Fostering Communication and Collaboration

The NIH Catalyst

A Publication for NIH Intramural Scientists

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OBSSR Retreat

Behavioral and Social Scientists Map Course in the Era of the Genome

by Christopher Wanjek with additional reporting by Rich McManus, NIH Record

The mantra "bench to bedside" conjures up many images, but perhaps not one of a bedside scene with a father reading *Curious George* to his child at nighttime.

On the NIH campus, where the focus traditionally has been on biomedical research, this concept may come across as an eye-opener: Translational research may not require lab coats and microscopes, catheters and IV clamps.

In the fields of behavioral and social sciences, the "bench" can be the rest of the world outside the laboratory, where a researcher might establish the mechanisms to change behavior. The "bedside" becomes the point of delivery of a thoroughly tested intervention: reading to a child to improve literacy; mentoring and athletics to reduce the risk of teen drug abuse; or school-based dental education programs to improve oral health.

OBSSR Acting Director Christine Bachrach poses one of many frank questions at the Behavior and Social Sciences Retreat.

Consider that in lieu of a vaccine, condoms and sex education have been the most effective means to reduce HIV transmission. Condoms were far less used a few generations ago. A behavior change has occurred. How's that for a bedside intervention.

continued on page 8

The Future of Cancer Stem Cell Research

An NIH Research Festival Report

by Vanessa C. McMains, NIDDK

This year's NIH Research Festival brought forward cutting-edge research questions and signaled new directions for top-notch NIH labs. One of these hot fields was featured in a symposium titled "Cancer Stem Cells and Tumor Biology: Challenges Today and Promises for the Future." This relatively new field extends back only about 10 years, during which time some major difficulties have persisted in simply classifying the specific types of cancer stem cells from different tumors. But progress towards understanding them is being made, and new cancer therapies are on the horizon from the research happening here at NIH. Vanessa McMains of NIDDK reports.

Cancerous to the Core

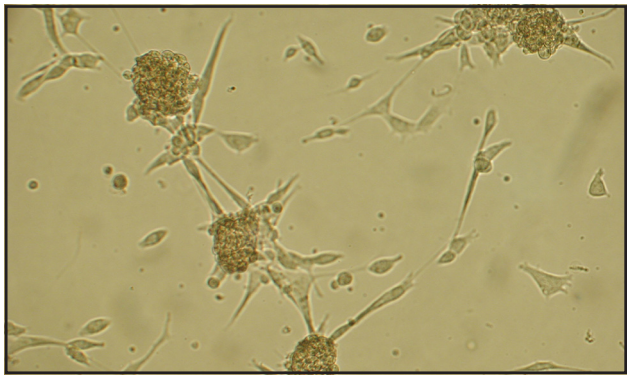
Cancer, as with all "tissue," appears to have its origin in stem cells. And just as skin cells die and are replaced with new cells, so too can cancer return after a vigorous course of treatment to kill it.

Stem cells are undifferentiated cells or precursor cells that give rise to other cell types that eventually mature into the specialized cells found in tissues. Adult stem cells are found in all body tissues and are responsible for maintaining the normal turnover of cells and regenerating damaged tissues.

When cells accumulate mutations that cause them to grow uncontrollably and migrate to other parts of the body, we cll this cancer. If one of the body's imperative stem cells becomes cancerous, it becomes a cancer stem cell. All the progeny born from that cancer stem cell will also be cancerous.

A cancer stem cell is also thought to arise from a specialized cell that becomes cancerous and reverts back to an undifferentiated state. This cell is then able to divide and give rise to more cancer cells.

This is not as straightforward, however, as it may seem. There's much dispute over how cancer stem cells come about. Typically, cells in a tumor are very heterogeneous. To get that sort of variety, these tu-



Skin cancer cells form spheres "tethered" to underlying irradiated NIH3T3 feeder layer. A small percentage of these cells can produce tumors, suggesting the presence of cancer stem cells. Photo courtesy Jonathan Vogel, NCI.

continued on page 10

CONTENTS

From the Deputy Director for Intramural Research

Revitalizing Clinical Research at the NIH

Michael Gottesman

Dan Kastner

With a new year and new administration upon us, it is with brimming optimism that we announce the creation of the Intramural Clinical Research Steering Committee (ICRSC) led by Dan Kastner, NIAMS clinical director and now the first Deputy Director for Intramural Clinical Research (DDICR). The overarching goal of the DDICR and ICRSC is to help revitalize clinical and translational investigations in the NIH intramural research program (IRP).

As detailed in previous issues of *The Catalyst*, we find ourselves at a critical juncture with the intramural clinical research enterprise having been eroded by a number of long-standing trends, some peculiar to the IRP and some common to the broader clinical research enterprise, exacerbated by five years of flat NIH budgets. Our challenge is to develop a visionary agenda and novel paradigms that will allow the IRP to take full advantage of its unique opportunities in clinical and translational research within the broader context of the NIH mission.

The IRP has been and should continue to be ideally suited to clinical and translational research, with the world's largest research hospital in close proximity to first-rate basic science, stable funding that permits patient cohorts to be followed over prolonged periods, a review system that encourages projects with substantial intellectual risk but the possibility of great benefit, and the ability to admit patients and perform studies without the permission of third-party payors.

In the setting of increased outside scrutiny by patient advocacy groups desperate for cures, a new administration sympathetic to renewed growth in biomedical research, and a new NIH director yet to be chosen, change of some sort is imminent; and it is incumbent upon us to bring our own experience to bear in formulating the best possible plan to maximize the clinical impact of the IRP.

In a subsequent issue of *The Catalyst*, Dan, my co-author for this editorial, will outline his own perspective on intramural clinical research, summarize what he believes to be the critical challenges facing clinical research in the IRP, propose essential steps to reinvigorate our intramural clinical research enterprise, and summarize the role of the DDICR in clinical research and the current activities of the ICRSC.

As spelled out in the ICRSC Charter, the DDICR chairs the ICRSC, approves appointments for tenure-track clinical Investigators, reviews the career pathways of Staff Clinicians, and serves on the NIH Clinical Compensation Panel, the NIH Compensation Committee, the Central Tenure Committee (ad hoc), and the Board of Scientific Directors (ex officio). The DDICR also advises the DDIR and the NIH Director on issues related to intramural clinical research.

The ICRSC was established by the DDIR as a forum for trans-NIH governance and policy development in the area of human subjects research. The current membership includes two IC Directors (Betsy Nabel of NHLBI and Griff Rodgers of NIDDK), two Scientific Directors (Lee Helman of NCI and Richard Nakamura of NIMH), four Clinical Directors (Richard Cannon of NHLBI, Bill Gahl of NHGRI, Markus Heilig of NIAAA and Carter Van Waes of NIDCD), two active clinical investigators (Steve Holland of NIAID and Shelia Zahm of NCI), an IRB Chair (Howard Austin of NIDDK), and an IRB Administrator (Jean Radcliffe of the Neurosciences Combined IRB).

Ex officio members include John Gallin, director of the Clinical Center; Cliff Lane, chair of the Medical Executive Committee; Charlotte Holden, director of the Office of Human Subjects Research; and Ezekiel Emanuel, head of Bioethics in the Clinical Center.

The current ICRSC Charter lists two specific areas of initial focus: (1) standards and strategies for the development, review, and implementation of human subjects protocols, including IRB operations, support, and accountability, and ethical interactions with the pharmaceutical industry (including technology transfer); and (2) standards and strategies for the development, review, and implementation of human subjects research more broadly, including the scientific review of protocols, and the BSC review of clinical programs.

The ICRSC will meet the second and fourth Monday each month in the CRC Medical Board Room. In addition to planned meetings with groups of intramural clinical investigators and human subjects protection professionals, Dan invites all members of the clinical research community to attend and participate in the discussions that will reinvigorate clinical research at the NIH.

Clearly, we stand at the threshold of a new adventure in the life of the NIH IRP. While the clinical program is not the only unique aspect of the IRP, it is certainly an important one. As stewards of this precious public resource, it will be our own responsibility and great privilege to have a role in refocusing clinical and translational research for a new era.

—Michael Gottesman, DDIR
—Dan Kastner, DDICR

Jennifer Lippincott-Schwartz: Down to the Nanometer

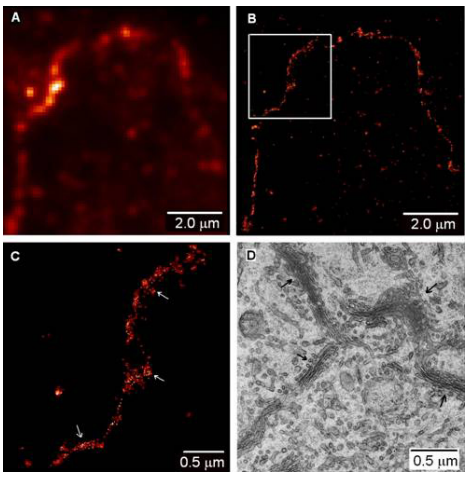
Anita B. Roberts Lecture Series, Distinguished Women Scientists at NIH

by Kara Lukasiewicz (NICHD) and Gail Seabold (NIAAA)

Jennifer Lippincott-Schwartz, head of the NICHD Section on Organelle Biology, delivered the fifth lecture in the Anita B. Roberts Lecture Series, Distinguished Women Scientists at NIH, on October 30.

One of 16 women elected to the National Academy of Sciences just a few months earlier, Lippincott-Schwartz discussed the latest advances in a rapidly expanding field she has helped create, employing fluorescent protein tags to attain nanometer-level resolution of cellular organelles. Her talk, "Emerging Fluorescence Technology for the Analysis of Protein Localization and Organelle Dynamics," attracted a capacity crowd to the Lipsett Amphitheater.

The lecture series, sponsored by the NIH Women Scientist Advisors Committee and Office of Research on Women's Health, honors Anita Roberts, a world-renown expert on transforming growth factor-beta (TGF-β) in wound healing and cancer. Roberts died in 2006 from gastric cancer after a stellar 30-year career at NCI. The series highlights outstanding research achievements of women scientists in the NIH Intramural Research Program.



As published in [1], comparative total internal reflection fluorescence, or TIRF, (A), and Photoactivation Localization Microscopy, or PALM, (B), images of the Golgi apparatus in a cryo-prepared thin section from a COS-7 cell expressing mEos-FP-tagged GalT. Higher magnification (C) of the box in (B) reveals a complex morphology not resolvable by TIRF, with thicker and thinner regions (arrows, C) similar to those seen in different cross-sectional TEM views of the Golgi apparatus (arrows, D) in a similarly prepared section.

Like Roberts, Lippincott-Schwartz is a highly regarded mentor and scientific pioneer. In 2002, she and NICHD colleague George Patterson revolutionized the field of fluorescent protein tags with the creation of photoactivatable green fluorescent protein (GFP). This allows for activation of a specific population of tagged protein by laser light, thus permitting the study of that specific population alone.

Not only has Lippincott-Schwartz created tools for the study of protein dynamics, but her laboratory also has developed photoactivated localization microscopy (PALM) in collaboration with Eric Betzig and Harald Hess of HHMI's Janelia Farm in Loudoun County, Virginia. This technology enables nanometer resolution of fluorescently tagged structures, a vast improvement over the typical resolution of standard confocal microscopy.

