

nih record



ABOVE • Their hearts weren't exactly on their sleeves, but the "Get Heart Healthy!" message got across. See p. 5.

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NIH, Industry and Non-Profits Partner to Speed Validation of Disease Targets

NIH, 10 biopharmaceutical companies and several nonprofit organizations launched an unprecedented partnership on Feb. 4 to transform the current model for identifying and validating the most promising biological targets of disease for new diagnostics and drug development.

The Accelerating Medicines Partnership (AMP) aims to distinguish biological targets of disease most likely to respond to new therapies and characterize biological indicators of disease, known as biomarkers. Through the Foundation for the NIH, AMP partners will invest more than \$230 million over 5 years in the first projects, which focus on Alzheimer's disease, type 2 diabetes and the autoimmune disorders rheumatoid arthritis and systemic lupus erythematosus (lupus).

SEE AMP, PAGE 6



NIH director Dr. Francis Collins unveils AMP at National Press Club on Feb. 4.

Neighborhoods Do Exert Influence

Fuchs Describes Importance of Niche in Stem Cell Biology

Dr. Elaine Fuchs has taken advantage of the abundance and regenerative capacity of hair and skin to do groundbreaking research on stem cells. To keep harmful microbes out, retain fluids and repair wounds, humans must constantly replenish their body surface, the epidermis. Hence the skin stem cells that achieve this practically announce their suitability for study.



Dr. Elaine Fuchs

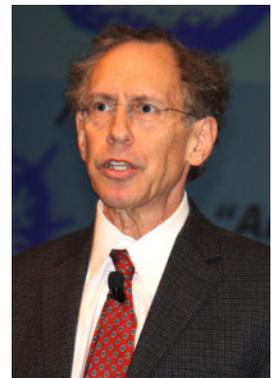
In her Jan. 15 talk "Carving Out a Niche for Stem Cells" in Masur Auditorium, Fuchs, who is Rebecca C. Lancefield professor of the laboratory of mammalian cell biology and development

SEE FUCHS, PAGE 4

Langer Makes a Career of Doing the Impossible

By Karin Lee

With a list of accolades that might make anyone blush, Dr. Robert Langer's career as an engineer and David H. Koch institute professor at MIT appears to have been thoroughly charmed by the STEM deities. So it was surprising to hear—over the course of his hour-long Wednesday Afternoon Lecture Series talk on Jan. 29—of the rejection that characterized his early career.



Dr. Robert Langer

As a young chemical engineer just out of school in Boston during the 1970s gas shortage, Langer found himself awash in job offers. "I went and interviewed at oil companies—20

SEE LANGER, PAGE 8



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NIH Record Office Bldg. 31, Rm. 5B41
Phone (301) 496-2125 Fax (301) 402-1485

Web address <http://nihrecord.od.nih.gov>

Editor
Richard McManus
Rich.McManus@nih.gov

Associate Editor
Carla Garnett
Carla.Garnett@nih.gov

Staff Writers
Jan Ehrman
Jan.Ehrman@nih.gov

Dana Steinberg
Dana.Steinberg@nih.gov

Belle Waring
Belle.Waring@nih.gov

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NIH...Turning Discovery Into Health

briefs

Cuervo To Give Pittman Lecture, Mar. 19

Dr. Ana Maria Cuervo of Albert Einstein College of Medicine will give the annual NIH Director's Margaret Pittman Lecture on Wednesday, Mar. 19 at 3 p.m. in Masur Auditorium, Bldg. 10. Her topic is "Did You Remember to Take Out the Trash? Your Cells Sure Did!"



Cuervo studies the role of protein-degradation in aging and age-related disorders, with an emphasis in neurodegeneration. Her group is interested in understanding how altered proteins can be eliminated from cells. Her laboratory has linked alterations in lysosomal protein degradation (autophagy) with different neurodegenerative diseases including Parkinson's, Alzheimer's and Huntington's disease. They have also proven that restoration of normal lysosomal function prevents accumulation of damaged proteins with age, demonstrating that removal of these toxic products is possible.

