists might not be attracted to the large-team-approach in tackling scientific problems because this was fundamentally contrary to the culture of universities, which rewards the individual for independent achievements. "We aren't training people for this," Tilghman stated. She then asserted that government-supported centers established in the past were not good models for group efforts because some of the research conducted there was not of the highest quality.

ACD member Susan Horwitz, a professor at Albert Einstein College of Medicine, added that often the potential members of integrated research teams—MDs and PhDs—spoke "different languages," and finding time to fit in cross-training would be very difficult because thesis projects are becoming increasingly complex.

As the ACD discussion moved on to other areas and toward the morning coffee break, there seemed to be a sense that Alberts' Sunday soundings had painted an exciting big picture, but that was actually the easy part. Resolving problems like changing the culture of science and creating integrated teams of cooperative scientists to pursue the vision would take more than 30 bright minds and one Sunday. ■

AU REVOIR

National Institutes of the Wacky Fun-page Grab-bag Last-But-Not-Least and Not-Exactly-Not a Dent Cartoon Thinga-majammy (copyright geekstuff incorp. 1998)



Top 10 Icky Lab Things

- 10) Computer keyboard layered with finger grime and food bits
- 9) Strange media spills in the tissue culture hood
- 8) Lyophilizer condensate
- 7) Old dusty things stored behind radioactive waste
- 6) The inside of a heavily used but never cleaned microfuge
- 5) The thick coating of dust on old chemical bottles
- 4) Lab microwave
- 3) Common lunch room microwave (particularly after heating fish)
- 2) Common lunch room floor
- 1) Burn box that hasn't been changed for three months



Lamest Cheer for Boosting Lab Spirit

"Give me an L, give me an A, give me a B, what's that spell?, LAB, LAB, YAY!, LAB!"

Top 3 Cartoon Ideas that Never Got off the Ground

- 3) So, you want to be a P.I.?
- 2) Cancer Commandoes
- 1) Studs of Science--

This is my pipetman, this is my gun, one is for manipulating DNA, the other's for fun



Choosing the Ideal Post-doctoral Fellowship: Choose your project, your labmates, your PI, and your lab environment! (Unfortunately, you only get one top choice, and you have to pick at least one number four choice. Example: Project #1, Lab-mates #2, P.I. #3, & Lab Env. #4)

Projects

- 1) Answers an important question, will get you a top-notch paper, and will help you get a job
- 2) Answers a question and gets you a good paper, doesn't really lead you anywhere
- 3) Answers a question that only three other people in the world care about and may or not be publishable
- 4) A total fishing expedition guaranteed to drive you insane

Lab-mates

- 1) A professional mix of students and post-docs who are competitive yet nurturing
- 2) A group of career-minded post-docs who don't care whether you sink or swim
- 3) A collection of career post-docs who lead a fun-filled life but are insecure about their work
- 4) A group of psychotic NIH veterans guaranteed to drive you insane

P. I.

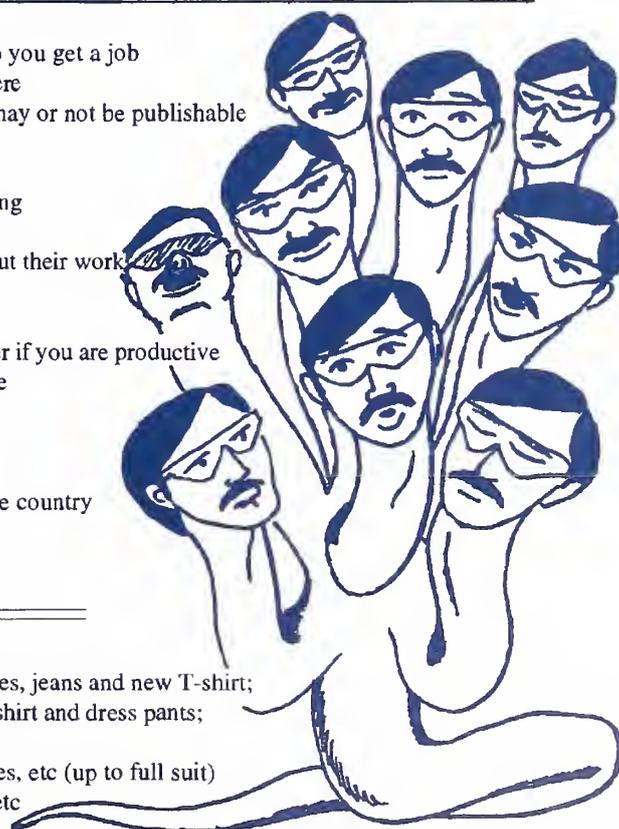
- 1) A smart, energetic, and respected researcher who will gladly further your career if you are productive
- 2) A smart and ambitious researcher who will burn you up like a two-cent candle
- 3) An over-the-hill codger who won't leave you alone
- 4) A psychotic martinet guaranteed to drive you insane