Her lecture discussed the evolution of imaging reagents, from the discovery of GFP—which earned Roger Tsien, Martin Chalfie and Osamu Shimomura the 2008 Nobel Prize in Chemistry—to the emerging technology that enables scientists to track the movement of single molecules in cells. She used examples from her lab to explain live cell imaging approaches that can be used to analyze the dynamic interactions of molecules in cells involved in protein transport, cytoskeleton dynamics, organelle assembly and disassembly, and the generation of cell polarity.

Lippincott-Schwartz also discussed the use of photoactivable GFP to assess the inter-compartment exchange of proteins that move from the endoplasmic reticulum (ER) to the plasma membrane, and proteins with photo-switchable tags, which turn from green to red with ultraviolet light and enable scientists to follow the photoconverted molecules overtime. She exploits this technology in PALM, using transmissive electron microscopy to better visualize cellular structures such as the ER network or to track single-molecule movements with quantum dots.

Lippincott-Schwartz told her audience how she foresees the use of iPALM (interferometry + PALM), being developed by Hess at HHMI, as a means to visualize three-dimensional organelles such as Golgi stacks and to create a topographical map of the cell terrain.

A major part of Lippincott-Schwartz's work is mentoring. She has trained many postdoctoral fellows to become independent academic investigators. "Jennifer taught me to not stick to the safe questions, to go for what's interesting," said Nihal Altan-Bonnet, a former postdoc now an assistant professor at Rutgers University, in a feature article about Lippincott-Schwartz in The Scientist. "I definitely wouldn't want to do science any other way." Altan-Bonnet has co-authored nearly a dozen papers with her mentor.

Jennifer Lippincott-Schwartz delivered the fifth lecture in the Anita B. Roberts Lecture Series, Distinguished Women Scientists at NIH, on October 30.

Similarly, Anita Roberts demonstrated that it is possible for women to balance an award-winning scientific career and great mentorship with a devoted family life. She had a "science is long, but life is short" attitude for herself and her lab members, said colleague Kathy Flanders of NCI.

Although Roberts had high expectations of her postdoctoral fellows, she was well known to encourage her lab members to live life to the fullest, especially outside of the lab. This attitude is part of the reason she will always be remembered as a mentor, not only to the members of her own laboratory, but to anyone in the TGF-β field. Her infectious enthusiasm helped recruit many talented scientists into the field, fostering a cooperative TGF-β research community. ■

1. E. Betzig, G. H. Patterson, R. Sougrat, O. W. Lindwasser, S. Olenych, J. Bonifacino, M. W. Davidson, J. Lippincott-Schwartz, and H. F. Hess, Imaging Intracellular Fluorescent Proteins at Near-Molecular Resolution. Science 313 1642-45 (2006).

The Exit Interview: Questions for Elias Zerhouni

Elias Zerhouni stepped down as NIH director at the end of October to pursue writing projects and explore other professional opportunities. A physician-scientist and world-renowned leader in radiology research, he had served as NIH director since May 2002.

Zerhouni came to the NIH speaking of a "perfect storm" with a new federal deficit, a teetering economy and a focus on terrorism conspiring to threaten NIH funding. And indeed he faced a stagnating budget as well as numerous ethical challenges, such as stem-cell research and conflict-of-interest cases. The former director looks back on his tenure in the following Catalyst "exit" interview.

§ § §

No one said the job would be easy. But what did you find particularly challenging about directing NIH as a whole and specifically its intramural program?

Truly, every day brought new challenges. In 2002 when I spoke to the Board of Scientific Counselors, I described a "perfect storm" as our government went from fiscal surpluses to deficits, facing a "teetering economy"—seeing many new security measures and expenses shifted to the war on terrorism—and what was then the "possibility" of a war in Iraq. All this just as NIH was to receive the final installment of its promised five-year budget doubling. As we are now, NIH was under a continuing resolution, and I needed to start off trying to create a soft landing. We were also receiving criticism from many parties for being too unwieldy and siloed and that the doubling of the NIH budget did not seem to have been strategically planned or implemented to maximize its potential.

I was determined that we would look at new ways of collaborating across the NIH and across the scientific enterprise and change those perceptions. We needed to adjust to many outside problems and some internal ones with conflict of interest. Throughout all the challenges, I was constantly inspired by the work of NIH's intramural scientists. At the end of the day, the remarkable work and the productive transfer of science that grows new science is a thrilling continuum. I will miss the stimulation of our intramural program and will remember this group with great pride and affection, especially the scientists with whom I interacted closely when I was excited by their research.

What qualities should the next president seek in choosing a new NIH director?

The new director will need the ability to lead and to listen. This is a remarkable place with so many dedicated and brilliant people committed to exploring scientific possibilities and improving human health that it is really the role of the NIH director to ensure the scientists have all the resources and the support that he or she can muster. This will increasingly mean finding ways to leverage not only physical resources, but [also] intellectual capital in collaborative ventures that take the most benefit from what we have with which to work.

Photo: ServicePhoto Elysée AR.

In April 2008, French President Nicolas Sarkozy awarded Algerian-born Elias Zerhouni the Légion d'honneur, the French National Order of the Legion of Honor, the highest decoration in France.

What challenges await the new director—challenges, perhaps, that you didn't have to face?

There are serious economic stressors, and those are likely not only to affect our technical resources [and] provide new pressures for our own staff in their professional and private lives, but also to stress the systems we work in and the general public. There are likely to be many challenges related to the prioritization of budget needs across so many areas. Leaving at this time, I am pleased to note that both candidates for president have expressed a commitment to science.

Photo: NIH

Elias Zerhouni was the 15th director of the National Institutes of Health, serving from May 2002 to October 2008.

I believe that the extramural community will be trying to sort out their best way to handle conflict of interest in the institutions across our portfolios. I hope that we have put in place some programs that will generate support for newly minted scientists and that future directors will meet the challenge of bringing the public to a better understanding of science. Moreover, I think that the intramural research program should continue to take risks and collaborate more on bold ideas, as the greatest risk for science in tough times is to stop taking risks.

The NIH press release announcing your departure listed your numerous accomplishments. What do you feel were your top accomplishments for the intramural program?

They are really your accomplishments! I am pleased to see the healthy growth of technology transfer and the new materials that have been put in place to help connect our researchers with those beyond our campuses.

"There are serious economic stressors and those are likely not only to affect our technical resources, but provide new pressures for our own staff in their professional and private lives…. I think that the intramural research program should continue to take risks and collaborate more on bold ideas, as the greatest risk for science in tough times is to stop taking risks."

Was there any issue you felt could have been handled better?

I am sure we all agree that we could have reached the conflict-of-interest solutions less painfully. However, we were in new territory for the agency, and we needed to assure the American public that we were being the best stewards of our privileged resources and maintain their full trust in NIH. But I wish we had more time to work together before so many external pressures came into the picture.

What unique opportunities do you see for the intramural program?

I see limitless opportunity in unlocking disease processes as well as conquering many acute and chronic diseases. Collaboration is going to make a significant difference in how we tackle the complex problems of obesity and addiction. We have gained so many insights into processes through both dissecting the genome and seeing through, behind, and around the technical walls that until the development of new imaging tools had limited our abilities. I see the growth and development of multi-disciplinary approaches and the preemptive, predictive and, in the best sense, personalized medicine here at NIH. I will look forward to seeing how nanomedicine and virtual tools will enhance your ability to explore.

"Collaboration is going to make a significant difference in how we tackle the complex problems of obesity and addiction…. I will look forward to seeing how nanomedicine and virtual tools will enhance your ability to explore."

You had some bittersweet moments here, such as taking second in the CFC kickoff country music dance contest. What ranks among your fondest memories at NIH?

This is one of the few times I've been honored to be second! Alfred [Johnson] really knew what he was doing. About fond memories: walking through the labs, talking to scientists, being fortunate enough to be able to hear about what is about to break before the news goes out into world. I have been moved by the words of the patients you have treated. Every Tuesday morning, I've enjoyed the advice and council of your leader, Michael Gottesman, a truly remarkable individual who looks out not only for the interests of the DIR, but also for those of science and scientists. I will miss working with him and with all of you.

Your letter to the NIH staff mentioned your interest in writing projects. Care to share what this might be? Fiction, or a stranger-than-fiction factual exposé on the NIH directorship?

No exposés! Life is much more interesting than fiction on most days. I've started working on several possibilities, but you can be assured however it turns out, it will be about science and my abiding belief that NIH is truly one of the wonders of today's world, bar none.

The NIH faces the possibility of a delay in the appointment of your replacement. Is there any unfinished business you would like to see completed within a year?

I am glad that the [DHHS] Secretary appointed Dr. Raynard Kington as acting director, He is "battle-tested" and has and will do great job in this transition. I have appointed twelve Directors, and all the IC Directors are working in a very collegial way through the governance structures I put in place. I am sure that finishing the reform of peer review will be important, and Raynard is committed to see it through as appropriate. I feel that NIH is in good hands to go through a smooth transition period, however long it turns out to be. ■

Photo: NIH Record

Yep, it's real. Zerhouni with NIDCD Director Lawrence Tabak, keeping his pledge to grow a beard if the 2007 CFC contribution goal was met. "I will miss the stimulation of our intramural program and will remember this group with great pride and affection," Zerhouni said upon his exit.

"…we all agree that we could have reached the conflict-of-interest solutions less painfully. However, we were in new territory for the agency…"

Highlights of Elias Zerhouni's Tenure

Elias Zerhouni, a physician scientist and world-renowned leader in radiology research, led the agency through a challenging period. One of the hallmarks of his tenure is the NIH Roadmap for Medical Research, launched in 2003.

Zerhouni also launched new programs to encourage high-risk innovative research, such as the Director's Pioneer Awards and New Innovator Awards, and focused especially on the need to support new investigators and foster their independence. During his tenure, Zerhouni worked to lower barriers between disciplines of science and encourage trans-NIH collaborations. He inspired significant interdisciplinary efforts such as the NIH Strategic Plan for Obesity Research and the Neuroscience Blueprint.

Other highlights include Clinical and Translational Science Awards, Molecular Libraries, Human Microbiome Project, Epigenomics Project, Structural Biology Roadmap, Pathway to Independence Awards, Transformative R01 Program, NIH Public Access, and the Public Trust Initiative.

The Training Page

From the Fellows Committee: Award Analysis—What's Fair is FARE

by Lori Keating (FDA) and Jennifer Shen (NCI), FelCom's FARE 2009 Co-Chairs

The Fellows Award for Research Excellence (FARE) competition recognizes outstanding scientific research performed by intramural postdoctoral fellows at the NIH and has been held annually since 1995. FARE winners receive travel award money to attend and present their work at a scientific meeting.

FARE is one of the major activities organized and implemented by the NIH Fellows Committee (FelCom), and it is sponsored and supported by the Office of Intramural Training and Education (OITE), the Office of Research on Women's Health (ORWH), and the Scientific Directors of Institutes and Centers at the NIH.

For the FARE competition, an applicant submits an abstract online and chooses three study sections related to his or her research. At the end of the submission period, these abstracts are assigned to each applicant's first, second or third study section choice. Abstracts in each study section are then evaluated by a panel of volunteer judges, which includes postdoctoral fellows and tenure-track and tenured investigators from the NIH community.