The lecture honors Dr. Margaret Pittman, NIH's first female lab chief, who made significant contributions to microbiology and vaccine development, particularly in the areas of pertussis and tetanus, during her long career at NIAID.

The lecture is part of the Wednesday Afternoon Lecture series. For information and reasonable accommodation, call Jacqueline Roberts, (301) 594-6747.

STEP Forum on 'Where Babies Come From'

The staff training in extramural programs (STEP) committee will present "Where Do Babies Come From? (Revised Edition)," on Tuesday, Mar. 11 from 9 a.m. to noon in Rockledge II, Rm. 9116.

Such a simple question, such a complicated answer in today's society. As fertility treatments have become widely available, tens of thousands of babies have been born using medically assisted reproductive technologies. What are the costs, what are the risks? Join us as we explore not only the latest technologies, but also access disparities, ethical issues and potential long-term outcomes for children and families.

Batter Up! Orioles, Nationals Ticket Sales

R&W will once again offer tickets to the Baltimore Orioles and Washington Nationals. To better serve the community, tickets will be sold online. Orioles tickets go on sale Tuesday, Mar. 11 at 8 a.m. at www.fedesp.com/nih/rw-services/rw-online-store/. Available are two regular season tickets (2 seats behind first base – Section 14BBB, seats 7-8). Nationals tickets go on sale Thursday, Mar. 13 at 8 a.m. at the same web address. Available are 2 seats in Section 219, Row D. Prices for all games will be announced on the R&W listserv and in the March R&W Newsletter. You must be a 2014 R&W member to purchase tickets. Memberships can be purchased at R&W stores or online and cost \$9 for the year. For details on auctions of opening day tickets for both the Nationals and Orioles, email nihrw@mail.nih.gov.

www.fedesp.com/nih/rw-services/rw-online-store/. Available are two regular season tickets (2 seats behind first base – Section 14BBB, seats 7-8). Nationals tickets go on sale Thursday, Mar. 13 at 8 a.m. at the same web address. Available are 2 seats in Section 219, Row D. Prices for all games will be announced on the R&W listserv and in the March R&W Newsletter. You must be a 2014 R&W member to purchase tickets. Memberships can be purchased at R&W stores or online and cost \$9 for the year. For details on auctions of opening day tickets for both the Nationals and Orioles, email nihrw@mail.nih.gov.

NIH Management Intern Program Recruits

Unlock a new career path with the NIH Management Intern Program, which is recruiting Apr. 7-11. The MI Program is a highly competitive, 2-year career-development program for current NIH employees. MIs come from a variety of job backgrounds including both scientific and administrative fields. Upon completion of the program, MIs transition into an administrative-management career in one of many areas throughout the NIH enterprise. Eligible employees are invited to apply. For program FAQs, upcoming information sessions and details about eligibility, visit <http://trainingcenter.nih.gov/intern/mi/>.

Changes Coming to HR Systems

The Department of Health and Human Services is implementing a program that will move HHS agencies to new human resources (HR) systems as well as change payroll service providers. HHS is calling this effort the HR Modernization Program, also referred to as the National Finance Center (NFC) migration. Agencies will be moving to the new systems in several waves, with NIH's migration estimated to be rolling out in early 2015.

NFC systems will replace three of NIH's current systems: myPay, the Integrated Time and Attendance System (ITAS) and Capital HR (EHRP) with a suite of integrated systems offering enhanced functionality, reduced costs, improved data accuracy and standardized processes throughout HHS.

Currently, NIH teams are working to ensure that the data housed in NIH's HR systems is current and accurate. This will assure a smoother transition when the new systems deploy. The NIH HR modernization program team has given presentations to administrative officers, executive officers and others to keep NIH staff informed.

As NIH gets closer to implementation, the team will ensure that NIH is prepared for the new systems. The team will provide change management tools for staff such as web sites, training and user guides, in addition to ongoing communication.