Lab Environment

- 1) Beautiful spacious facilities, windows with a view, in a desirable region of the country
- 2) Beautiful spacious facilities, windows with a view
- 3) Average facilities, no view, in a not so desirable region of the country
- 4) An older NIH lab, guaranteed to drive you insane

Clothes and Advancement in Science

- 1) Graduate student: old sneakers, shorts and old T-shirt; 2) Post-doc: tennis shoes, jeans and new T-shirt;
 - 3) Asst. Prof: loafers, slacks and polo shirt; 4) Tenured Prof: dress shoes, dress shirt and dress pants;
 - 5) Senior Prof: dress shoes, dress shirt with bow tie, dress pants, blazer
- For M.D.-- post-doc wears level three clothes, Asst. prof wears level four clothes, etc (up to full suit)
 For Californian-- Post-doc wears level one clothes, Asst. prof wears level two, etc



Analogies to science:

- CellScienceNature paper (first/last author)
- Attend meeting
- Speak at big meeting
- Graduate student
- Post-doc
- Asst. prof.
- Tenured prof.
- Prof. Emeritus
- Nobel prize

baseball

- big league home run
- on the road
- on the all-star team
- college ball
- minor leagues
- major leagues
- big money contract
- retired
- hall of fame

pop music

- top ten hit
- on tour
- sell out Madison Square Garden
- garage band
- club band
- signed to record label
- three platinum albums
- has-been
- legendary artist

fast food industry

- bonus
- attend motivation session
- give motivation session
- dishwasher
- french fry guy
- cashier
- manager
- industry giant
- own the franchise

CALL FOR CATALYTIC REACTIONS

In this issue, we are asking for your reactions in four areas: fostering research teamwork, interest group experiences, spending preferences, and cartoon creation.

Send your responses on these topics or your comments on other intramural research concerns to us via e-mail:
<catalyst@nih.gov>;
fax:402-4303; or mail:
Building 1, Room 209.

In Future Issues...

- NIAID's Big Sky Laboratory
- Catalytic Cauldron: Tales from the Labs
- TLC and TCB: Social Work at NIH

1) What steps can NIH take to encourage the formation and function of effective research teams?

2) Are you satisfied with the scope and organization of the current roster of NIH interest groups? What have you gotten out of your participation in an interest group?

3) How would you recommend NIH spend expanding research money?

4) Alex Dent's farewell *potpourri* appears on the other side of this page, as have his "Joe Postdoc" cartoon adventures since the January 1994 issue of the *Catalyst*. He's off to Indiana, from whence we hope he'll favor us with cartoons from the other side from time to time. But we are repeating our call (first aired last issue) for closet NIH cartoonists to push some of their efforts under our door (or fax them to 402-4303). A few of you have already done so (thank you, thank you, you'll be hearing from us), and we'd like a few more—kind of a rotating cartoon corner to display the multiplicity of humors bubbling on the NIH campus.

The NIH Catalyst is published bi-monthly for and by the intramural scientists at NIH. Address correspondence to Building 1, Room 209, NIH, Bethesda, MD 20892. Ph: (301) 402-1449; fax: (301) 402-4303; e-mail: <catalyst@nih.gov>

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