Several fellows raised concerns recently that abstracts might have been unfairly judged if placed in the second or especially the third choice of study section. To determine whether there is a correlation between the FARE competition outcome and the assigned study section, the FelCom FARE subcommittee analyzed the FARE 2009 data and obtained the following results:

- 798 of the 1043 abstracts (77%) were assigned to their first choice of study section.
- For abstracts placed in first, second, and third choice of study section, 26%, 28%, and 23%, respectively, won an award.
- Based on the FARE 2009 data, it was concluded that there is no correlation between the study section assignment and FARE competition outcome.

A similar conclusion was drawn based on 2008 data analysis. For abstracts placed in the first, second, and third study section of choice, 24%, 27%, and 28%, respectively, won an award. In summary, analysis based on FARE 2008 and FARE 2009 data has discredited the belief that assignment to the first study section of choice warrants better FARE competition outcome.

We welcome your comments, as we are always working to improve the FARE process. We want to ensure that abstracts are judged fairly and anticipate the continued and increased participation from the NIH community.

We would like to remind those considering applying for FARE 2010 that the earlier an abstract is submitted, the greater the chances that it will be placed in the first choice of study section. Look for the call for applications in early spring, 2009. Fellows who would like to get involved are encouraged to join the FelCom FARE subcommittee for next year's competition. ■

From the Fellows Committee: Calls for WALS

by Ram Kumar Mishra (NICHD), FelCom Publicity Committee

The Director's Wednesday Afternoon Lecture Series (WALS) is one of the main opportunities at the NIH to hear top researchers in basic and medical sciences from across the world. Held most Wednesdays at 3 p.m. in Masur Auditorium, the WALS has been an outstanding forum to bring leaders of scientific distinction to the NIH community since it was conceived in 1952 and in the present format since 1994.

In November, the Office of Intramural Research issued a call for nominations for the 2009–2010 WALS season, which remains open until December 31, 2008. Anyone can nominate individually, although groups such as FelCom and the multitude of NIH Scientific Interest Groups have had great success in having their nominations chosen. This is because nominations from these groups reflect a consensus among many scientists.

Thus, FelCom is collecting nominations for WALS on behalf of the NIH fellows. You can nominate an admired scientist whom you met at a conference, collaborated with, or simply appreciate for his or her scientific achievements. Two speakers in the current WALS season were selected from the nominations made by fellows.

Nominating a speaker can be a fulfilling experience. If your nominee is selected for a WALS lecture, you may be an integral part of hosting the speaker. You could travel with the speaker from the airport or have a meal with him or her. You may even be asked to introduce the speaker at the seminar. This is an excellent opportunity to meet an admired scientist.

To nominate a scientist for a WALS lecture, send e-mail to Julie Wu (wujulie@mail.nih.gov) with "WALS nomination" in the subject line by December 26. Please furnish the nominee's name, professional title, institutional affiliation and contact information. A brief paragraph highlighting the nominee's research interests and qualifications always helps.

Please check the WALS website (http://www1.od.nih.gov/wals) to avoid nominating a recent speaker, because preference is given to individuals who have not presented recently. WALS special lectures are also listed at this website. Fellows may also nominate speakers for the WALS Cultural Lecture. This lecture is given by a speaker with an ability to communicate fascinating aspects of science; this year's speaker is Atul Gawande, *New Yorker* magazine columnist and Associate Professor of Surgery at Harvard Medical School, who will present a lecture titled "Ignorance vs. Ineptitude: Science and the Causes of Failure in Medicine."

In addition, any fellow can enjoy lunch with WALS speakers to discuss scientific ideas. Go to the WALS website to sign up for lunch with WALS speakers.

Don't be shy: Take this opportunity to nominate your favorite scientist! ■

From the Office of Intramural Training and Education: Recruit Top Quality Graduate Students to your Lab

by Caroline Duffy, OITE

The NIH might not grant degrees, but that doesn't keep its Intramural Research Program from recruiting top-quality graduate students to its laboratories. And your lab can tap in to this resource.

More than 550 graduate students hailing from more than 100 universities around the world are working and studying here. Graduate students are active members of the community who serve as mentors to postbacs, lead journal clubs for summer students, teach FAES classes, and contribute a creative and energetic research approach.

Each February, OITE's Graduate Partnerships Program (GPP) invites approximately 120 candidates to interview for one of our 16 institutional partnerships. Candidates learn about intramural research, meet current graduate students, tour NIH labs, and discuss science with investigators interested in recruiting them for the upcoming year. After the visit, approximately 45 candidates join the GPP.

In preparation for the interviews, to identify scientists with whom they would like to speak, candidates use a GPP database of over 450 investigators who have indicated interest in mentoring graduate students in their labs. Any tenured or tenure-track investigator can be included in this database. If you are interested, discuss it first with your Scientific Director and then visit <https://gpp-nih.symplicity.com/investigator> to register.

If you have previously registered, we encourage you to visit the website to update your information. If a student asks to meet with you, the GPP will be in touch in January or early February to arrange a meeting during one of the recruitment days.

Whether in their senior year as undergraduates or in postbac positions, these candidates apply to the GPP for the chance to be a part of the NIH community and to access the outstanding scientific resources. The science here sells itself. Our main recruitment goal, therefore, is to showcase the student-friendly and supportive community. Your help is greatly appreciated. We would want you to chat with the prospective students about why science excites you, introduce them to the members of your lab, discuss the contributions of trainees to your research, and remind them that career and professional development opportunities are available through the institute/center training offices and through the OITE.

GPP recruitment will occur on Wednesdays and Thursdays during the last three weeks of February. Mark your calendars and join the database. ■

HERC: Herculean Tool for Recruitment

by Joslyn Yudenfreund Kravitz, AAAS Science & Technology Policy Fellow

Finding a job is never easy, but finding two jobs for a dual-career couple can be extremely challenging. In an effort to make that task a little easier for current and potential NIH employees, the NIH has partnered with Loyola College, the University of Richmond, and Washington and Lee University to establish the Mid-Atlantic Higher Education Recruitment Consortium (M-A HERC).

Twenty-two member institutions, including Georgetown University, American University, the University of Virginia, two campuses of the University of Maryland, and the FDA, now comprise the M-A HERC.

The main component of the HERC is its website, <http://www.midatlantic-herc.org>, which posts every available job at each of the member institutions. The website is unique in that it enables dual-career couples to link their individual areas of expertise and job requirements and search for two jobs simultaneously.

The M-A HERC is part of the National HERC, which includes ten other regional HERC affiliates. National HERC is working with JobTarget, the firm that manages the websites for the regional HERC affiliates, to implement the capability to search the job listings of multiple HERCs simultaneously, which would help job seekers look at jobs at institutions across HERC regional borders.

In October, representatives of the member institutions met at Natcher Conference Center for the inaugural meeting of the M-A HERC. Paula Alfone, the M-A HERC director based at Loyola College, opened the meeting, followed by NIH representatives Christine Major, director of the Office of Human Resources, and Joan Schwartz, assistant director of the Office of Intramural Research.

The main event was a talk by Ethan Bloomfield, JobTarget's vice president of sales operations. Bloomfield presented the OneClick Network, a listing of national and regional job boards, websites of professional societies, diversity-focused job boards and more. Member institutions can select up to seven sites from the network to which to send each position announcement in addition to the M-A HERC, and JobTarget will automatically post the job to those sites as well.

The day wrapped up with a roundtable discussion of how the member institutions can best take advantage of the M-A HERC network. Ideas generated included establishing an online discussion forum and topics for future meetings, such as best practices in diversity hiring and family-friendly policies.

The M-A HERC website.

The first HERC was developed in 2000 by colleges and universities in northern California. Plans for the M-A HERC were underway by late 2007 and quickly gelled, because the Mid-Atlantic region is so rich in colleges, universities, teaching hospitals and government agencies with a focus on research and training.

NIH's participation in the HERC was, in part, an effort of members of the NIH Working Group on Women in Biomedical Careers, co-chaired by NIH Director Elias Zerhouni and Vivian Pinn, director of Office of Research on Women's Health. ■

Behavior and Social Sciences Retreat

continued from page 1

The Framingham Heart Study, now part of the NIH intramural research program, provides an instructive example of a melding of behavioral and social science with biomedical science. Epidemiological perspectives made risk factors visible. The physiologists and other scientists leading this study were but loosely aware of them until biometricians digested the data that behavioral scientists were collecting.

NIH Acting Director Raynard Kington offered frank insight in his closing remarks.

Today at Framingham several massive and unprecedented genotyping projects are underway, searching for genetic risk factors that will best make sense in the context of environmental and behavioral risk factors.

The very essence of Public Health, with capital P and H, is the marriage of these disciplines. This was the case in the beginning of the 20th century, with hand-washing and vitamin-fortification programs. And it remains essential now as we unravel the entanglement of genetics and environment for the goal of making medicine more predictive, personalized and preventive.

How well does the NIH, and in particular its intramural programs, perform in this endeavor? This was a key question discussed at a November 12 retreat organized by the Office of Behavioral and Social Sciences Research (OBSSR) and a trans-NIH planning committee.

There was no sugarcoating of the issues. Questions on the agenda included "How do we thrive as behavioral and social scientists in an institution that is predominantly biomedical in orientation?" and "What lessons have we learned about how to successfully advance and integrate our sciences and their contributions to the NIH mission?"

"We have a gold mine of behavioral and social science research talent at NIH," said OBSSR Acting Director Christine Bachrach in her welcoming address to the more than 300 NIH-only retreat attendees at the Natcher Conference Center. "But we are scattered. I hope the retreat empowers and connects the field."

Glass One-Third Filled

Bachrach was pleased that nearly 30 percent of the retreat attendees came from the intramural community. "We do a much better job connecting with extramural than intramural."

She was also pleased with the representation from higher office. NIDA Director Nora Volkow and NIMH Director Thomas Insel were among those leading panel discussions. NIMH Deputy Director Richard Nakamura hosted one of nine breakout roundtable discussions, titled "Conversations with Senior Staff." NIGMS Director Jeremy Berg was in attendance, and NIH Acting Director Raynard Kington provided closing remarks.

NIDA Director Nora Volkow participated in a panel discussion.

Each was frank and critical of NIH's ability to incorporate biomedical research with behavioral and social science research and pointed to "big science" as the place where the largest gains can be made.

"Behavioral and social science research must continue to define their roles in the next generation of genomics research," said Kington, who led the OBSSR from 2000 to 2003 and whose research has focused on the role of social factors, especially socioeconomic status, as determinants of health. "Mapping the human genome is the biggest scientific achievement of our lifetimes. There has to be a vision for the behavioral and social sciences in understanding gene-environment interactions."

NIDA and NIMH are among the institutes most invested in behavioral and social science research. "I certainly believe we can improve the integration of what is considered behavioral versus biomedical sciences," said NIDA's Volkow after the retreat. "Brain imaging and genetics offer a good bridge to do this."

Berg, too, supports such interdisciplinary collaboration but maintains a slightly different stance. "I see this apparent barrier between behavioral and biomedical sciences as artificial, outdated and not helpful," he said.

NIGMS has initiated an extramural Ph.D. training program called "Behavioral-Biomedical Sciences Interface." The goal is to train students to be fluent in both behavioral and biomedical sciences and to bring the faculty together to develop a competitive program. And NIGMS's Models of Infectious Disease Agent Study (MIDAS) is a computational biology program to develop computer models that simulate how diseases spread through populations. This includes computer scientists, epidemiologists and infectious disease specialists, as well as demographers, sociologists and economists.

