THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

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Diversity Course

Crucial Lessons for Scientists

BY IRENE AVILA, NIA

Participants stood silently in a circle, stepping forward in response to prompts that ranged from lighthearted statements about musical tastes—"I like rock and roll music"—to more serious ones—"I have more than five friends of a different racial or ethnic background," "I or someone I care about is lesbian, gay, bisexual, or transgendered," or "My parents paid for my college tuition."

There was palpable relief when many people stepped into the circle together and discomfort when one or only a few stepped in or were left behind. At the end of the exercise, everyone shared feelings about the experience. Someone pointed out how many things people have in common; another commented on how difficult it can be to acknowledge differences; and the group agreed that some prompts made them feel uneasy especially because the exercise seemed so public.

This "Difference Circle" exercise was part of a 12-week NIH course "Building the World We Dream About: Diversity in a Multicultural Society." The course, which was offered by the NIH Office of Intramural Training and Education (OITE), created a safe environment for people from different backgrounds to talk openly and explore their own attitudes and subtle biases; understand the meaning of diversity in the lives of individuals, groups, communities, society, and the scientific community; and consider

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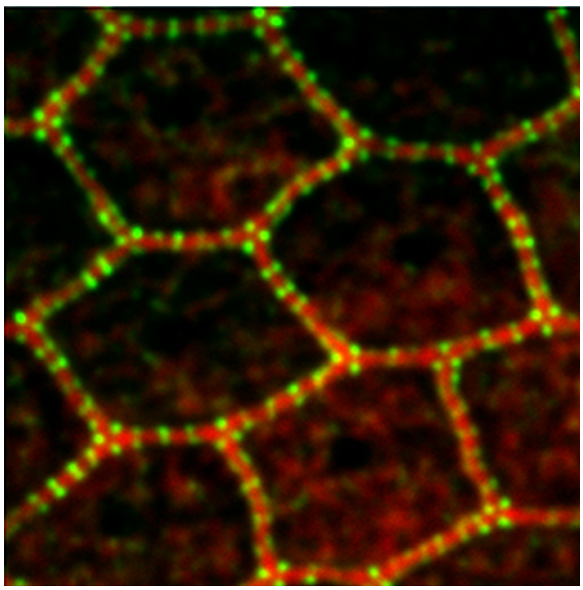
Chain Reaction

NIH Researchers Find Dynamic Ties among Epithelial Cells

BY SHARON REYNOLDS, NIDCD

A new finding from researchers at the National Institute on Deafness and Other Communications Disorders (NIDCD) has uncovered a never-before-seen method of intracellular physical communication among epithelial cells in the inner ear. The finding offers scientists a potential new pathway for developing ways to treat hearing loss and diseases in many different organ systems. The research was published in a recent issue of *Current Biology* (*Curr Biol* **23:**731–736, 2013).



NIDCD LABORATORY OF CELL STRUCTURE AND DYNAMICS

Fluorescent probes attached to proteins in the epithelial belt show the precisely structured network connecting individual epithelial cells.

Epithelial cells line our internal organs and passages to the outside world, such as the throat and nose, and act as a protective shield against germs and injury. They also play an active role in some of our sensory organs, such as the ear, where they are a key part of structures that allow us to hear.

Each epithelial cell in the body has a "cord" that wraps around its boundary, called the epithelial belt. This belt can tighten or relax, changing the cell's size and shape.

Researchers know that two muscle proteins, myosin and actin, play a role in powering the movement of the epithelial belt. Now, a study led by **Bechara Kachar**, chief of NIDCD's Laboratory of Cell Structure and Dynamics, has shown that these two proteins form a remarkably precise chainlike configuration within the epithelial belt similar to that

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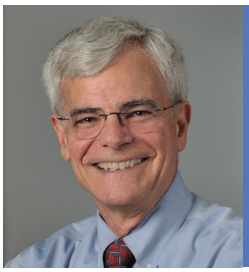

Celebrating the Global Community of Scientists at the NIH

BY MICHAEL GOTTESMAN, DDIR

Look to your right and your left in the labs or clinics at the NIH and you are likely to spot a scientist who was born outside the United States and got their primary training elsewhere. At NIH, about 40 percent of our approximately 7,000 scientists and trainees are foreign nationals from more than 100 countries and with various work visas (mostly J-1 and H-1B). And many of our principal investigators were also born outside of the U.S. Why does NIH have this enormous wealth of talented individuals from nearly every part of the world?

The United States has benefited from a huge influx of highly educated and talented biomedical researchers from other countries. Their desire for an outstanding research experience is matched by our open and inclusive attitude towards our international colleagues in providing opportunities (including salary and research support) to pursue important research. The NIH intramural research program is perceived as being one of the top research facilities in the world. For many foreign researchers, a successful postdoctoral experience at the NIH is often a ticket to future success in a scientific career either back home or in the United States.

We all benefit from what an international cadre of scientists have to offer—a kaleidoscope of cultures, religions, abilities and disabilities, worldviews, and perceptions that can be harnessed to solve almost every problem that nature has thrown our way. At NIH, our international community brings many different points of view to bear on important problems in basic biology, public health, and clinical practice. Think about the teams of NIH's U.S. and foreign scientists who cracked the genetic code, developed cancer chemotherapy, or responded to the HIV epidemic, and you will appreciate the wonderful tapestry of culture and intellect that makes up our scientific community.

The United States has benefited from a huge influx of highly educated and talented biomedical researchers from other countries.

One of the strong indications of the value to the global research effort of a research experience at the NIH is the fact that more and more countries are developing programs to send their postdocs to the NIH for advanced training. We recently signed an updated memorandum of understanding with the Japan Society for the Promotion of Science, which fully supports two years of postdoctoral training at the NIH for Japanese fellows. This program, ably managed by our own **Keiko Ozato**, a senior investigator in the National Institute of Child Health and Human Development, has been providing research support for Japanese fellows at the NIH for 18 years.

In addition, we have an agreement with Quebec to provide full stipend support for Canadian fellows who, if successful, are then offered independent positions in Quebec when they return to Canada. Newer programs with Russia, Brazil, and Korea provide varying levels of support to allow their fellows to work in NIH laboratories. All of these programs continue the strong NIH tradition of providing advanced training to fellows from all over the world.

We have done less well in tapping the enormous talent and diversity of Americans. Scientists at the NIH who are American citizens don't reflect the many groups that are traditionally underrepresented in biomedical research including racial and ethnic groups (black or African-American; Hispanic; American Indian and Alaskan Native; and Pacific Islanders) and persons with disabilities.

Efforts are under way to understand this deficit and to provide the opportunities needed to fully realize the potential of our own citizens. NIH's success in creating a global community of scientists indicates that we appreciate the value of including all kinds of backgrounds and points of view in our scientific community. So we are confident that we can ultimately succeed at home as we have done in the wider world.

NIHers have a long history of celebrating our international colleagues by learning more about their cultures (including food, of course!) and by forming lifelong friendships and collaborations. The strength of this institution reflects the importance of the global community of scientists at the NIH. ●

Blogging About Your Science

Blogs Can Augment Regular Communications

BY KATHERINE BRICCENO, NINDS

Do you blog and tweet for work? NIH Director **Francis Collins** does both: On his NIH Director's Blog, he highlights new discoveries in, and fascinating facts about, biology and medicine; you can also follow him on Twitter as he tweets about biomedical research and health. Several institutes and centers (ICs) are also using social media as a part of their overall communication strategy. Have you considered blogging about your research?

The word "blog" comes from a contraction of the term "Web log." Bloggers provide regular posts—including text, images, and links to other Web pages—on particular subjects and invite readers to comment. Blogs are not the only way to convey information, but can foster interactions with people who share common interests.