For more information, visit <http://hr.od.nih.gov/hr-systems/nfcmigration.htm>. You may also join the HR modernization Yammer group by logging into www.yammer.com.

Questions? Contact NFCMigration@mail.nih.gov.

nih record



Attendees gather for the recent NIAMS Coalition outreach and education meeting. The coalition is a group of nearly 90 professional and voluntary organizations concerned with the NIAMS portfolio.

NIAMS Coalition Comes Together for Outreach, Education

More than 40 representatives of the NIAMS Coalition recently attended its Outreach and Education Meeting: Creating Connections for Science. Attendees expanded their knowledge of the programs and opportunities available at NIH and NIAMS, interacted with staff and shared ideas about how best to collaborate with the institute and each other. The coalition is a group of nearly 90 professional and voluntary organizations concerned with the NIAMS portfolio.

NIH director Dr. Francis Collins welcomed participants and called the event “a celebration of accomplishments in science, education and outreach.” He provided an overview of recent events and urged attendees to spread the word about how NIH helps to grow the economy, in part, by reducing the burden of chronic disease. “I hope today you can learn more and create some inspirational ideas. Thank you for the work you do,” he concluded.

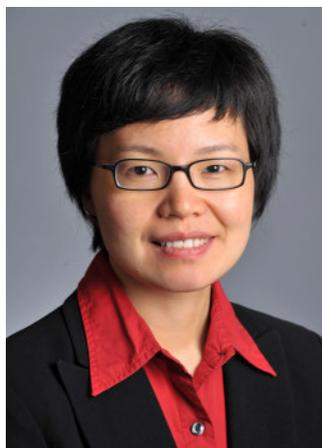
NIAMS director Dr. Stephen Katz offered research highlights and briefly discussed the impact of the 2013 government shutdown. He noted that there was one bright spot for NIH during the shutdown. In almost every mention—from scientific journals, to news outlets and even on the floor of Congress—the importance of the work NIH does was emphasized. “It was a difficult time, but it was heartening for us to hear how much NIH’s work is valued by every community throughout this nation,” Katz said.

Attendees heard about the importance of public-private partnerships from Dr. David Eckstein of NCATS and Dr. Maria Freire of the Foundation for the National Institutes of Health. Both gave examples of current ini-

tiatives that show how combining the forces of the public and private sectors can accelerate development of technologies and therapies for prevention, early detection, diagnosis and treatment of disease.

Breakout sessions covered topics such as collaborations to foster innovative research and training, partnerships in outreach to underserved populations and effective communication with key audiences. The meeting concluded with a presentation by Dr. James Onken of the Office of Extramural Research. He discussed how coalition organizations can leverage existing tools and resources such as RePORT to track and analyze NIH-supported research.

“The coalition leads efforts to educate stakeholders on the importance of the research funded by the NIAMS. Learning about the activities of the institute through meetings and events like this one makes us better at what we do,” said coalition co-chair Kim Cantor of the Lupus Foundation of America.—Sara Rosario Wilson



NLM Lecture Features Weng, Mar. 5

The National Library of Medicine Informatics Lecture Series will feature Dr. Chunhua Weng on Wednesday, Mar. 5, from 2 to 3 p.m. in Natcher Bldg., balcony A. She will speak on “Bridging the Semantic Gap Between Clinical Research Eligibility Criteria and Clinical Data.”

With the burgeoning adoption of electronic health records (EHRs), vast amounts of clinical data are increasingly available for computational reuse. However, there is a semantic gap between the raw clinical data and free-text human-provided eligibility criteria. Weng will describe the evolving understanding of the semantic gap and

approaches to overcoming it in the context of EHR-based phenotyping and clinical trial prescreening.

Weng is the Florence Irving assistant professor of biomedical informatics at Columbia University, where she has been a faculty member since 2007.