"The interplay between behavior and biology is crucial to many of the most important questions" that intramural NIH scientists ask each day, he said. "Even simple organisms can teach us much about human health and disease, and I am sure that behavioral traits will not be an exception."

Behavior Changes at NIH

Robert Croyle, director of NCI's Division of Cancer Control and Population Sciences, was a driving force behind the conception and organization of the retreat. He,

NCI's Robert Croyle (left) and NIMH Director Thomas Insel field questions from the audience.

too, participated in the morning panel discussion, "A Framework for the Future of BSS at NIH."

"We need to broaden the definition of translational research so that we're not just talking about drug development all the time," Croyle told attendees.

For the behavioral scientists who work here, the NIH "is like a university without a college of arts and sciences," he said. "Behavior and social science could be a linking discipline across the institutes… a tremendous amount of collaboration could occur at NIH, but does not because many institutes lack a critical mass of behavioral and social science researchers."

The presence of institute directors and other top biomedical scientists was encouraging to both intramural and extramural scientists in attendance, Croyle said, for the community used to feel like "fourth-class citizens" but have since ascended to second-class status.

Now, it seems, the opportunity is ripe for collaboration.

"The growth of team science has provided contexts within which biomedical and behavioral scientists can collaborate to address common problems through a broader set of methods," Croyle said after the meeting.

Nearly 300 NIH researchers attended the daylong behavioral and social sciences retreat at the Natcher Conference Center. About 30 percent of the attendees were from NIH intramural programs.

Biomedical and Behavioral Ivory Towers

Some attendees, speaking off the record, felt that the NIH has far to go in providing the kind of fluid academic environment that the best universities capitalize on.

For example, behavioral and social sciences themselves seem rigidly defined at the NIH, with research agenda incorporating quantitative aspects of psychology and sociology but little anthropology, economics, history or political science.

Also, disciplinary boundaries have been eroding for some time, and multiple disciplines now address common scientific objects or questions. Who is a cancer researcher? A geneticist, an epidemiologist, a biophysicist, an immunologist, an anthropologist? How does this situation jibe with the traditional NIH funding and reward mechanisms based on *intra*-disciplinary peer review?

There are physical barriers as well, Bachrach said, that hinder intramural collaborations. In the extramural community, scientists considering RFAs (request for applications) have access to an early notification system alerting them to grants pending in other NIH institutes and centers, which can spark collaboration. There is no such system linking what intramural and extramural scientists are doing.

Setting a Course

Other retreat topics included health disparities; community-based participatory research and community engagement; brain and behavior; health promotion, prevention and adherence; theories of behavior change; technology and health; measures, methods and data; health policy and quality of care; and social, environmental and psychological factors related to health.

Kington's advice to attendees was to "emphasize interventions for the short run, for the here and now, while continuing to expand our knowledge base for understanding fundamental causal pathways." He said "the [behavioral and social sciences] community should be leaders in portfolio analysis and the management of science."

John Haaga, deputy director of NIA's Division of Behavioral and Social Research, collecting ideas at one of the several breakout sessions asking such questions as "How do we thrive as behavioral and social scientists in an institution that is predominantly biomedical in orientation?"

Kington also didn't mince words about dwindling budgets and getting the most bang for the buck by forging interdisciplinary collaborations. "We're on the verge of a deep and lengthy recession, [so] more sophisticated arguments are needed in lean times," he said. "We will all be asked to do more with less."

The daylong event was filled with ideas and criticisms, which the OBSSR plans to digest in the coming months. But the retreat's goals were met. "We got people talking," Bachrach said. ■

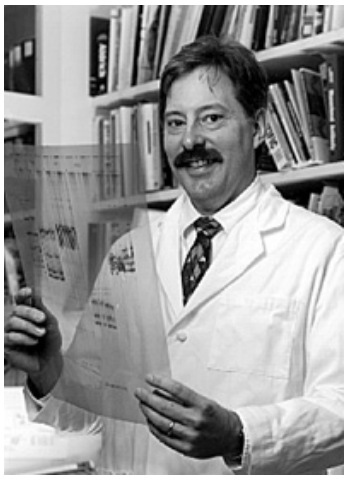
All photos by Michael Spencer, NIH MAPB.

Future of Cancer Stem Cell Research

continued from page 1

mor cells likely would have to come from cancerous stem cells, rather than cancerous specialized cells.

Treatment with cancer drugs eradicates tumor cells, yet years later the tumor can grow back. Why? Perhaps this is because cancer stem cells do not have the same characteristics of the tumor cells, for they are undifferentiated, and may be protected by the surrounding tumor or unaffected by the anti-cancer treatment administered. If a small population of cancer stem cells remains alive, they can propagate new tumor cells causing the cancer to return.



Jonathan Vogel's research festival talk was "Tumor Initiating Cells in Human Squamous Cell Carcinoma."

Worse, often the remaining cancer stem cells become resistant to the original treatment used in the first incidence of cancer, and so the same treatment will not work at a later time. In some types of cancers, as few as one cell in 10,000 is a cancer stem cell, but this tiny entity nonetheless can establish a whole new tumor.

By studying and understanding cancer stem cells, researchers can design specific treatments to specifically target and kill the cancer stem cells so that the tumor loses the ability to generate new cells. That's the research gamble, anyway.

There are many challenges in the field of cancer stem cell biology. Researchers must find a way to distinguish cancer stem cells from other cells in the tumor to allow these cells to be analyzed. Typically do so by detecting specific surface proteins or markers found on cancer stem cells from a specific tissue.

One of the caveats to these markers is that each tissue's stem cells may express different markers, and over time the profile of the markers may change. Finding ways to culture the cancer stem cells so they can be studied for any length of time is also important. Familiarity with the workings of cancer stem cells then allows new therapeutics to be designed to specifically target them. The combination of current anti-tumor treatments with additional anti-cancer stem cell treatments promises to be a powerful duet in the fight against cancer.

NIH investigators discussed four different cancer stem cell systems at the NIH Research Festival: skin, liver, breast and blood. Each of these individual systems is in its own stage of understanding and development. Some projects are in the early stages, and just getting cancer stem cell to grow in culture and characterizing them are important focuses. Other projects are entering the translational stage of knowledge to drug therapy.

Stem Cells: A History

by Dan Lednicer, Office of NIH History

The steps in the formation of adult life forms from a single cell had been satisfactorily elucidated by the 1890s. But the mechanism whereby some cells, such as those found in blood, were continually renewed was less clear. Russian biologist Alexander Maximow presented a theory of hematopoiesis in 1909 that accounted for blood cells' origin and differentiation. This formulation proposed that the various cells found in blood all derive from a common cell type: the stem cells. This still-current concept was to be found in Maximow's *A Textbook of Histology*; the seventh edition (W. Bloom co-editor) of this widely used book was published as recently as 1957.

The first clinical application of stem cells involved blood malignancies. Mouse experiments in the 1950s demonstrated the possibility of replacing diseased blood by blood-forming marrow from closely related healthy animals. Test animals were exposed to high-dose total-body irradiation to kill all blood cells. By the early 1960s researchers isolated stem cells in murine marrow and found that they both self-renewed and could become any type of blood cell. Administration of bone marrow, in effect, blood stem cells, then led to formation of new blood devoid of malignant cells. This technique was first applied to human patients in 1959, although it was difficult to find immunologically matched donors. The procedure involved administration of a sample of the patient's own blood marrow, collected just before irradiation. This method met with some success in various types of leukemia and is still used today.

Stem cells are present at the earliest stages of an organism's development— in blastocysts and later in their descendants, embryos—when different cell types are forming. These can produce any number of structures and organs and are thus pluripotent, in contrast to stems cells found in bone marrow, whose progeny comprises only hematopoetic cells. Stem cells were obtained from rabbit blastocysts in 1966. Murine embryonic stem cells, however, weren't cultured in vitro successfully until 1981. Stem cells from human blastocytes were first isolated and cultured in 1998.

The human embryonic stem cell's potential to develop into any of the 220 cell types is no longer present in adult stem cells. Thus, embryonic stem cells offer the greatest potential to treat diseases marked by loss or malfunction of specific tissues. Spare embryos from fertility clinics are at first glance an attractive source of embryonic stem cells. Only one or a very few embryos are selected for implantation in mothers-to-be from the group produced by in vitro fertilization of human ova. The rest are, as the euphemism has it, discarded. The proposal to use the discards for collecting stem cells for research has engendered a very emotional controversy among scientists, disease advocate associations, ethicists (on both sides) and spokespeople for various religious sects.

This controversy has in addition led to a widespread search for another source for pluripotent stem cells. It often seems that not a month passes without yet another announcement of a new source.

[This sidebar represents a new feature in *The Catalyst* to provide historical perspective on more recent NIH research advances.]

Snorri Thorgeirsson spoke on "The Case for Cancer Stem Cells in Human Liver Cancer."

Culturing: Skin Cancer Stem Cells

Research on skin cancer stem cells is in the early phases. Determining whether cancer stem cells are found in skin cancer tumors, such as squamous cell carcinoma, and harvesting the cells are the goals in the laboratory of Jonathan Vogel, a senior investigator in the NCI Dermatology Branch.

Atsushi Terunuma and Girish Patel, a staff scientist and visiting fellow in Vogel's laboratory, respectively, have developed *in vitro* assays to grow both normal keratinocyte stem cells and skin cancer initiating cells on feeder layers of irradiated human skin fibroblasts. The normal skin keratinocytes form a monolayer on the fibroblast feeder layer while the skin cancer cells form floating spheres that remain tethered to underlying feeder layer. The tethered spheres can be plucked up and re-cultured in a new flask containing a fibroblast feeder layer or transferred into mice. Only a few of the cells in each skin cancer sphere has the ability to form or initiate new tethered spheres.

Taking culturing to the next level, these investigators wanted to create more life-like conditions for growing human skin cancer stem cells, rather than as balls of cells, which is not the typical morphology in the body. After two and a half years, Vogel's lab has developed a system to grow the human skin cancer cells in the skin of immunocompromised mice. Human fibroblasts, 3-dimensional gel foam, and Matrigel are used to create a human-like environment that is needed to successfully grow the human skin cancer cells. In this culture system, the cells maintain their original cancer morphology (that is, they do not form strange spheres) and can be analyzed further.

Now that Vogel's lab has shown the existence of skin cancer cells and enabled them to grow in a more natural cultural system, they will begin observing changes that occur over time as the cells are transferred from one mouse to another, known as passaging. From here they can begin to study what properties define a skin cancer stem cell.

Jonathan Keller presented "Inhibitor of DNA-Binding (Id) Proteins as Potential Therapeutic Targets in Hematopoietic Malignancies."

Characterizing: Liver Cancer Stem Cells

Cancer stem cells in liver cancer still remain to be clearly defined. Liver cells, or hepatocytes, themselves have many characteristics in common with stem cells, such as longevity, the ability to proliferate extensively, and self-renewal; and they define a heterogeneous population of cells. The liver itself is one of the most resilient organs in the human body, able to completely regenerate if as much as 70 percent is destroyed.

The research focus of Snorri Thorgeirsson, chief of NCI's Laboratory of Experimental Carcinogenesis, is to identify the origins of liver cancer with data from human, mice and rat liver tissue and tumors in a process called Integrative Functional Oncogenomics. He and his colleagues compare the expression of genes between samples to find common or distinguishing characteristics that define the tumor types.