If you are thinking of starting a work-related blog, there are a few things you need to know. To start, it is important to contact your IC's communications office early in the process. For general information about policies, check the Department of Health and Human Services (HHS) "HHS Blog Guidance" Web site (http://www.hhs.gov/web/socialmedia/getting_started/blog_guidance.html).

"A blog represents the agency so you need good coordination and consistency," said **Dan Luxenberg**, senior advisor for Social Media and Collaborative Technologies in NIH's Center for Information Technology.

"You need a plan," said **Scott Prince**, chief of the Online Information Branch (OLIB) in the Office of the Director. Blogs require knowing who your audience is; identifying your goals; and committing the time and resources necessary to regularly write and edit posts and respond to comments by readers.

NIH already has several blogs. Some are for intramural audiences such as the "OITE Careers Blog" managed by the Office of Intramural Training and Education. It provides career development information for postdocs, postbacs, and graduate students.

Other blogs are dedicated to research. For example, the National Cancer Institute (NCI) and the National Heart, Lung, and Blood Institute (NHLBI) each have blogs aimed at specific areas of epidemiology. The National Center for Complementary and Alternative Medicine (NCCAM) blog focuses on research developments in complementary medicine.

The National Institute on Aging's (NIA) "Inside NIA: A Blog for Researchers" also covers research, with a focus on grants and funding policies as well as on scientific meetings and priorities. The blog welcomes posts from NIA intramural staff, according to **Britt Ehrhardt** of NIA's Office of Communications and Public Liaison, who manages the blog with **Robin Barr**, director NIA's Division of Extramural Activities.

The National Institute of General Medical Sciences' (NIGMS) "Feedback Loop" blog—established in 2009, making it one of the oldest on campus—shares funding, research, and other news. Ideas come from a steering committee that meets three times a year and from NIGMS staff. In addition, if a question is asked at least three times on the blog, it deserves a post making the blog "a forum for discussion and clarification of confusing topics," said **Emily Carlson**, NIGMS's blog manager.

Still other blogs cover research funding, NIH policies, meetings, and other topics of interest to extramural audiences. Deputy Director for Extramural Research **Sally Rockey**'s "Rock Talk" blog focuses on extramural grant policies, programs, and resources.

To learn more about blogs, see the "How to Start a Blog" sidebar. ●

How to Start a Blog

- Visit the HHS Blog Guidance site http://www.hhs.gov/web/socialmedia/getting_started/blog_guidance.html
- Contact your IC's communications office because each IC has its own guidance for social media.
- Notify the OLIB (Scott Prince): Although official sign-off is not required, OLIB likes to know about new social media accounts.
- Determine who your audience is and the best platform to interact with its members.
- Decide whether to post on certain days or on specific topics.
- Identify your goals.
- Ensure that you have the time and resources to generate and review posts and to moderate and respond to comments.
- Create policies for generating blog content and moderating comments.

Visit Other NIH blogs:

- NIH Director's (directorsblog.nih.gov)
- Inside NIA: A Blog for Researchers (http://www.nia.nih.gov/research/blog)
- NCCAM Research Blog (http://nccam.nih.gov/research/blog)
- NCI Biomedical Informatics Blog (http://ncip.nci.nih.gov/blog)
- NCI Cancer Epidemiology Matters Blog (http://blog-epi.grants.cancer.gov)
- NHLBI Challenges in Cardiovascular Epidemiology (http://nhlbiepi.wordpress.com)
- NIGMS Feedback Loop Blog: A catalyst for interaction with the scientific community (http://loop.nigms.nih.gov)
- OITE Careers Blog (http://oitecareers-blog.wordpress.com)
- Rock Talk: Dr. Sally Rockey, Deputy Director for Extramural Research (http://nexus.od.nih.gov/all/category/blog)

For a more complete list of social media and outreach efforts at NIH, go to http://www.nih.gov/Subscriptions.htm.

FROM THE OFFICE OF INTRAMURAL TRAINING AND EDUCATION

The NIH Academy

BY CASEY LYONS, FDA

For the past eight months, I have been one of more than 100 postbacs who attend the NIH Academy's weekly meetings to wrestle with one of the hottest topics in public health: health disparities. The term "health disparities" refers to inequalities in vulnerable populations in rates of disease incidence, prevalence, morbidity, and mortality.

The NIH Academy is a 12-year-old program that empowers the next generation of researchers and clinicians in the fight for health equity. In September 2012, OITE launched an expanded version of the Academy. The old Academy trained 12 to 16 postbacs a year, but the new NIH Academy, which offers a certificate program and a more intensive fellows program, has already trained 115 people in just one year. The program emphasizes the need for multidisciplinary collaboration among policy makers, communities, and public-health workers, as well as scientists, to bring about change.

In college, I became passionate about the social determinants of health after studying abroad, but I came to my postbac fellowship at NIH knowing little about health disparities in the United States. The NIH Academy provided an opportunity to explore issues affecting Americans of all stripes and quickly became the highlight of my week.

Through journal clubs, research talks, and community outreach, we covered a variety of topics related to health disparities. We have spoken with investigators who are using techniques as disparate as genomics, psychology, and community-based participatory research in order to document and address health disparities; we have read about and discussed cutting-edge research; and we took a multisession diversity course that allowed us to reflect on our own privileges and challenges so we can better connect with future patients and research collaborators.

Through all our activities, a central theme emerged: Communication—among researchers, clinicians, policy makers, public-health workers, patients, and the community—is essential to eliminating health disparities. Good communication can increase the public's knowledge and awareness of health issues and refute misperceptions. Often, that communication occurs best when conducted in partnership with community members.

One of our first lectures walked us through the process of developing animated public service announcements to prevent gun violence in Philadelphia. The animations were produced with the help of many city youth and were used in several other cities, demonstrating the vast impact that one idea can have. In another lecture, we looked at Asian-language pamphlets that were intended to decrease the stigma associated with hepatitis C. Developed with community representatives, each pamphlet addressed particular community fears about the virus. I came away from both lectures in awe of the creativity of these interventions. My time in the Academy has strengthened my commitment to resolving health disparities and reminded me that this work can be fun, too!

Trainees who are interested in participating in the next session of the NIH Academy (September–May) are invited to submit letters of interest emphasizing a strong desire to learn about health disparities. For more information, visit http://www.training.nih.gov/new_nih_academy_home or contact Shauna Clark (clarkshauna@mail.nih.gov or 301-594-3753.) ●

ERNIE BRANSON

U.S. Senator Harry Reid Visits NIH Clinical Center

Senate majority leader Harry Reid (D-Nev.) visited NIH on June 17, 2013, and met with Clinical Center Director **John Gallin** (left) and NIH Director **Francis Collins** (right) and others to tour the Clinical Center (model shown) and to learn about recent advances in NIH science. A few days later, he extolled the virtues of NIH in a 15-minute address to fellow Senators. "It would be impossible to count the lives that NIH innovation has already saved," he said, "and researchers are not close to realizing the limits of modern medicine."

Four Generations of Mentors and More

BY ROLAND OWENS, OIR

Great mentoring produces great scientists, great science, and more great mentoring.

Nowhere is this adage more evident than at the National Institute of Drug Abuse (NIDA), where four successful mentors were recognized at its annual Poster Day and Mentoring Awards Ceremony, held on May 8, 2013, in Baltimore. Three of the awardees represent four generations of mentors.

"Mentoring provides the core of a postbac, graduate, or postdoc training experience," said **Stephen Heishman**, director of NIDA's Office of Education and Career Development. NIDA has several mentoring programs—a Mentoring Plan, a four-week Mentoring Seminar, and Mentoring Awards—that Heishman hopes "will foster a successful mentoring experience for our trainees."