The talk will be broadcast live and archived at <http://videocast.nih.gov/>. Sign language interpreters will be provided. Those who need reasonable accommodation to participate should contact Ebony Hughes, (301) 451-8038, Ebony.Hughes@nih.gov or the Federal Relay (1-800-877-8339).

FUCHS

CONTINUED FROM PAGE 1

and HHMI investigator at Rockefeller University, described work that has pointed lately in the direction of determining the cause of squamous cell carcinomas of the skin, head and neck, tackling one of the most common and life-threatening cancers world-wide.

Fuchs also demonstrated that those who think the era of stem cell biology began only recently are more than a century late to the party; the term “stammzelle” was first used in 1877 by Ernst Haeckel. In the early 1900s, Alexander Maximov proposed that blood cells arise from a stem cell. In the mid-1970s, Fuchs’ mentor, Dr. Howard Green at MIT, was the first to culture stem cells. They were epidermal stem cells and Green applied his methods to treat burn victims by using their stem cells to create sheets of cultured skin.

Green’s work repairing burned skin led to a number of new

insights: the lab-grown skin never showed any signs of promoting cancer, thus eliminating one worry about this particular stem cell therapy. And the “artificial” sheets of skin were incapable of growing hair or sweating, which eventually resulted in the realization that a niche, or a cell’s neighborhood, sends powerful signals orchestrating normal development; Fuchs’ studies have shown that hair follicles, sebaceous and sweat glands have their own stem cells apart from epidermal stem cells.

In the eye as well, regenerative medicine has already laid down milestones: transplants of corneal epithelial cells have restored vision in at least 100 patients over the past decade, Fuchs said.

Regardless of which epithelial stem cell she interrogates, Fuchs finds that stem cells rely on heterologous neighbors, or their niche, to fulfill function.

Hair follicle stem cells are particularly abundant in most mammals such as the laboratory mouse. The ability of hair follicles to undergo cycles or spurts of follicle regeneration and hair growth makes it an ideal model for studying how stem cells toggle between resting states when they aren’t making tissue and active states when they are, she explained. Governing

that cycle are cues from the microenvironment, or cell signals.

“As we began to delve deeper into how the hair follicle stem cells respond to these cues to become activated,” Fuchs said, “we realized that if we genetically manipulate them to become more responsive, the skin of the mice becomes prone to developing cancer.”

It turns out that stem cells are regulated by both heterologous and progeny niche cells—it’s a continuous feedback loop. “This is why wound repair has a ‘stop’ signal eventually,” Fuchs explained. “This system is perturbed in cancer... Cancer hijacks how stem cells transition from quiescence to activation.”

Fuchs and her team have isolated and characterized cancer stem cells from squamous cell carcinomas of the skin. It turns out that squamous cell carcinoma arises from a niche of its own, she said.

“We have discovered more than 700 differences between cancer stem cells and normal stem cells. The problem we face is similar to that faced by the National Cancer Institute’s human cancer sequencing project, where hundreds of mutations have been found in human squamous cell carcinomas that are not found in normal human skin. Which of these differences is causal to cancer and which are mere bystanders?”

Most exciting, Fuchs’ team has developed a new method to carry out large-scale screens in mice, similar to what makes the worm and fly such amenable organisms for geneticists. In screening the gene alterations in cancer stem cells and those from human head and neck cancers, the group identified seven new tumor suppressor genes, previously unconnected to cancer. They presented their new work at NIH for the first time. It was published recently in *Science*.

As detailed and complicated as the pathways they are searching turn out to be, Fuchs let a last slide serve as a motto: “Don’t get so engrossed in details that you miss the big picture.”

And, as if niche only played a role in determining cell behavior, Fuchs reminded her audience of the importance of niche in the production of talented scientists: NIH director Dr. Francis Collins (who introduced Fuchs’ talk) inherited his first graduate student (now a professor at Duke) from Fuchs’ lab. And Fuchs’ lab begat NHGRI’s Dr. Julie Segre, who was recently celebrated as federal Employee of the Year.