His group selected 511 genes that are expressed differentially during normal liver development in the rat. Eighty of these genes were co-expressed in all the analytical platforms—that is, mouse, rat and human. Clustering these 80 genes with gene expression data from human liver tumors identified a distinct group of tumors having stem cell-like phenotype and displaying bad prognosis, essentially short survival from diagnosis. These data suggest that gene expression profiles from adult or fetal liver stem cells—and presumably from other organ specific stem cells—can be used to identify tumors derived from cancer stem/initiating cells.

Barbara K. Vonderhaar's talk was "Breast Cancer Stem Cells: Fact or Fiction?"

Thorgeirsson's research is currently aimed at identifying and characterizing human liver cancer stem cells in order to both better classify liver tumors and to provide better therapeutic options for the patients.

Redefining: Breast Cancer Stem Cells

The story of breast cancer stem cells is slightly different, because there have been reports that claim to identify breast cancer stem cells. Previous studies reported that breast cancer cells expressing high levels of the surface protein marker CD44 and low levels of CD24 are the stem cells that are able to create new tumors. But Barbara Vonderhaar, Chief of NCI's Mammary Biology and Tumorigenesis Laboratory, reports that these defining characteristics of breast cancer stem cells are plastic.

Her laboratory has observed that where the breast cancer tumor cells are injected in an immune-compromised mouse influences tumor growth and latency, meaning the microenvironment, or niche, is important in determining the behavior of the breast cancer stem cell. For instance, if putative breast cancer stem cells are injected just under the skin of the mice, fewer, smaller tumors arise. If the tumor cells are injected into the mouse mammary fat pad, a more compatible microenvironment, the breast cancer stem cells produce more and larger tumors.

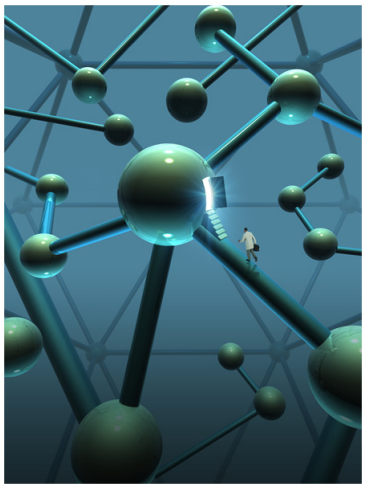
Once the selected breast cancer tumor cells are injected into the orthotopic or correct site and a new tumor develops, the defining signature of the surface marker proteins on the breast cancer stem cell can change, Vonderhaar's group has found. Although the CD44 marker seems to be needed for tumors to form, the expression of CD24 is dynamic and the levels of CD24 change. The histological appearance of the tumor cells is similar to the primary tumor and the hormone receptor profile remains the same, yet the defining signature changes.

The previously defined breast cancer stem cell may need some reworking on

continued on page 12

Future of Cancer Stem Cell Research

continued from page 11



"Cancer Stem Cells and Tumor Biology: Challenges Today and Promises for the Future" was one of several concurrent symposia sessions during the NIH Research Festival on October 15. A major paradigm shift in cancer biology and treatment has occurred in the past decade that implicates the "cancer stem cell" or the "cancer initiating cell with stem-like properties" as the central entity in tumor biology. However, numerous challenges, both conceptual and practical, need to be resolved in order to clearly define the nature and role of these cells in the tumorigenic process. In this session NIH researchers explored the state of the art for identification, isolation and characterization of cancer stem cells from four organ systems to more clearly define their potential as targets for prevention and treatment.

NCI's Gilbert Smith, not mentioned in this article, joined Thorgeirsson, Vonderhaar, Vogel and Keller with a talk titled "The Influence of the Stem Cell Niche."

identifying markers. "CD44 and at least two other markers will give a better identified cancer stem cell," Vonderhaar said.

Therapeutics: Blood Cancer Stem Cells

When blood stem cells known as hematopoietic stem cells become cancerous, leukemia results. Hematopoietic cancer stem cells already have been identified and characterized. In leukemia patients, the hematopoietic stem cells continue proliferating, but they have lost the ability to differentiate into blood cells. The challenge that remains is how to use this knowledge to come up with viable therapeutics for leukemia patients.

Jonathan Keller, head of NCI's Hematopoiesis and Stem Cell Section, has been studying the pathways of differentiation that are disrupted in hematopoietic cancer stem cells to identify targets for leukemia treatment. His strategy is to overcome the cancer stem cell's ability to differentiate and force it to become a blood cell, which would also prevent it from dividing. Once the cells are differentiated into blood cells, they would no longer pose a high-risk cancer threat, because the cells would be unable to divide and make new cancer cells. Differentiated blood cells also are the main line of immune defense and come into harm's way when fighting off pathogens, causing many of them to be short-lived, another plus for eliminating the cancer cells.

Keller's lab has found a protein called inhibitor of DNA binding (Id) that represses differentiation of stem cells to blood cells. In human leukemia his group found mutations that caused the Id gene to be highly expressed, which prevented the stem cells from becoming blood cells.

This research has revealed Id to be a prime target for anti-leukemia drugs. The next step is to find small molecules that inhibit or block the function of Id proteins that force the hematopoietic cancer stem cells to become blood cells, which would reduce their ability to proliferate and form tumors.

To Infinity and Beyond

From learning to culture, characterizing and designing therapies that target specific cancer stem cells, much research still needs to be accomplished before any real therapeutics can be used in patients. But the research is moving in the right direction and within a few years we should expect major breakthroughs.

Understanding the biology behind cancer stem cells is essential if we are to win the battle against cancer.

"The challenge to future researchers will be to determine the origin of cancer stem cells from normal cancer stem cells or their progenitors or any other cell that becomes stem-like," Vonderhaar said. "If we understand the process and zone in on cancer stem cells, then we can detect them earlier and target them with new treatments." ■

[*Editor's note*: For a provocative discussion on the efficacy of cancer stem cell research, refer to "Efficient tumour formation by single human melanoma cells" by Quintana et al. in Nature, vol. 456, 4 Dec 2008, doi:10.1038/nature07567. The URL is http://www.nature.com/nature/journal/v456/n7222/full/nature07567.html.]

Translational Research Informatics Seminars

Dr. Zerhouni has gone, but his Roadmap's emphasis on translational research lives on in the Biomedical Translational Research Information System (BTRIS), a research data repository and tool that will provide investigators with electronic access to, and analysis capabilities of, both clinical and non-clinical data.

BTRIS 1.0 is set for release in July 2009. In anticipation of this event, Jim Cimino, BTRIS project manager and chief of the Laboratory for Informatics Development, will host a Translational Research Informatics Seminar Series. This series begins in January 2009 and will bring to the Clinical Center leading figures in the study and use of translational information systems. Each seminar will be a valuable opportunity to learn more about current technology developments and to discuss the future of informatics in bench-to-bedside research.

The seminars will be held in the Lipsett Amphitheatre from 2 to 3 p.m. on:

Wednesday, January 21, 2009
Tuesday, February 17, 2009
Tuesday, March 17, 2009
Tuesday, April 21, 2009
Tuesday, May 19, 2009
Tuesday, June 16, 2009

For more information about BTRIS, please visit http://btris.nih.gov.

We're #17

That's not too shabby. The NIH ranked 17th in The Scientist's annual listing of the best places to work in academia. Our strengths were research resources and tenure; our weaknesses were management and policy issues. Oh? Topping the list were J. David Gladstone Institutes in San Francisco, Princeton University, and the Trudeau Institute in Saranac Lake, N.Y.. The NIH edged out the University of Pennsylvania, Dana-Farber, Baylor, Duke and UCLA. (Harvard wasn't even in the top 40). The list appeared in the November 2008 issue.

The SIG Beat

News from and about the NIH Scientific Interest Groups

Three New SIGs

Tissue Microdissection Interest Group

Laser-based microdissection has become a powerful tool for biomedical research. Since its initial development at NIH over 10 years ago, diverse variations on technological design have evolved and today there are several commercial systems available, each with advantages and disadvantages.

Many laboratories in the NIH Intramural Program now have laser microdissection instruments that researchers use for a variety of challenging applications, including integrating dissected cells with newly developed, high-throughput molecular profiling assays. For this reason we have created the Tissue Microdissection Interest Group to facilitate the interchange of ideas, experiences, and protocols among investigators across campus who are either actively using laser microdissection or who have an interest in doing so in the future.

For more information, contact Jaime Rodriguez-Canales at <rodrigja@mail.nih.gov>, Jeffrey Hanson at <hansoje@mail.nih.gov> or Michael Emmert-Buck at <buckm@mail.nih.gov>.

Biospecimens Interest Group

One of the major goals of this interest group is to promote and facilitate interaction between intramural and extramural scientists who are interested and involved in a variety of clinically oriented research using biospecimens. We intend to use this interest group as a forum where investigators can get together to exchange scientific data, ideas and information, using biospecimens for research and validation of assays and technologies development.

In addition, this forum will be used to discuss ways to access high-quality biospecimens and better harmonize and standardize procedures and SOPs for collecting, handling, and storing samples to ensure maximum reproducibility of outcome, while protecting the privacy of the patients (donors) and adhering to the ethical and legal requirements associated with the use of biospecimens.

For information, contact Yaffa Rubinstein at <rubinsty@mail.nih.gov> or John Gillespie at <jgill@mail.nih.gov>.

Patent Law Interest Group

We provide educational and networking opportunities for NIH scientists interested in patent law and technology transfer. This interest group hopes to attract current members of the NIH Office of Technology Transfer, bench scientists with interests in intellectual property, and past fellows who have transitioned into applicable careers in local companies. We will feature seminars inviting representatives from the U.S. Patent and Trademark Office, law firms and biotechnology and pharmaceutical companies to discuss issues important to this field.

Additionally, we will provide an environment in which junior scientists can learn about different career opportunities in this field and steps they can take to become competitive for these positions. On other occasions we may take turns presenting articles discussing important changes in the field and how these changes affect the NIH community.

For information, contact Thomas Paul at <paulth@mail.nih.gov>.

Glycobiology Scientific Interest Group
Sweet New Series on Glycobiology

The NIH Glycobiology Scientific Interest Group (GBIG) is sponsoring the new "Special Topics in the GlycoSciences" seminar series. The series, which began in November, is for those working in the glycosciences as well as those interested in learning more about this emerging field of study.

Researchers from laboratories across the intramural NIH and the FDA will speak on a broad range of topics in the glycosciences. Seminars include an extended introduction to an area of glycobiology or glycochemistry and highlight exciting research in progress in the investigator's laboratory.

Those who wish to learn more about the glycosciences in general, or the special topics being covered by these seminars in particular, are encouraged to take part in the series and review relevant information in "Essentials of Glycobiology" available freely only at <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=glyco2>.

Seminars are on Thursdays, although time and location vary. The remaining talks in this series are listed below. Contact Pamela Marino of NIGMS at <MARINOP@nigms.nih.gov> for more information.

December 18, 2–3:00 p.m., Bldg. 40/1201-1203, "Clinical Glycobiology," by Donna Krasnewich, NHGRI deputy clinical director; background materials: chapter 42

January 15, 2–3:00 p.m., Bldg. 40/1201-1203, "Proteoglycans and Principles of Structural Analysis," by Yasuhiro Katagiri, NHLBI; background materials: chapters 16 and 47.