Mentoring is "doing for my mentees what was done for me," said Investigator Mentoring Award winner **Kenner Rice** (http://irp.nih.gov/pi/kenner-rice). He thanked his mentor, the late **Everette May**, an NIH chemist noted for his work on analgesics and drug abuse, for being a "gentleman [who] led by example." Rice was recognized for being "generous with his time, often working in the lab for hours, elbow-to-elbow with his trainees."

Rice in turn mentored **Amy Newman** (http://irp.nih.gov/pi/amy-newman), recipient of this year's Investigator Diversity Mentoring Award. Mentoring has been "a lifelong lesson that I hope to pass on to the next generation," said Newman, who was acknowledged in the citation for her ability to give feedback that is "sympathetic to the personal needs of her mentees." She also understands that good mentoring often requires a commitment to the mentee's career that lasts beyond the fellowship. Newman was recognized for mentoring individuals from groups that are underrepresented in the biomedical sciences.

DOUGLAS HANSEN, NIDA

Mentoring by successful scientists begets more successful scientists. (Left to right) Stephen Heishman, director of NIDA's Office of Education and Career Development; winners of NIDA's 2013 mentoring awards Jennifer Bossert, Thomas Keck, Kenner Rice, and Amy Newman; OIR Assistant Director Roland Owens; and NIDA Scientific Director Antonello Bonci.

She has already passed the lesson of good mentoring on to her mentee **Thomas Keck**, who received the Postdoctoral Fellow Mentoring Award. Keck considers mentoring as "creating a new generation of scientists that I want to work with."

Jennifer Bossert, the recipient of the 2013 Staff Scientist Mentoring Award, is starting her own mentoring lineage with postbaccalaureate fellows like **Robyn St. Laurent**, whose poster ("Context-induced Relapse after Suppression of Heroin Seeking by Adverse Consequences and an Alternative Palatable Food Reward") was one of 37 presented at the annual event.

The mentors honored on this day represented well the legacy of Everette May, who had all the attributes of a good mentor. May "had a keen interest in our science," said Rice. Furthermore, he "encouraged and helped all his students achieve their full potential." ●

Resources

"A Guide to Training and Mentoring in the Intramural Research Program at NIH"
http://sourcebook.od.nih.gov/ethic-conduct/TrainingMentoringGuide_7.3.02.pdf

"Guidelines for Mentors at the National Institutes of Health"
http://sourcebook.od.nih.gov/ethic-conduct/guidelines-mentors.htm

"Thoughts on Choosing a Research Mentor"
https://www.training.nih.gov/mentoring_guidelines

Career services for NIH Trainees
https://www.training.nih.gov/career_services

Diversity Course

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OITE

The group here represents some of the NIHers who have participated in OITE's 12-week diversity course, which is designed to create a safe environment for people from different backgrounds to talk openly and explore their own attitudes and subtle biases; understand the meaning of diversity; and consider the consequences of social exclusion and oppression. Michael Sheridan (front row, center), from The Catholic University of America, is the instructor.

the consequences of social exclusion and oppression, including health disparities and other inequities.

Underrepresented minorities (black or African American; Hispanic; American Indian and Alaskan native; Pacific Islanders; and others) are the fastest-growing segment of the U.S. population, yet the percentage of biomedical scientists from those groups fails to mirror the diversity of the population.

NIH and other organizations have long known that building a diverse scientific workforce is important: Teams made up of scientists from different backgrounds—compared with homogenous groups—are better equipped to expand the range of research questions, interact more effectively with colleagues around the world, and address the needs of underrepresented racial and ethnic minorities in order to reduce health inequities. But achieving that diversity has been difficult.

OITE Director **Sharon Milgram** developed the diversity course as one way to address the problem. She based the course on discussions she had had with trainees about how being different—whether it had to do with gender and gender identity, ethnic background, sexual orientation, race, religion, immigrant status, socioeconomic status, or disability—made some of them feel uncomfortable at NIH. And Milgram herself, as well as other principal investigators (PIs), wanted to learn how to make their trainees feel more welcome.

"Hundreds of students and fellows have been trained in my lab, with a large portion coming from different ethnic, cultural, and religious backgrounds, underrepresented minorities, women, and low-income families," said one NIH scientist. "I felt the need to enhance my understanding of diversity so that I can be a better leader to my trainees."

In 2009, Milgram charged OITE Leadership and Professional Development Coach **Julie Gold** with finding a suitable instructor for a diversity course. Gold found Michael Sheridan, an associate professor in the National Catholic School of Social Service at The Catholic University of America (Washington, D.C.). Sheridan has been teaching courses in diversity and social justice around the world for nearly 20 years. She began teaching the NIH course in 2011.

Sheridan "is superb in her ability to foster group [and] team dynamics and interaction," said course participant **Patricia Cole**, director of OITE's Intramural Loan Repayment Program. She "challenges you to do personal reflections, which reinforce the course material."

"This course really opened my eyes to areas that I had been oblivious to," said **Sheila Caldwell**, a program director for the Native American Research Centers for Health in the National Institute of General Medical Sciences. "We don't intentionally discriminate, but our ignorance or lack of cultural understanding leads us to be less understanding and less patient. Seeing things through another's eyes . . . can provide us with a personal perspective."

"It was interesting to see how everyone, even the most conscientious and accepting individuals, have some biases," said **Philip Wang**, deputy director of OITE's Graduate Partnerships Program.

The course not only helped participants to become more self-aware, but has also propelled many to make changes in the way they interact with others.

"I can now talk with young people about what my biases are and what I struggle with," said **Rita Devine**, an assistant director for science administration in the National Institute of Neurological Disorders and Stroke. "That gives them the green light to ask me why and to also challenge some of their own perceptions about me or others."

"Personal experiences with those close to me like a deaf housemate, gay friends, and elderly parents (who are also immigrants) have helped me learn not to be so judgmental," said **Jameela Khan**, a former postdoctoral fellow in the National Institute of Allergy and Infectious Diseases. "I

try putting myself in their shoes and that is when it hits home the most."

Course participants were also encouraged to make personal commitments to change that would have positive effects both within NIH and in the broader community. For example, **Michelle Bennett**, deputy scientific director in the National Heart, Lung, and Blood Institute, was concerned that some women in lower socioeconomic groups were having an especially hard time finding jobs. She decided to create a leadership program for these women in Washington, D.C., "to help them build self-awareness and skills to increase their effectiveness and become competitive for new positions or the next step on their career ladder," she said. They are applying what they are learning to their professional lives.

Several participants were sensitized to the difficulties that NIHers with disabilities face. OITE's Wang and **Philip Ryan** (who were former NIH graduate students and postdocs) spearheaded the purchase of scooters as a small pilot program for trainees with mobility issues to get around campus. Another student alerted custodial staff to the empty, five-gallon water jugs that blocked drinking fountains and doorways, making them inaccessible to people in wheelchairs. The jugs were removed.

NCI postdoc **Christiane Kuschal**, along with another postdoc, started the Lesbian, Gay, Bisexual, and Transgender (LGBT) Fellows and Friends Group to help LGBT trainees connect and build community. (To join the LISTERV, go to https://list.nih.gov/cgi-bin/wa.exe?SUBED1=NIH-LGBT-FF&A=1.)

In fact, the 12-week diversity course has been so successful that elements of it have been incorporated into several other OITE programs including a workplace dynamics management series; a mentoring course for fellows who have summer students; Scientists Teaching Science; and the NIH Academy (for postbacs interested in health disparities). In addition, OITE is developing plans for a monthly diversity discussion group.

One powerful message from the course is reflected in a poem that Sheridan shared with the class: Antoinette Sedillo Lopez's "On Privilege." The poem's final line, "You only notice privilege when you don't have it," struck a chord with the class. By learning about the dynamics and consequences of both privilege and oppression, reviewing current research findings, and sharing and listening to one another's stories, participants deepened their understanding of health disparities and other inequities that determine life opportunities for many.

"The hope is that each participant will become an ally for diversity and social justice," said Milgram. "They will be more open to discussing difference and more aware of what they can do to be a part of making the NIH and scientific communities more welcoming and inclusive." ●

The next "Building the World We Dream About: Diversity in a Multicultural Society" course will be offered in 2014, beginning Tuesday, January 21 (3:00–5:00 p.m.). For more information about the course and other programs, contact Julie Gold at goldje@od.nih.gov. The course is open to NIH trainees and intramural and extramural staff.

To learn more about NIH's overall efforts to improve multicultural diversity in the intramural and extramural communities, go to http://acd.od.nih.gov/dbr.htm. In 2011, the Advisory Committee to the NIH Director formed a Working Group on Diversity in the Biomedical Research Workforce to analyze the problem and provide recommendations toward improving the recruitment and retention of underrepresented groups. A draft report was issued in 2012.

NEWS FROM AND ABOUT THE NIH SCIENTIFIC INTEREST GROUPS

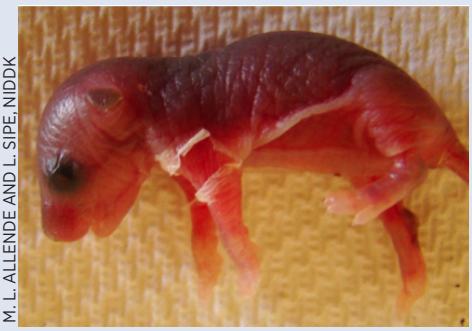
NEW SIG: Natural Products

The Natural Products SIG was created to bring together NIH program officials and intramural investigators who are interested in natural products research. "Natural products" are chemical substances with distinctive pharmacological effects that are produced by living organisms, most notably marine invertebrates, plants, fungi, and bacteria. Single chemical entities as well as their mixtures in natural product extracts have a long history of use as drugs, drug precursors, and/or complementary health adjuvants. Such materials have provided the source or inspiration for a vast number of FDA-approved agents and continue to be one of the major sources of inspiration for drug discovery. The SIG will meet quarterly and is open to all persons within NIH and associated agencies (FDA, USDA, etc.) who share an interest in natural products research. The group currently has 60 members—including intramural researchers and extramural program and review staff—and encourages collaborations among intramural researchers. For more information or to be added to the LISTSERV, contact John Williamson at williamsonjs@mail.nih.gov.

Neurodevelopmental Disorders

Coming soon: The Neurodevelopmental Disorders (NDD) Interest Group is being reconstituted. The NDD SIG will foster collaboration among NIH intramural investigators who are involved in both basic and clinical research that is related to autism spectrum disorders and other neurodevelopmental disorders. Monthly meetings are planned (stay tuned for meeting dates). The group moderator is Carolyn Beebe Smith, a senior investigator in NIMH's Section on Neuroadaptation and Protein Metabolism. To join the NDD SIG and received notifications of meetings and other events, contact Geeta Strange at strangegk@mail.nih.gov.

Intramural Research Briefs



M. L. ALLENDE AND L. SIPE, NIDDK

The peeling skin on the forelimb of this four-day-old mouse is caused by a missing gene that controls the concentrations of a lipid molecule called sphingosine-1-phosphate.

NIDDK: DISRUPTING THE INTEGRITY OF SKIN

Psoriasis and other skin diseases may be caused by disturbances in the balance between the growth and the differentiation of keratinocytes, the major cell type in the outer layer of skin. NIDDK researchers have found that a lipid molecule called sphingosine-1-phosphate (S1P) plays a key role in controlling the differentiation of keratinocytes. Mice missing the gene controlling intracellular S1P concentrations suffered from stunted growth and thickened skin that was prone to peeling within the first few days of life. Most of the mutant mice died but the ones that survived had skin abnormalities—their keratinocytes had high concentrations of S1P, which enhanced keratinocyte differentiation. The findings suggest that manipulating S1P concentrations may be a way to alter the abnormal growth and differentiation of keratinocytes. The researchers say that one possible treatment for psoriasis—a disorder in which there is a hyperproliferation of keratinocytes—might be to increase S1P concentrations. (NIDDK authors: M.L. Allende, L.M. Sipe, G. Tuymetova, K.L. Wilson-Henjum, W. Chen, and R.L. Proia, *J Biol Chem* **288**:18381–18391, 2013)

NIDCR: WHAT TRIGGERS ITCHING?

"What is an itch?" is a question that five-year-olds have used to stump Ph.D.s for years. Now, thanks to two scientists at NIDCR, we are closer to an answer. Itching was once thought to be a low-level form of pain, but the NIDCR scientists determined that a neurotransmitter called natriuretic polypeptide b (Nppb) is released in the spinal cord and carries the sensation of itch to the brain. They showed that mice lacking either Nppb or cells expressing its receptor in the spinal cord did not itch when administered itching agents, but were still sensitive to pain. Furthermore, an injection of Nppb led to the increased production of a previously identified itching molecule, the gastrin release peptide. The NIDCR scientists suspect that blocking Nppb might one day be a cure for chronic itching conditions such as eczema and psoriasis. (NIDCR authors: S. K. Mishra and M. A. Hoon; *Science* **340**:968–971, 2013)

NICHD: WOMEN'S BRAINS ARE HARDWIRED TO FOCUS ON INFANT'S CRIES

Mothers have long suspected that women's brains are hardwired to respond to the cries of a hungry infant. After all, a baby's survival depends on being fed, and in nature, it's females who need to respond. An NICHD researcher, in collaboration with other scientists, has shown that women's brains do indeed react differently than men's to a baby's cries. The nine men and nine women in the study were told to let their minds wander as they listened to a 15-minute recording of white noise interspersed with the sounds of an infant crying. Functional magnetic imaging scans of the participants' brains showed that, in the women, patterns of brain activity abruptly switched to an attentive mode when they heard the infant cries, whereas the men's brains remained in the resting state. The results were the same regardless of whether the participants were parents or nonparents. Such studies documenting the brain activity patterns of adults represent the first stages of neuroscience research to understand how adults relate to and care for infants. (NICHD author: M. Bornstein, *NeuroReport* **24**:142–146, 2013)

CONTRIBUTORS: KRYSTEN CARRERA, NIDDK; KATHERINE WENDELSDORF, NIAID

NIAAA: ANTI-SMOKING MEDICATION SHOWS PROMISE FOR TREATING ALCOHOL DEPENDENCE

Alcohol dependence is a chronic disease that includes symptoms such as craving, loss of control over drinking, withdrawal symptoms after stopping drinking, and tolerance (the need to drink greater amounts of alcohol to feel the same effect). NIAAA researchers, in collaboration with clinical investigators at other institutions, found that varenicline (marketed under the name Chantix), approved in 2006 to help people stop smoking, significantly reduced alcohol consumption and craving among 200 alcohol-dependent adults. Varenicline may work by partially stimulating receptors for nicotinic acetylcholine, a promising molecular target implicated in both nicotine and alcohol disorders. This hypothesis was supported by early animal studies, which showed that varenicline decreased alcohol consumption. The researchers conclude that longer treatment with varenicline and follow-up assessments to determine whether there are sustained effects would be a valuable next step in the development of this medication for alcohol problems. [NIAAA authors: R. Litten, J. Fertig, D. Falk, and M. Ryan, *J Addict Med* DOI: 10.1097/ADM.0b013e31829623f4 (2013)]

NIAID: HOW HIV KILLS IMMUNE CELLS

Untreated human immunodeficiency virus (HIV) infection destroys a person's immune system by killing infection-fighting cells, but precisely when and how HIV wreaks this destruction has been a mystery until now. New research by NIAID scientists revealed how HIV triggers a signal telling an infected immune cell to die. This finding has implications for preserving the immune systems of HIV-infected individuals. HIV replicates inside infection-fighting human immune cells called CD4+ T cells through complex processes that include inserting its genes into cellular DNA. The scientists determined that during this integration step, a cellular enzyme called

DNA-dependent protein kinase (DNA-PK) becomes activated. DNA-PK normally coordinates the repair of simultaneous breaks in both DNA strands. As HIV integrates its genes into cellular DNA, single-stranded breaks occur where viral and cellular DNA meet. Nevertheless, the scientists discovered, the DNA breaks during HIV integration surprisingly activate DNA-PK, which then performs an unusually destructive action: It elicits a signal that causes the CD4+ T cell to die. The cells that succumb to this death signal are the very ones mobilized to fight the infection.