February 26, 2:30–3:30 p.m., Bldg. 49/1A51-1A59, "Heparan Sulfate Proteoglycans Mediate Developmental Cell Signaling by Multiple Mechanisms," by Kenneth Kramer, NHLBI; background materials: chapters 16 and 35.

March 12, 2–3:00 p.m., Bldg. 49/1A51-1A59, "Proteins That Recognize Glycans," by Gerardo Vasta, University of Maryland Biotechnology Institute at Baltimore; background material: chapter 26.

March 26, 2–3:00 p.m., Bldg. 49/1A51-1A59, "O-Glycosylation During Eukaryotic Development," by Kelly Ten Hagen, NIDCR; background material: chapters 9 and 38.

April 30, 2–3:00 p.m., Bldg. 49/1A51-1A59, "Glycobiology in Biotechnology and Medicine: Glycan Arrays and Vaccine Development," by Jeff Gildersleeve, NCI; background material: chapter 51.

June 4, 2–3:00 p.m., Bldg. 49/1A51-1A59, "Mass Spectrometry of Carbohydrates as a Tool for Characterization of Bacterial Vaccines and Pathogens," by John Cipollo, CBER FDA; background material: chapter 47.

Colleagues

Recently Tenured

Daniel H. Appella *obtained his bachelor's degree in chemistry from Oberlin College in 1993 and his Ph.D. in organic chemistry from the University of Wisconsin-Madison in 1998. From there, he performed postdoctoral work for three years at MIT and then started his independent career in 2001 as an assistant professor in the chemistry department of Northwestern University. In 2005, Appella moved to NIDDK's Laboratory of Bioorganic Chemistry as a tenure-track investigator and was promoted to tenure in September 2008.*

Chemistry is an enabling science that finds solutions to broad problems. Over the past several decades, medicinal chemistry has generated libraries of low-molecular-weight molecules, most of which target the active sites of enzymes. This genre of molecules accounts for the majority of compounds present in all chemical libraries currently used to identify binders to biological targets. However, the associations that frequently occur between biological macromolecules (such as proteins and nucleic acids) involve arrays of interactions that are significantly more complex than the forces that direct the binding between a small molecule and an enzyme active site. Therefore, new chemical approaches are essential to develop synthetic molecules that interact with complex biological targets for which there are a lack of antagonists. The NIH has a unique set of medical and biological capabilities that will interface with and benefit from this type of research.

Dan Appella

The goal of my research program is to develop new classes of synthetic molecules that are able to selectively bind to and disrupt interactions between nucleic acids and proteins, and then to take advantage of NIH's resources to develop the biomedical applications of our molecules.

Peptide nucleic acids (PNAs) are a class of non-natural nucleic acids that we have modified to improve their properties for DNA detection. PNAs retain the natural nucleobases from DNA but hybridize to complementary DNA with significantly higher affinity and selectivity than corresponding natural oligonucleotides. PNA is resistant to degradation from both nucleases and proteases, thus making it a very stable platform for numerous applications.

Traditionally, PNAs have been difficult to modify to improve binding to nucleic acids. My group has overcome this obstacle and developed chemically modified versions of PNA to improve its properties for a range of biomedical applications. For instance, we have developed a cyclic constraint that may be incorporated into the PNA backbone to increase the binding affinity of PNA for a target nucleic acid.

At the same time, this chemical modification enhances the single-base mismatch discrimination of PNA for complementary sequences. We have recently developed a sandwich-based strategy based on our chemically-modified PNAs to improve the detection limit of a DNA sequence from anthrax. Because the base sequence of PNA may be easily altered to target other DNA (or RNA) sequences, nucleic acid sequences from other pathogens and diseases can potentially be detected.

A second research goal in my lab is to elucidate the molecular requirements of small molecules to target the three-dimensional folds of RNA. Currently, RNA is significantly underused as a target for drug development because there is a lack of basic knowledge about how to design a molecule to target a single, folded RNA over other RNAs. In many cases in which protein-RNA interactions are important biochemical signals, the RNA folds in order to create a protein-binding site. Such folded RNA structures commonly approach the complexity of folded protein structures.

Because RNA can possess folded, three-dimensional structures, it should be possible for chemists to design new molecules that bind a target RNA approaching the affinity and specificity seen in nature. Such molecules could ultimately evolve into new types of drugs that exert their biological effects by targeting RNA and disrupting protein-RNA interactions. We have developed a class of molecules we call Multivalent Binding Oligomers (MBOs) and are investigating their binding to HIV-related RNA structures, such as the TAR and RRE sequences. Association of specific proteins with these RNA structures is essential for HIV replication, and molecules that prevent the protein–RNA associations could be used as antiviral therapies.

Recently, we have developed MBOs with very strong binding affinity to TAR that also exhibit antiviral activity in HIV-infected peripheral blood mononuclear cells. We are examining the basic binding properties of these MBOs to TAR to improve their biological activity and also to guide development of MBOs that target other disease-related RNAs.

Lastly, my group is investigating molecular scaffolds as inhibitors of protein-protein interactions. There is significant interest among chemists to design molecules that target the interfaces at which proteins interact. Inhibition of protein-protein interactions can interfere with regulatory pathways in cells and could constitute a new strategy for drug discovery. However, it is challenging to design inhibitors to match the molecular nature of the interfaces between proteins.

In many cases, the contact surface area between proteins is two to ten times as large as that observed with protein and small molecule interactions and commonly lacks well-defined substrate binding sites present in enzymes. Therefore, novel classes of molecules will necessarily have to be developed to target protein-protein interactions, and it is likely that such molecules will possess complex molecular scaffolds from which functional groups project and interact with a protein surface.

One such scaffold is illustrated by peptoids, oligomers of nitrogen-substituted glycine in which the sidechains are attached to the backbone amide nitrogen instead of the α–carbon as in polypeptides. A wide variety of sidechains can be attached to the peptoid backbone, and peptoids are resistant to proteolytic digestion. My lab has demonstrated that peptoids can be designed to target the p53 binding site of the human homolog of the mouse "double minute2" (HDM2) protein.

HDM2 is a negative regulator of p53, and overexpression of HDM2 has been linked to tumor aggressiveness and drug resistance. Inhibition of the interaction of HDM2 and p53 can restore p53 function and prevent cancer growth. Our development of the first peptoid-based inhibitor of HDM2 shows that peptoids may be useful inhibitors of protein-protein interactions. Current efforts in this area are now focused on refining our initial peptoid scaffold to improve binding and cellular uptake. §

Robert A. Colbert *received his M.D. and Ph.D. degrees from the University of Rochester School of Medicine's Medical Scientist Training Program in 1987, and completed his pediatric residency training there in 1990. Following postdoctoral research training in Microbiology and Immunology and a clinical fellowship in Pediatric Rheumatology at the University of North Carolina at Chapel Hill and Duke University, he joined the faculty at Cincinnati Children's Hospital Medical Center in the Division of Rheumatology in 1994. He was associate director of the University of Cincinnati's Physician-Scientist (M.D.-Ph.D.) Training Program from 1998 to 2008. He was promoted to full professor in 2005 and served on the Executive Committee of the Center for Immunological Research and as director of the Cincinnati Children's Trustee and Procter Scholar Awards Programs from 2006-2008. Colbert was division director in Rheumatology from 2006 to 2008, and then joined the NIH in September 2008 as senior investigator and chief of NIAMS' newly formed Pediatric Translational Research Branch.*

Research in the Pediatric Translational Research Branch (PTRB) aims to understand more about spondyloarthritis, an immune-mediated inflammatory disease. People with spondyloarthritis, and in particular the prototypic form ankylosing spondylitis (AS), develop severe inflammation in the spine that is painful and eventually leads to ankylosis, or fusion, of the axial skeleton, resulting in significant loss of mobility.

Robert Colbert

AS is considered a complex genetic disease that is estimated to be caused by approximately 10 genes in combination with ubiquitous, but poorly defined, environmental influences. A major goal of PTRB research is to understand how susceptibility genes work together to cause this inflammatory disease and concomitant abnormal bone formation. It is anticipated that these studies will lead to a better understanding of how to treat individuals with AS and other spondyloarthropathies.

Ongoing studies in my laboratory have led to the discovery that the HLA-B27 gene, long recognized to play a major role in susceptibility to spondyloarthritis, encodes a protein with a propensity to misfold and activate an evolutionarily conserved stress response known as the unfolded protein response (UPR). Recently, using an animal model, we discovered that the UPR, when active in certain cells of the immune system, alters the induction of a group of highly pro-inflammatory cytokines that may create a set of upstream signals that initiate the inflammatory response. Development of disease in these animals is highly strain dependent. My fellow PTRB investigators will take advantage of these differences to identify genes and pathways that regulate the development of inflammation in experimental spondyloarthritis. The animal studies will inform and guide translational approaches in human subjects to confirm relevant pathogenic mechanisms. My group plans also to investigate connections between susceptibility genes and the immunobiology of abnormal bone formation.

Spondyloarthritis is difficult to recognize in its earliest stages, particularly in children, in whom the axial skeleton is often spared. In addition, not all patients with juvenile-onset spondyloarthritis (referred to as enthesitis-related arthritis, or ERA) go on to develop ankylosing spondylitis. Our ongoing studies are comparing gene expression signatures in juvenile-onset disease to define critical differences that distinguish these patients from those with other forms of juvenile idiopathic arthritis, and also to predict whether AS will develop. We hope to incorporate emerging genetic findings into this analysis to better predict outcome.

Robert J. Lederman *received a bachelor degree in molecular biophysics and biochemistry at Yale University in 1986, and a medical degree at Case Western Reserve University in 1990. He was a resident and chief resident in internal medicine at University Hospitals of Cleveland from 1990 to 1994. He was a clinical fellow in general cardiology at University of California at San Francisco from 1994 to 1996, interventional cardiology at University of Michigan from 1996 to 1997, and peripheral artery interventions at Duke University from 1997 to 1998. He was a junior faculty member in cardiology at University of Michigan until early 2001, when he moved to the NHLBI Division of Intramural Research as a tenure-track investigator in late 2000. He was awarded tenure in spring 2008.*

Our work applies advanced imaging tools to guide novel, minimally-invasive (catheter-based) treatments as alternatives to surgery. We have found two avenues to be fruitful. We have worked closely with the imaging physics lab of Elliot McVeigh, formerly with NHLBI and now relocated to Johns Hopkins University. We adapted real-time magnetic resonance imaging (rtMRI) to guide catheter-based cardiovascular interventional procedures. Most work to date has been in models of disease in large animals. We have used rtMRI to target and deliver therapeutic cell preparations to precise myocardial targets and to track them *in vivo*. We also have used rtMRI to guide endovascular repair of aortic coarctation, a common congenital abnormality. Other investigators, such as Keith Horvath in the NHLBI Cardiothoracic Surgery Research Program, are exploring this technology for MRI-guided surgical procedures. In addition, we work closely with Andrew Arai and colleagues in the Laboratory of Cardiac Energetics to understand better how noninvasive cardiovascular imaging, such as MRI and cardiac CT, enhance interventional treatment planning.

Traditional X-ray-guided catheter procedures often require "blind faith" to ensure appropriate device positioning. We have used rtMRI to help safely traverse anatomic boundaries inside the heart, and to recanalize chronically occluded arteries. We also are working closely with the NHLBI core catheter engineering team led by Ozgur Kocaturk to develop clinical-grade catheter devices to apply this technology to patients at the NIH Clinical Center.