The new findings suggest that treating HIV-infected individuals with drugs that block early steps of viral replication—up to and including activation of DNA-PK and integration—not only could prevent viral replication, but also may improve CD4+ T cell survival and immune function. The findings also may shed light on how reservoirs of resting HIV-infected cells develop and may aid efforts to eliminate these sites of persistent infection. (NIAID authors: A. Cooper, M. Garcıa, C. Petrovas, T. Yamamoto, R. A. Koup, and G. J. Nabel; *Nature* **498**:376–379, 2013)

NCI, NIAMS, CC, OD: LINK BETWEEN ALLERGIC AND AUTOIMMUNE DISEASES

NIH scientists and their colleagues in Qatar and Japan have discovered that a gene called *BACH2* may play a central role in the development of diverse allergic and autoimmune diseases, such as multiple sclerosis, asthma, Crohn's disease, celiac disease, and type 1 diabetes. Previous research had shown that people with minor variations in the *BACH2* gene often develop allergic or autoimmune diseases, and that a common factor in these diseases is a compromised immune system. In this study in mice, the *Bach2* gene was found to be a critical regulator of the immune system's reactivity. The finding that a single component of the immune system plays such a broad role in regulating immune function may explain why people with allergic and autoimmune diseases commonly have alterations in the *BACH2 gene*.

Genome-wide association studies showed that DNA from patients with diverse autoimmune disorders often had minor alterations in the *BACH2* gene, which laid the foundation for this research. The team found that if mice lacked the *Bach2* gene, their cells became inflammatory and the mice died of autoimmune diseases within the first few months of life. When they re-inserted *Bach2* (using gene therapy) into *Bach2*-deficient cells, the ability to produce regulatory cells was restored. These findings have implications for treating cancer as well as allergic and autoimmune diseases. The scientists are now working toward manipulating the activity of the *Bach2* gene, with the goal of developing a new cancer immunotherapy. (NIH authors: R. Roychoudhuri, K. Hirahara, K. Mousavi, J. J. O'Shea, N. P. Restifo, D Clever, C. A. Klebanoff, Z. Yu, M. Rao, P. Muranski, J. G. Crompton, L. Gattinoni, M. Bonelli, G. Sciumè, G. Vahedi, H. Takahashi, Y. Kanno, H. Zare, V. Sartorelli, B. Dema, J. Rivera, H. Liu, D. Bedognetti, E. Wang, F. M. Marincola, G. Punkosdy, and V. Hoffmann; *Nature* DOI: 10.1038/nature12199)

NIH TO REDUCE THE USE OF CHIMPANZEES IN RESEARCH

NIH announced recently that it plans to substantially reduce the use of chimpanzees in NIH-funded biomedical research and to designate for retirement most of the chimpanzees it currently owns or supports. NIH Director **Francis Collins** accepted most of the recommendations made by an independent advisory council (http://dpcpsi.nih.gov/council/working_group.aspx#Summary) for implementing a set of principles and criteria (http://iom.edu/Activities/Research/Chimpanzees.aspx) defined by the Institute of Medicine (IOM). NIH plans to retire about 300 government-owned chimpanzees and to retain, but not breed, up to 50 chimpanzees for future biomedical research. The chimpanzees that will remain available for research will be selected based on research projects that meet the IOM's principles and criteria for NIH funding. The chimpanzees designated for retirement could eventually join more than 150 other chimpanzees already in the Federal Sanctuary System, which is overseen by NIH.

NIH's decision "culminates more than two years of intensive deliberations among NIH leadership, independent chimpanzee experts, researchers, bioethicists, and members of the public," said **James M. Anderson**, NIH deputy director for program coordination, planning, and strategic initiatives, whose division oversees the NIH Chimpanzee Management Program. "We are grateful to all who have contributed their insight and expertise during the advisory process."

NIH's full response to the recommendations and public comments can be found at http://dpcpsi.nih.gov/council/working_group.aspx.

NIH

Pumpkin, a 24-year-old chimpanzee at the Alamogordo Primate Facility (APF), Alamogordo, N.M., loves coconuts and kiddie swimming pools. APF is a chimpanzee reserve where no research is conducted.

Chain Reaction

CONTINUED FROM PAGE 1

found in muscle cells. These chains extend across adjacent cells, allowing whole sheets of epithelial tissue to coordinate clear-cut changes in tension and shape.

The interlinked chains form a network across the entire epithelium, according to **Seham Ebrahim**, a visiting fellow in Kachar's lab and co-leading author of the study. "Any contraction or relaxation happening to one cell isn't just a local effect," said Ebrahim. It "is transmitted to the whole epithelial sheet to make sure all the cells are always in sync."

Using a mouse model, the researchers examined the epithelial belt in the organ of Corti, the part of the inner ear that shelters the sensory hair cells that turn the mechanical vibrations of sound into nerve impulses. The researchers tagged two types of myosin with fluorescent probes and then used powerful microscopes to visualize the order of the molecules within and between each cell.

These advanced techniques showed the precise links between epithelial cells. When the researchers used a drug to force the epithelial belt to relax, they were able to reveal that these links coordinate a dynamic dance that changes the tension between cells. In a relaxed state, the subunits making up the connections between cells maintained precise—if wider—spacing. When tension was restored, the subunits slid back into place. The scientists found the same linkage patterns between epithelial cells in the intestines and stomach, indicating that this coordination likely exists in organs throughout the body.

Mutations in the genes for the types of myosin studied in these experiments have been linked to many human diseases, not only hearing loss, and their mechanisms offer potential new pathways for developing interventions to treat diseases or disorders of the ear, eye, and lungs (among others) related to dysfunction in the epithelial sheet.

The study was also supported by the intramural division of the National Heart, Lung, and Blood Institute (NHLBI) and the Ministry of Education, Culture, Sports, Science and Technology/Japan Society for the Promotion of Science. ●

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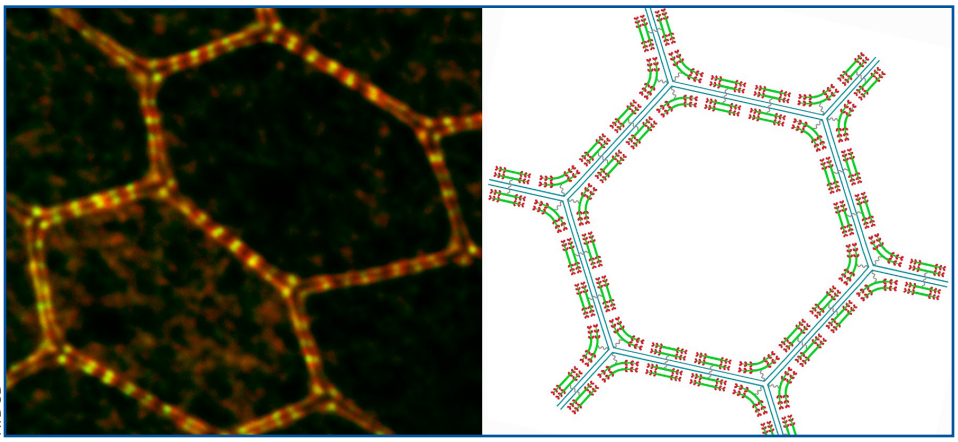

NIDCD

Fluorescence confocal image of the surface of an epithelial sheet (left) showing non-muscle myosin molecules arranged as contractile "dumbbell"-shaped units with their globular heads (red) flanking a rod-like region (green). The schematic (right) shows how the contractile units are oriented end-to-end (and interlaced with actin filaments, not shown) to form a belt that wraps around each cell and line up perfectly with their counterparts in neighboring cells to create an integrated network across the epithelium.

NIH ABBREVIATIONS

CBER: Center for Biologics Evaluation and Research, FDA
CC: NIH Clinical Center
CCR: Center for Cancer Research, NCI
CDC: Centers for Disease Control and Prevention
CIT: Center for Information Technology
DCEG: Division of Cancer Epidemiology and Genetics, NCI
DOE: Department of Energy
FAES: Foundation for Advanced Education in the Sciences
FelCom: Fellows Committee
FDA: Food and Drug Administration
FNL: Frederick National Laboratory
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCATS: National Center for Advancing Translational Sciences
NCCAM: National Center for Complementary and Alternative Medicine
NCBI: National Center for Biotechnology Information
NCI: National Cancer Institute
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: Eunice Kennedy Shriver National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OD: Office of the Director
ODS: Office of Dietary Supplements
OITE: Office of Intramural Training & Education
OIR: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women's Health
OTT: Office of Technology Transfer

Wei Yang: Deciphering the Three Rs of DNA

BY JENNIFER SARGENT, NIAMS

Fifteen years ago, the scientific world was skeptical when structural biologist **Wei Yang** reported she had identified unexpected enzymatic activity in one of the proteins that played an essential role in maintaining genome stability. Other scientists attributed her findings to contamination during a protein purification process.

But Yang persisted. She demonstrated adenosine triphosphatase (ATPase) activity in MutL, a key protein that corrects DNA replication errors. ATPase catalyzes a reaction that releases energy to be used in cellular metabolism. Until Yang's discovery no one understood how MutL worked. She also showed that MutL underwent a conformational change that modulated its specificity for binding DNA and protein cofactors. Her results, although controversial, were finally published in *Cell* in 1998 and 1999 (*Cell* **95:**541–552, 1998; *Cell* **97:**85–97, 1999). This year, in recognition of all her scientific accomplishments, Yang was elected to the National Academy of Sciences.

Yang, a section chief in the Laboratory of Molecular Biology in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), uses X-ray crystallography and other methods to study the enzymes involved in DNA repair, recombination, and replication—the "3 Rs" of DNA maintenance. X-ray crystallography is a technique used to deduce the 3-D structure of a protein—or a protein-substrate complex—by aiming X-rays at a crystal of the macromolecule and measuring the pattern and intensity of the scattered X-rays.

In a recent presentation to the scientific directors, Yang demonstrated how 3-D structures of protein-DNA complexes provide unique insights into dynamic interactions between proteins and their substrates. Her studies on DNA polymerase eta (Pol eta), an enzyme involved in DNA repair, have led to a better understanding of the molecular events underlying the genetic skin disorder xeroderma pigmentosum. Patients with the disorder are highly sensitive to the sun's ultraviolet rays and are at increased risk for developing skin carcinomas.

Early in her training, Yang never imagined she would become a structural biologist. When she began her graduate work, in 1985, at Columbia University's (New York) Department of Biochemistry and Molecular Biophysics, she had every intention of studying oncogenes and gene regulation. But during a rotation in a biophysics lab, one of her professors described structural biology as "molecular biology in three dimensions." These words stuck a chord with Yang and she shifted her doctoral studies from gene hunting to molecular biophysics.

In 1992, Yang joined the lab of future Nobel laureate Thomas Steitz at Yale (New Haven, Conn.). She wanted to examine the mechanisms of recombination activating gene (RAG)–mediated V(D)J recombination, the process by which antibodies and receptors are assembled in the immune cells. But she was ahead of her time—the tools needed were underdeveloped—and Steitz discouraged her from embarking on the project. Instead, she focused on gamma delta resolvase, an enzyme involved in DNA recombination in bacteria.

When Yang came to NIDDK in 1995 as an independent investigator, she was impressed with the collaborative environment of the NIH intramural community. She has since collaborated on many projects with NIH intramural investigators. She even had the opportunity to revisit her fascination with understanding V(D)J recombination by working with **Martin Gellert** (NIDDK).

Among Yang's other collaborators are **Robert Crouch** at the National Institute of Child Health and Human Development, and **Stuart Le Grice** at the National Cancer Institute. Their structural work provides insights into the molecular mechanism for HIV resistance in a broad range of antiretroviral therapy drugs. Yang hopes their work will lead to the development of novel anti-HIV therapeutics.

NIDDK scientist Wei Yang studies the enzymes involved in DNA repair, recombination, and replication—the "3 Rs" of DNA maintenance.

Yang's work goes beyond determining the 3-D nature of protein structures. By studying the 3Rs of DNA metabolism, she has contributed to our knowledge of enzymes that bind to and process DNA and extended these findings to clinical applications. For example, the same gene that is mutated in patients with xeroderma pigmentosum directs the production of an enzyme that interferes with a chemotherapy drug that kills cancer cells. Yang and her colleagues are using their knowledge of the structure and function of Pol eta to develop inhibitors that could increase the efficiency of anticancer drugs.

And so Yang returns to her roots—oncogenes and gene regulation—but now with a 3-D view. ●

An Interview with Hynda Kleinman

The Matrigel-Maker's Story

BY LAURA STEPHENSON CARTER

Hynda Kleinman

Hynda Kleinman revolutionized cell-culture research when she co-invented Matrigel cell-culture substrate at NIH in the 1980s. Until then, scientists grew cells in a flat layer in plastic culture dishes.

Matrigel is the most popular trade name for a protein mixture, secreted by certain mouse tumor cells, that assembles into a three-dimensional matrix that closely resembles the natural environments in which most mammalian cells grow. This invention allows researchers to grow and study cells that were previously difficult or impossible to culture and to observe complex cell behaviors in a more realistic environment. Today, Matrigel has widespread applications in research laboratories worldwide for studying angiogenesis, cancer, stem-cell differentiation, and other processes.

Kleinman worked at NIH from 1975 to 2006 in the National Institute of Dental and Craniofacial Research (NIDCR) and served as chief of the Cell Biology Section in NIDCR's Laboratory of Cell and Developmental Biology (1985–2006). Her laboratory was the first to report the wound-healing effects of thymosin beta 4 (TB4), a synthetic version of a naturally occurring molecule. Her research accomplishments also include identifying various angiogenic and antiangiogenic molecules and characterizing sites on laminin for adhesion, migration, neurite outgrowth, angiogenesis, metastases and inhibition of metastases, and the respective receptors.

She has more than 400 publications and 11 patents including two for Matrigel, which was one of the top royalty generators at NIH; served on editorial boards; and received many awards and fellowships within NIH as well as from outside organizations. In the 1990s and 2000s, she served on the Task Force on the Status of NIH Intramural Women Scientists (as chair from 1992 to 1994), which addressed gender-inequity issues.

Kleinman received her B.S. in chemistry from Simmons College (Boston) in 1969 and her Ph.D. from the Massachusetts Institute of Technology (MIT; Cambridge, Mass.) in 1973. She did postdoctoral training at Tufts University (Boston) before coming to NIH in 1975. She is currently a consultant to several biotech companies, an adjunct professor at George Washington University Medical Center (Washington, D.C.), and a guest researcher in NIDCR.

The following is an edited interview with the *NIH Catalyst*. A longer version is available online at http://irp.nih.gov/catalyst/v21i4/alumni-news.

CATALYST: Are you surprised that Matrigel was so successful?