While real-time MRI is promising, translating these developments into clinical care will take time. In the meantime, as a second avenue of research, we have used three-dimensional MRI information ("roadmaps") registered with live X-ray fluoroscopy to enhance clinical procedures that require additional soft-tissue information. In this way we hope to offer some of the best features of both. We have demonstrated this so-called X-ray Fused with MRI (XFM) to guide cell injections to infarct borders and to simplify and dramatically shorten radiation exposure in repair of a complex congenital heart defect (membranous ventricular septal defect), among other applications.

We hope to offer our image-guidance technologies to related clinical collaborators, including in interventional radiology for oncology and in pediatric heart disease. A little-known service that we in the Clinical Cardiovascular Section can offer to members of the NIH and regional communities is consultative cardiology, cardiovascular imaging such as MRI and CT, and revascularization such as coronary and peripheral stenting services, which can be provided at the NIH Clinical Center as part of our "teaching protocols."

Colleagues

On Tenure Track

Laufey Amundadottir is a genome biologist studying how common heritable genetic variation contributes to cancer development and progression. She is an investigator in NCI's newly formed Laboratory of Translational Genomics using genome-wide association studies and other techniques to identify risk factors for various cancers including pancreatic, prostate and breast cancer.

Laufey Amundadottir

Amundadottir received her B.S. in biology and an additional degree in genetics at the University of Iceland; she then went on to get her Ph.D. in cell biology at Georgetown University in 1995. After completing her studies, she conducted her post-doctoral training at Harvard University before returning to Iceland to become the Head of the Division of Cancer Genetics at deCODE Genetics, a biotech company that specializes in genomics and drug discovery. In 2007, Amundadottir moved back to the states to join the NCI.

At the NCI, she joined PanScan, a genome-wide association study of pancreatic cancer performed within the framework of the NCI-sponsored Cohort Consortium. The aim of this study is to identify common susceptibility variants for pancreatic cancer, one of the most deadly cancers, with a five-year survival rate of less than five percent. The study involves genotyping hundreds of thousands of common DNA variants, called single nucleotide polymorphisms, or SNPs, in a large number of patients with pancreatic cancer and in matched control individuals and analyzing the association to pancreatic cancer risk.

Amundadottir's group is working on functional characterization of risk variants identified in PanScan. Most risk variants identified in GWAS studies to date do not fall within protein coding regions of the genome; and although many are located in the vicinity of known genes, others are very far from known genes. This means that every region will require a slightly different approach. One of the first tasks is to characterize all sequence variation surrounding PanScan risk variants with deep sequencing approaches. These new sequence variants will then be assessed with regard to risk of pancreatic cancer in large sets of cases and controls to see if they associate more strongly to cancer risk than the SNPs discovered in the initial GWAS study. Additional approaches aim at correlating risk variants to molecular phenotypes, such as binding of proteins to DNA, gene expression levels, epigenetic signatures or other molecular changes that ultimately result in increasing an individuals risk of cancer.

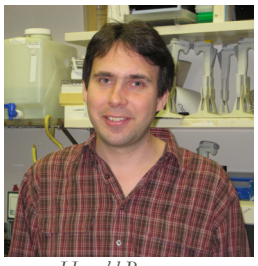
Another project in her lab involves assessing the role of Y-chromosome variation in prostate cancer risk. This chromosome is not well covered on the current genome-wide genotyping platforms, and there is ample biological evidence that it may be involved in cancer as it has been shown to regulate expression of a wide variety of genes on the autosomes and X chromosome. This project entails examining about 5,000 prostate cancer cases and 5,000 control subjects to address whether specific risks for prostate cancer are linked with gene variations found specifically on the Y chromosome.

The final aim of her studies is to unravel the path from susceptibility variants to the functional pathways that initiate cancer to provide insight into how to better prevent and treat these devastating diseases. As her research involves using multiple different approaches to study a research problem, she advises junior researchers to work together with people of different backgrounds—whether it is biology, medicine, bioinformatics or statistics—to work with large high-quality data sets through collaborations with multiple research groups to achieve their research goals. This multidisciplinary approach is how she sees the future of biology heading.

—text by Vanessa McMains

Harold Burgess leads the NICHD Unit on Behavioral Neurogenetics, where he uses high-speed imaging and other techniques to study the darting movements of larval zebrafish. His work is revealing the neural patterns underlying this goal-directed, navigational behavior—from sensory perception and motivation to movement execution and control.

Raised in Australia by parents working in cancer research, Burgess was set on the science track early and did his graduate work at the Weizmann Institute of Science in Rehovot, Israel, a place he affectionately likens to the NIH. Before arriving at the NIH this year, he conducted postdoctoral research at the University of Pennsylvania, where he developed complex data-acquisition software to analyze zebrafish movement captured by a camera at 1,000 frames per second. By digitizing the body axis of the fish, he could describe and quantify their behavior in terms of curvature. Resulting sinusoidal traces represent stereotypical behaviors such as startle responses, simple forward swims, or small navigational turns. He obtained and analyzed large amounts of data quickly via experimental manipulation of many fish simultaneously.



Harold Burgess

Burgess anticipates exciting collaborative opportunities at the NIH, with access to knowledge and scientific tools unparalleled by most research institutions in the world. "Neuroscience is a bit like the Wild West; you never know what [tools] you're going to need next," he said. His work on zebrafish aims to "trace the pattern of connectivity that actually underlies behavior to the level of single cells," he said, to uncover molecular, cellular and genetic underpinnings of complex behaviors.

The neural architecture of zebrafish brains is analogous to mammalian brains with a similar fundamental pattern of connectivity. The advantage of using zebrafish is that they might have a network of only two cells responsible for a certain task, compared with thousands of cells in a rodent model. These few cells can be ablated, and then a battery of tests can be run, such as pre-pulse inhibition (PPI) of a startle response or phototaxis (attraction to the light) to determine the phenotype or behavior controlled by that region. Burgess recently showed that PPI in larval zebrafish and pharmacological sensitivity of PPI is very similar to that in humans—particularly interesting and clinically relevant, because impairments in human PPI is linked to psychiatric disorders such as schizophrenia.

"Sometimes you just don't know where your inspiration is going to come from," he said, seemingly searching for a way to articulate the obvious passion and enthusiasm he has for his work in particular and science in general. "The greatest thing about being in science is that you can go to a lecture... then suddenly you realize that almost by chance someone has done an experiment and interpreted the results in a way that you realize you can apply to an experiment. I'm really sure that being here I'm going to have these moments of inspiration."

—text and photo by Katherine Jakubs

Take a Sabbatical, Win a Marathon

Like many visiting scientists at the NIH, Cate Fenster has taken advantage of her short stay to see the sites of the Washington, D.C., area—from Arlington Cemetery to Georgetown, over to the White House and down through the National Mall and Tidal Basin.

The only difference is that she did it all by foot in one day, in 2 hours, 48 minutes and 55 seconds, to be exact, which earned her first place in the women's division of the Marine Corp Marathon on October 26. What's more remarkable is that this was her first marathon.

Fenster is on sabbatical from the College of Wooster in northern Ohio, where she is an assistant professor of biology. She's working in the lab of Andrés Buonanno, chief of NICHD's Section on Molecular Neurobiology. Her stay is brief—only five months, the approximate time it would take this writer to run 26.2 miles—but she's hoping the experience will bring new opportunities for her teaching and research back home.

The sabbatical has been a win-win experience for Buonanno and Fenster. Buonanno's group studies the cellular mechanisms that regulate glutamate-mediated neuorotransmission at central synapses. Maladaptations in this intricate process can result in developmental abnormalities, psychiatric disorders, chronic pain, addiction, and neurodegenerative disorders such as Alzheimer's disease.

More specific, Buonanno's lab focuses on the role of neuregulins in neuronal plasticity. His team has found how the gene for neuregulin-1 (NRG-1) influences synaptic plasticity, which is thought to form the basis of neuronal adaptations required for learning and proper neurological function.

Buonanno was able to bring Fenster to his lab essentially for free as an adjunct scientist through the NIH Special Volunteer Program, for which "the paperwork required was reasonable by NIH standards," he said. Fenster, whose college pays for the sabbatical, found Buonanno listed in the AAAS fellowship database as a potential mentor. Fenster was awarded a modest grant from the Henry Luce III Fund, too, to cover expenses for reagents and equipment.

Fenster's sabbatical work builds upon Buonanno's findings by providing a more comprehensive understanding and description of the acute effects of NRG-1 on the function of two classes of glutamate receptors, AMPA and NMDA receptors. She uses a combination of cellular and electrophysiological approaches to study this.

"As a basic scientist, this is an exciting project because not only may it lead to a better understanding of the cellular mechanisms that fine tune neuronal signaling under normal conditions, but it may also have implications for understanding and treating schizophrenia," she said.

Fenster's experiments in her first few months at NIH, starting in the summer, didn't yield the results she was expecting, but nevertheless they have set her on new paths. She hopes this work will lead to resources for her students and her school when she returns in January.

Cate Fenster, after catching her breath

Fenster is now well positioned to continue her research project at Wooster, provided she can get funding for basic equipment based on her preliminary data and quite possibly a journal article from her NIH stint. Undergraduates at Wooster must complete a research project and written thesis. So Fenster's experience at NIH ultimately might lead to an unprecedented opportunity for her students at this small, independent liberal arts college.

Her success in the marathon also has opened up new opportunities. Her winning time was just shy of the qualifying time for the Olympics, currently 2 hours and 47 minutes. She hopes to beat that time in Columbus, Ohio, next year.

"I highly recommend NIH scientists to consider 'sponsoring' scientists for sabbaticals, because they bring fresh perspectives to the laboratory," Buonanno said. "My group has certainly enjoyed having Cate in the lab."

—text by C. Wanjek

NCI Researcher Wins Salzman Virology Award

Alberto Bartesaghi of NCI's Laboratory of Cell Biology has won the 2008 Norman P. Salzman Memorial Award in Virology for his work on HIV. An electrical engineer by training, Bartesaghi develops computational imaging technologies to determine the structure of various viral components involved in the neutralization and cellular entry of SIV and HIV.

Bartesaghi received his award on November 13 at a half-day symposium at the Natcher Conference Center honoring the memory of Norman Salzman, a pioneer in the field of molecular biology and one of the giants of NIH. With a career at NIH spanning over 30 years, mostly at NIAID, where he served as chief of the Laboratory of the Biology of Viruses from the mid-1960s to his retirement in 1986, Salzman made major contributions to the field, including being among the first to characterize viral mRNAs and to visualize replicating viral DNA.

Alberto Bartesaghi

Salzman also turned his laboratory into a training ground for young researchers. Six of his trainees have been elected to the National Academy of Sciences, and one has won the Nobel Prize.

The Salzman award, now in its tenth year, is given for innovative and creative research in the field of virology to an outstanding postdoctoral fellow from NIH, FDA or SAIC-Frederick. The awardee's mentor—this year, NCI's Sriram Subramaniam—also is honored and recognized at the ceremony.

The symposium was a who's who in virology, with several hundred researchers in attendance from around the country, including many of Salzman's trainees. NIAID Director Anthony Fauci, who worked with Salzman during the early days of the AIDS epidemic, opened the day with a tribute. NIAID's Bernard Moss provided the keynote presentation, during which he relayed the tale of how Edward Jenner couldn't get his small pox paper published. (It was rejected because he had a sample size of only three.)