KLEINMAN: I'm shocked that it's this useful and that no one has invented anything better. It's still made the exact same way we made it 25 years ago.

CATALYST: What are your other patents?

KLEINMAN: Among my patents are two for TB4, a small actin-binding protein. One is for wound healing and the other is for hair growth.

CATALYST: How does TB4 work?

KLEINMAN: It prevents cell death and stimulates stem cells to do repair. So whether the repair is a damaged muscle or an injury from a bullet to the brain or a burn to the skin, it works on all of them. It doesn't matter where you inject it, it knows where to go.

CATALYST: How well is it working?

KLEINMAN: It works very well in the eye for different kinds of eye problems such as dry eye. For the skin, clinical trials have shown that TB4 has a positive effect on accelerating the healing of certain kinds of pressure ulcers.

CATALYST: How do you know when a discovery is worth patenting?

KLEINMAN: Sometimes you know what other people are patenting, and you say, "Okay, I've got something that's better than that." Other times, it's a guess. I urge scientists to patent their discoveries. The success rate is 25 percent, which is higher than the grant-application success rate. It's an easy process. The NIH Office of Technology Transfer (OTT) handles patents and licenses. [For details on OTT's process, see http://www.ott.nih.gov.]

CATALYST: What got you hooked on science?

KLEINMAN: My family was very interested in nature. We were the only people in our neighborhood with a garden, and we always went fishing and hiking in the woods. In school, I was more interested in the biological and chemical sciences than I was in literature, reading, and history. In college, I got a National Science Foundation fellowship to work in a lab at Yale University [New Haven, Conn.]. From then on, it was absolutely clear what my path was going to be.

CATALYST: What challenges did you face as a woman scientist early in your career?
KLEINMAN: During my interview for grad school at MIT, they asked me what my husband did and what his plans were. He was a graduate student at Harvard. They were concerned that I would disappear with my husband to wherever his career took him. I said, "If you want to interview him, you should call him." They were a little surprised at that.

CATALYST: How did you help other women?
KLEINMAN: I had gone to an all-girls high school and an all-girls college. Then I went to male-dominated MIT. So my antennae were up. When I went to publish my paper on Matrigel, I looked at the journal's editorial board and saw it was all men. So I wrote a letter to them, and later to other journals, complaining about that. George Martin [then chief of NIDCR's Laboratory of Developmental Biology and Anomalies] signed the letters. Later, when I felt more comfortable, I signed them myself. I learned that if I was going to complain, I also had to give them a list of five women to consider. People at NIH knew that I was writing these letters [laughs]. So they thought of me when Bernadine Healy [NIH Director, 1991–1993] created the committee to investigate the status of women at NIH.

CATALYST: Have things improved for women scientists at NIH?
KLEINMAN: For awhile things seemed a little better. I think the women who survive are the ones with good mentors who protect them and support them and promote them.

CATALYST: Who was *your* mentor?
KLEINMAN: George Martin. He was at NIH for 30 years—in NIDCR and later as the scientific director at the National Institute of Aging. He's an emeritus and a consultant now.

CATALYST: How did he encourage you?
KLEINMAN: He was very accessible and generous with his time. He offered us [his mentees] ideas and opportunities. He would encourage us to go to meetings, to give talks, and to ask questions at seminars. He really promoted us. He introduced us to other scientists when they visited and even invited us to have lunch with them. Things like that are normal today, but not back then. He was unusual for his time.

CATALYST: What have you enjoyed most in your career?
KLEINMAN: The students and postdocs. It's been fun watching them grow and seeing how much they can do. They did very well. I try to keep in touch with most of them. Most of the students went on to medical school.

CATALYST: One last question. How did you wind up being listed in the credits for the 2001 horror movie classic *Session 9*?
KLEINMAN: My husband's cousin was a movie set director and needed sets for a lobotomy lab. *Session 9* was being filmed at an abandoned mental hospital in Massachusetts. I went to the National Library of Medicine to look at old books with pictures of lobotomy tools and of people who had had lobotomies. I collected a bunch of old lab equipment and got permission to send them to my cousin-in-law. He outfitted a lobotomy lab with old, cracked beakers, giant tweezers and tongs, and other things that could pass for old lobotomy tools—at least on a movie set. I never saw the movie myself.

To read more about the Matrigel story:
Semin Cancer Biol **15**:378-386, 2005
Curr Opin Cell Biol **22**:677-689, 2010
To see a video of Hynda Kleinman's presentation at the Philip Chen, Jr., Lecture, on November 15, 2012, go to http://videocast.nih.gov/launch.asp?17665.

Other Alumni News

Tee. L Guidotti, a former clinical associate in the National Institute of Metabolism and Digestive Diseases (1977 to 1979) and considered a thought-leader in the field of occupational and environmental medicine, was recently awarded the William S. Knudsen Award for Lifetime Career Achievement in Occupational and Environmental Medicine. His 30-year academic career in medicine and public health included founding an internationally important program at the University of Alberta (Canada) and, more recently, positions including a department chair at George Washington University, from which he retired in 2009 in order to launch a second career. He served as president of the American College of Occupational and Environmental Medicine in 2006 and of the Association of Occupational and Environmental Clinics in 2002. Guidotti has over 300 academic publications and seven books to his credit and is also editor-in-chief of *Archives of Environmental and Occupational Health*.

The Knudsen Award is the highest honor in the field and is given by the American College of Occupational and Environmental Medicine. Guidotti was recognized for his book *The Praeger Handbook of Occupational and Environmental Medicine*, which has been described as "transformative to the field," as well as his research and academic contributions made during his career. He is now a full-time consultant with Medical Advisory Services in Rockville, Md.

Recently Tenured

MICHAEL GRIGG, NIAID

SUSHIL RANE, NIDDK

MICHAEL GRIGG, PH.D., NIAID

Senior Investigator; Chief, Molecular Parasitology Unit, Laboratory of Parasitic Diseases

Education: University of British Columbia, Vancouver, Canada (B.Sc. in biochemistry); Imperial College of Science, Technology, and Medicine, University of London, London (Ph.D. in biochemistry; D.I.C.)

Training: Howard Hughes Medical Institute senior fellow, University of Washington (Seattle); postdoctoral scholar, molecular parasitology, Stanford University (Stanford, Calif.)

Before coming to NIH: Assistant professor of medicine, microbiology, and immunology at the University of British Columbia

Came to NIH: In 2006 as a tenure-track investigator

Selected professional activities: Fellow of the Canadian Institute for Advanced Research's Integrated Microbial Biodiversity Program

Outside interests: Running marathons; rowing; kayaking; spending time outdoors

Research interests: The Molecular Parasitology Unit uses population-, forward-, and reverse-genetics techniques to understand the molecular basis of virulence and pathogenesis in parasitic protozoa. Protozoal zoonoses (diseases that can be naturally transmitted from animals to humans) are serious pathogens of humans and animals throughout the world. By studying these protozoa, scientists have gained significant insights into fundamental processes such as antigenic variation, virulence shifts, and RNA editing.

My program's focus is on the food- and water-borne parasite *Toxoplasma gondii*, a pathogen that causes lethal infections in developing fetuses and immunocompromised patients. It also causes blinding chorioretinitis, an inflammation of the retina, in children and adults. In all hosts, *T. gondii* establishes life-long infections. Despite its prevalence as a human pathogen, surprisingly little is known about how it causes disease. What's more, there is no vaccine or drug that can control it.

Our laboratory has developed new genetic, genomic, and molecular-imaging techniques to identify—in animal models of infection—the genes that enable these parasites to enter and colonize host cells, evade the immune system, and cause virulent disease. Virulence is a critical pathogen-enhancing determinant of infectious diseases. Our studies are establishing how virulence emerges, how it is propagated by parasite sexual cycles, and how it is maintained in complex genetic populations circulating in the vast array of intermediate hosts these parasites infect. Our work deals with the genetic origins of outbreaks caused by a large and diverse group of eukaryotic pathogens, including species of Toxoplasma, Plasmodium (the causative agent of malaria), Cryptosporidium, Leishmania, and Giardia.

Because little is known about eukaryotic pathogenic processes compared with those of bacterial or viral pathogenesis, entirely new mechanisms and principles of pathogenesis are emerging from our work.

SUSHIL G. RANE, PH.D., NIDDK

Senior Investigator; Chief, Cell Growth and Metabolism Section

Education: University of Bombay, Mumbai, India (B.S. and M.S. in biology and biochemistry); Temple University, School of Medicine, Philadelphia (Ph.D. in biochemistry)

Training: Postdoctoral fellowships at Bristol-Myers Squibb Pharmaceutical Research Institute (Princeton, N.J.) and at Fels Research Institute (Philadelphia)

Came to NIH: In 2001 as NCI Scholar; in 2006 became a tenure-track investigator in NIDDK

Selected professional activities: Reviewing manuscripts; organized a TGF-beta Special Interest Group on campus

Outside interests: Coaching baseball teams that his two sons play on

Research interests: My research group studies the molecular underpinnings of glucose and energy balance to better understand obesity and diabetes. We focus on the cell cycle—how cells divide and replicate. Using mouse models, we study how the cell cycle influences glucose regulation, energy homeostasis, and beta cells.

Beta cells store and release insulin and are found in the pancreas. My group showed that a key cell-cycle protein, Cdk4, regulates beta-cell mass, a finding that may have potential clinical applications for diabetes therapy. Currently, we are investigating molecular pathways involving cell-cycle regulators that lead to increases in beta-cell mass and improvements in beta-cell function.

We also study how cell-cycle proteins influence the growth, development,

differentiation, and death of cells that comprise the organs that maintain normal glucose tolerance and glucose homeostasis. Our goal is to determine how the expression of cell-cycle molecules and their resultant biological pathways differ in obesity and diabetes.

We demonstrated that the TGF-beta signaling pathway regulates glucose tolerance and energy homeostasis and that it controls the acquisition of properties of metabolically beneficial brown fat within the often problematic white fat. The switch of white fat to brown fat may protect against obesity and diabetes. We strive to further characterize the mechanisms involved in the switch.

We hope our findings will provide an integrated view into multiorgan communication as it relates to glucose homeostasis and energy balance. Ideally, this information will deepen our understanding of the pathogenesis of diabetes and obesity, and contribute to the development of rational therapies. ●

NIH IN HISTORY

The NIH Stetten Museum loaned an early HIV test kit and a 1983 notice to blood donors about AIDS to the New York Historical Society's new exhibit "AIDS in New York: The First Five Years." The exhibit explores the impact of the AIDS epidemic on personal lives, public health and medical practices, culture, and politics in the first years (1981–1985) of recognition of the mysterious and fatal disease. The exhibit opened on June 7, and will run through September 15, 2013. Find out more at http://www.nyhistory.org/exhibitions/aids-new-york-first-five-years

For more news about the NIH Office of History, visit http://history.nih.gov.

ANNOUNCEMENTS

SUMMER POSTER DAY 2013
Thursday, August 8, 2013
9:00 a.m.–3:00 p.m.
Natcher Conference Center (Building 45)
NIH Investigators, staff scientists, and scientific administrators are encouraged to visit posters by NIH summer interns and engage their authors in discussion. For more information, visit https://www.training.nih.gov/summer_poster_day.

WALS RETURNS IN SEPTEMBER
Kickoff on Monday, September 9
Most Wednesdays, 3:00–4:00 p.m.
Masur Auditorium (Building 10)
The 2013–2014 Wednesday Afternoon Lecture Series (WALS) starts on a **Monday (September 9)** with Cori Bargmann, from The Rockefeller University (New York), who will talk about brain mapping. Then the Wednesday schedule resumes with on September 11 with Jeffrey Esko from the University of California, San Diego, School of Medicine (La Jolla, Calif.) who will present "Proteoglycans: Arbiters of Lipoprotein Metabolism." The full schedule will be posted soon at http://wals.od.nih.gov.

2013 RESEARCH FESTIVAL
October 7–11, 2013
FAES Academic Center (Building 10)
Masur Auditorium (Building 10)
The theme this year is "Sixty Years Later: The Double Helix in the Clinical Center." For more information visit http://researchfestival.nih.gov, or contact Jacqueline Roberts at 301-594-6747 or robertsjm@od.nih.gov.

"INFLAMMATION, MICROBIOTA, AND CANCER" SYMPOSIUM
September 19–20, 2013
8:30 a.m.–5:00 p.m.
Masur and Lipsett Auditoriums (Building 10)
NCI's Center for Cancer Research is hosting a national symposium, which promises to be an exciting forum for discussion and debate on the current understanding of cancer and inflammation. Topics include inflammation and microbiota; cancer, microbiota, and metabolism; miRNAs, cancer and inflammation; and cancer, inflammation, and immunity. Registration is free, but seating is limited; visit http://ncifrederick.cancer.gov/events/microbiota/default.asp.

SYMPOSIUM ON CARDIOVASCULAR REGENERATIVE MEDICINE
September 25–26, 2013
Natcher Conference Center (Building 45)
NHLBI's fifth Symposium on Cardiovascular Regenerative Medicine will bring together experts in basic stem-cell biology and experts in clinical cardiovascular medicine to discuss the emerging basic science, preclinical animal models, and potential clinical applications. Topics will include general and cardiovascular stem cells, clinical applications, tissue engineering, developmental biology, and large-scale proteomics and metabolomics as a tool to identify new clinical deliverables. There will also be a poster session. For more information and to register (registration is free, but required), go to http://www.nhlbi.nih.gov/news/events/2013-nhlbi-cvregenmed/.

NATIONAL GRADUATE STUDENT RESEARCH CONFERENCE
October 6–8, 2013
FAES Academic Center (Building 10)
Natcher Conference Center (Building 45)
Ninety advanced graduate students will visit NIH, share their cutting-edge research, and learn about scientific advances at NIH. Investigators will have the opportunity to recruit participants, who are selected competitively from a pool of more than 500 racially and ethnically diverse applicants. The agenda includes workshops and poster sessions. NIH investigators and current postdoctoral fellows are encouraged to visit the posters to discuss potential collaborations and learn about approaches that could enhance their investigations. For information visit https://www.training.nih.gov/events/recurring/nih_national_graduate_student_research_festival. ●

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CATALYTIC REACTIONS?

If you have a photo or other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation or confession that scientists might appreciate and that would be fit to print in the space to the right, why not send it via e-mail: catalyst@nih.gov; fax: 301-402-4303; or mail: *The NIH Catalyst*, Building 1, Room 333.

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

History Mystery

The *NIH Catalyst* thanks readers who responded to the NIH Office of History's mystery photo that appeared on the back page of the May–June 2103 issue (http://irp.nih.gov/catalyst/v21i3/nih-in-history). We hope to share the results soon.

PHOTOGRAPHIC MOMENT

Sunrise

SAMARENDRA SINGH, NIDDK

Samarendra Singh arrived at the NIH Bethesda campus one morning at 5:00 a.m. to tend to his experiments. But before he headed to the lab, he stopped long enough to set up his tripod camera mount on the grass near the Natcher Building (Building 45) and wait until the light was just right to snap this photo. "The sky was cloudy but the light dispersed by the rising sun was magical," he said. Singh is a visiting postdoctoral fellow in NIDDK's Laboratory of Molecular Biology.

HAVE A LATE-NIGHT LABORATORY CONFESSION OR A SPECTACULAR PHOTOGRAPH TO SHARE?
SEND IT TO CATALYST@NIH.GOV AND WE JUST MIGHT PRINT IT.

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