The symposium is archived at <http://videocast.nih.gov/Summary.asp?file=14766>.

Major Shared and Multi-Institute Research Resources in the NIH Intramural Research Program

The NIH Intramural Research Program has a long history of interactions and shared resources among its investigators. These include core facilities that support crucial research activities, such as a sequencing center, a magnetic resonance imaging facility, a mass spectroscopy service, and a protein expression service. The most prominent example is the Warren Grant Magnuson Clinical Center, the nation's largest hospital devoted entirely to clinical research, providing comprehensive services and facilities in support of clinical research sponsored by the Institutes and Centers. In addition, the NIH Office of Intramural Training and Education organizes and sponsors a variety of training and career development activities for the entire intramural community. Various mechanisms are used to support these resources, including contributions from participating NIH Institutes and Centers such as the management funds, user fees, and program support from the Office of Intramural Research. The OIR has updated its list of shared resources for the Scientific Director's orientation book. We thought this list might be of interest to all intramural investigators.

RESOURCES AVAILABLE TO ALL INSTITUTES AND CENTERS

Research Resource	*Location*	*Participants*	*Governance*	*Contact*	*Research Services*	*Review*
Bioengineering (Lab of Bioengineering and Physical Sciences)	Building 13	Lead IC: NIBIB	NIBIB	R. Leapman, scientific director	Drug delivery, molecular interactions, image analysis, instrumentation development, supramolecular structure, nanoscale immunodiagnostics	SRS, ICs, Coordination Committee
Center for Information Technology (CIT) Division of Computational Bioscience	Building 12 complex		CIT	B. Trus, acting director	Image processing, bioinformatics, computational methods and algorithms, computer engineering, bioscience, molecular modeling, mathematical and statistical computing	SRS, ICs
Medical Arts and Photography Branch	Building 10, B2 level		ORS	L. Canady, chief	Medical illustration, photomicroscopy, photomacroscopy, scientific posters	
NIH Library	Building 10		ORS	S. Grefsheim, director, http://nihlibrary.nih.gov	Full-service library, including electronic journals, electronic document desktop delivery and translations	Users committee, ICs
Scientific Equipment and Instrumentation Branch	Building 13		ORS	J. Robbins, chief, http://seib.od.nih.gov	Maintain scientific equipment and computers; design and fabricate custom instruments; lease and sell scientific and medical equipment	SRS, ICs
Veterinary Resources Program (VRP)	Building 14–28 complex; Bethesda; Poolesville	Office of Research Services (ORS)		M. Eckhaus, acting director	Veterinary services (surgery, radiology, pharmacy, nutrition, rodent genetic repository, animal behavior and enrichment); animal husbandry, procurement, quarantine, and health surveillance; diagnostics (pathology, bacteriology, parasitology, serology); embryo cryopreservation and rederivation	Shared Resources Subcommittee (SRS), ICs

MULTI-INSTITUTE SHARED SERVICES

Research Resource	*Location*	*Participants*	*Governance*	*Contact*	*Research Services*	*Review*
Biotechnology unit (pilot plant)	Building 6, Room B1–33	Lead IC: NIDDK; Major client: NICHD		J. Shiloach, director	Production and purification of biological material, especially scale-up protein production and purification	BSC, ICs
Bone Marrow Stromal Cell Transplantation Center	Building 10	Steering Committee: CC, NIDCR, NIAID, NIAMS, NIBIB, NCI, NINDS	Oversight Committee: NINDS, NIAID, NCI, NIDCR	H. Klein (CC), P. Robey (NIDCR)	Production facility for bone marrow stromal (mesenchymal) stem cells for clinical research	
Center for Inherited Disease Research	Bayview Research Campus, Baltimore	Lead contracting IC: NHGR; all ICs may participate	Review: CIDR Board of Governors	D. Valle, Johns Hopkins University PI; Access Committee: http://www.cidr.jhmi.edu; Review: CIDR Access Committee (Jerry Roberts, NHGRI)	Genotyping, DNA banking, statistical genetics consultation, mouse genotyping	
Integrative Neural Immune Program	Multiple locations	NIMH, NINDS, NCI, NIAID, NIAMS, NIA		Esther Sternberg, director	Lecture series, conferences, workshops, retreat; training that bridges neuroscience and immunology; cyberlab to oversee virtual cores	

MULTI-INSTITUTE SHARED SERVICES (continued)

Research Resource	*Location*	*Participants*	*Governance*	*Contact*	*Research Services*	*Review*
Imaging Probe Development Center(IPDC)	9800 Medical Center Dr., Rockville, MD, Building B, Room 3042	Lead IC: NHLBI	Roadmap Initiative	Garry Griffiths, http://nihroadmap.nih.gov/molecularlibraries/ipdc/contact.asp	Production of new imaging probes for the intramural NIH research community	
Mass spectroscopy	Building 8A, Room B2A19–21; Building 10	Lead ICs: NIDDK, NHLBI, NIMH, NIAID, NINDS			QTOF–LCMS; high-resolution magnetic sector; MALDI, LC-ion trap	BSC, ICs
Microarray services	1. Multiple sites	1. NHGRI, NCI, NIA			1. Chips prepared by special arrangement	ICs
Microarray services	2. Building 12A	2. CIT with contributions from NINDS, CC, NHLBI, NIAID, NCI			2. Analysis, database storage and retrieval, bioinformatics services for microarray data	ICs
Mouse Imaging Facility	Building 10, In Vivo NMR Center	Lead ICs: NINDS, NHLBI; Participants, all ICs but NIEHS are paid charter members		A. Koretsky, director, and steering committee.	Mouse radiologic imaging (from fall 2001); 7T rodent MRI, microCT, high-frequency ultrasound, laser Doppler	SRS, ICs, steering committee
NIH Chemical Genomics Center (NCGC)	9500 Medical Center Drive, Rockville, MD	Lead IC: NHGRI		C. Austin, director;	Ultrahigh-throughput screening center of the Molecular Libraries Screening Center Network that generates chemical probes to understand molecular and cellular functions and serve as starting points for drug development, particularly for rare and orphan diseases	
NIH Intramural Sequencing Center (NISC)	5625 Fishers Lane, 5th Floor, Rockville, MD	Participants: NHGRI, NCBI, NIDCD, NIAAA, NIDA, NHLBI, NIDDK, NICHD, NEI, NIAMS, NINDS, NIDCR, NIEHS, NIMH	Users Committee	E. Green, director; Multi-Institute Access Review Committee: http://www.nisc.nih.gov	Production-scale DNA sequencing, assimilation and analysis of sequence data, acquisition and development of new sequencing chemistry, instrumentation, sequence analysis software	Users Committee
NIH Magnetic Resonance Imaging Facility	Building 10, In Vivo NMR Center	Lead IC: NINDS; all ICs except NIEHS		A. Koretsky, director, and steering committee	Human and animal MRI; other IC MRI instruments available	SRS, ICs, steering committee
PET Imaging	Building 10, Room 1C401	Lead IC: CC		P. Herscovitch and steering committee	State-of-the-art facility with three medical cyclotrons and ten hot cells to produce positron-labeled radiopharmaceuticals as well as four PET scanners	
Protein Expression Lab	Building 6B, Room 1B130	Lead IC: NIAMS; Participants: NHGRI, NCBI, NIDCD, NIAAA, NIDA, NHLBI, NIDDK, NICHD, NEI, NIAMS, NINDS, NIDCR, NIEHS, NIMH; any IC may request service		P. Wingfield, chief	Expression, purification, and structural characterization of HIV and HIV-related proteins via a variety of techniques; protein EXE software; supply HIV-1 protease	IATAP, ICs
Stem Cell Facility	Building 35, Room 3A201	Lead IC: NINDS		R. McKay	Facility uses a standardized paradigm to conduct side-by-side comparisons of the available cell lines on the NIH Human Embryonic Stem Cell Registry and shares the results with the scientific community	
Structural Biology NMR	Buildings 5, 6A, and 50	All ICs		Lead ICs: NIDDK, A. Bax; NHLBI, J. Ferretti; NIDCR, D. Torchia	Molecular structural imaging: 500MHz cryoprobe NMR spectrometer; 800MHz NMR spectrometer; now shopping for 900 MHz NMR spectrometer	ICs
Synchrotrons:						
1. Advanced photon source	1. Argonne National Lab	DOE		1. http://www.aps.anl.gov	1. High-brilliance X-ray beams	
2. National synchrotron light source	2. Brookhaven Nat'l Lab	Lead IC: NCI; Major Users: NIDDK, NIEHS, NIAID, NHLBI		2. http://www.nsls.bnl.gov	2. Intense focused beamlines throughout the spectrum	
Center for Human Immunology (CHI)	CRC		Board of Governors	N. Young, Director		
Warren Grant Magnuson Clinical Center	Building 10/future Clinical Research Center	Access to the Clinical Center is available to all ICs	Board of Governors	J. Gallin, director	Research hospital that accommodates 300 inpatients and outpatients and provides comprehensive services and facilities in support of clinical research sponsored by the ICs	Joint Comm. on Accreditation of Healthcare Organizations, BSC; Advisory: CC Research Steering Committee, CC Board of Governors

Catalytic Reactions?

If you have a photo or other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation that scientists might appreciate that would be fit to print in the space to the right, why not send it to us via e-mail: catalyst@nih.gov; fax: 301-402-4303 (temporarily out of service); or mail: Building 2, Room 2E26.

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

In Future Issues...

- Heart Imaging
- Biospecimens
- Pain Relief

Special Icelandic Issue

This issue of *The Catalyst* featured two researchers originally from Iceland: Snorri Thorgeirsson and Laufey Amundadottir. Iceland's population is only 300,000. Thus, we can proclaim this to be the special Icelandic issue, with 1/150,000 of the population represented. No issue of *The Catalyst* has ever been so representative of a single nationality. We'd need 6,000 Chinese-born researchers in a single issue to match this kind of representation. Most issues feature only 1 in 15 million American-born people. The frequent presence of English-, Australian- and Canadian-born researchers in the pages of *The Catalyst* also doesn't come close to matching the Icelandic numbers. And so we say, "Nei, hættu nú (þú hlýtur að vera að grínast)."

Ideas Needed

The NIH Catalyst needs ideas for this back page. In the past we have featured Kids' Catalyst, calendars of events, direct questions to the intramural staff, images of NIH life, ads for the National Library of Medicine's online bookshelf, crazy demographic trivia, and leftover stuff that didn't fit on the other pages. We would like to publish a regular feature on this back page. If you have suggestions for a column or feature, please e-mail them to the *Catalyst* editor at catalyst@nih.gov. No knowledge of Icelandic necessary.

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<**http://www.nih.gov/catalyst**>

Publisher
Michael Gottesman
Deputy Director
for Intramural Research, OD

Editors
John I. Gallin
Director, NIH Clinical Center

Henry Metzger
Scientist Emeritus

Writer-Editor
Christopher Wanjek
Director of Communications, OIR

Copy Editor
Shauna Roberts

Contributing Writers
Vanessa C. McMains, Dan Lednicer
Kara Lukasiewicz, Gail Seabold
Lori Keating, Ram Kumar Mishra
Caroline Duffy
Joslyn Yudenfreund Kravitz
Katherine Jakubs

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U.S. Department of Health and Human Services
National Institutes of Health
Building 2, Room 2E26
MSC 0235
Bethesda, Maryland 20892

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