The full lecture is on view at <http://videocast.nih.gov/summary.asp?Live=13556&bhcp=1>.



“We have discovered more than 700 differences between cancer stem cells and normal stem cells,” said Fuchs. Looking on is NIH director Dr. Francis Collins, who introduced her.

PHOTOS: ERNIE BRANSON

Berger To Discuss Senescence, Aging In Mahoney Lecture

Dr. Shelley L. Berger will discuss “Epigenetic Regulation of Senescence and Aging” Mar. 12 at 3 p.m. in Masur Auditorium, Bldg. 10. She will give the annual Florence Mahoney Lecture on Aging, sponsored by NIA and part of the NIH Director’s Wednesday Afternoon Lecture Series.



Berger is a leader in the field of eukaryotic gene regulation, unifying understanding of transcription and chromatin regulation. Her pioneering studies elucidated mechanisms of histone modifications, modifier enzymes, their complexes and their coordination.

For the Mahoney lecture, she will discuss the role epigenetic changes play in human cellular senescence and aging. Current thinking holds that aging is plastic and its pace can be slowed or even reversed; epigenetic alterations may be key to this potential reversibility. Cellular senescence is a state of proliferation arrest in response to cellular stress, such as long-term cell replication in differentiated cells. While senescence is protective to the organism against stress in the short-term, the cells also undergo damage contributing to “aging,” a highly deleterious consequence. Berger’s work has uncovered dramatic alteration of the epigenetic landscape in senescence and aging, providing potential for epigenetic therapy to address deterioration on a broad front to improve health span.

Since 2009, Berger has been the Daniel S. Och university professor at the University of Pennsylvania and is a faculty member in the cell & developmental biology department in the Perelman School of Medicine. She also serves as founder and director of the epigenetics program at Penn School of Medicine. She received her Ph.D. and B.S. in biology from the University of Michigan. Berger is the recipient of an Ellison Foundation Senior Scholar Award and an HHMI collaborative research award. She is a member of the American Academy of Arts and Sciences and Institute of Medicine of the National Academies. She also helped create the NIH-sponsored Human Epigenome Project.

There will be a reception and an opportunity to talk with the speaker in the NIH Library following the lecture.



Heart Health Awareness Gets Boost

“Get heart healthy!” shouted more than 100 NIH’ers who gathered in the Clinical Center’s atrium on Feb. 3 to help make a video to promote National Wear Red Day on Feb. 7. The group created an 18-foot-wide heart to help raise awareness about women and heart disease. February is American Heart Month. Over the past decades, NIH research has played a key role in the dramatic decline in heart disease mortality. “Help us to spread the word that heart disease is preventable,” said NHLBI director Dr. Gary Gibbons. “By making healthy lifestyle changes and taking steps to manage risk factors, we can reduce the risk for heart disease.” Gibbons is in the front row at bottom, along with NIH director Dr. Francis Collins, CC director Dr. John Gallin, NIDDK director Dr. Griffin Rodgers and ORWH director Dr. Janine Clayton.

PHOTO: GREG LAVINE

Campus Feels Effects of Unusual Snow Season

The Bethesda campus showed the impact of an unusually snowy winter so far in the D.C. area. Some communities saw upwards of 3 feet of the white stuff over the course of a 2-week span—the largest measurable amounts since “Snow-mageddon” in 2010. Grounds and buildings were closed to all but the essential on a couple of occasions when travel was deemed unfit for the masses.

PHOTOS: BILL BRANSON, ANDY HARBERT



Right:

In addition to Collins (l), other speakers assemble to discuss AMP.

“What we would like to have is a precise navigation system—a GPS for human disease,” said Dr. Mikael Dolsten (c), president of worldwide research and development at Pfizer.

Lupus patient Shanelle Gabriel, a performance artist, said, “To see everyone in here teaming up together to try to find better ways to help people like me...it means a lot.”



AMP

CONTINUED FROM PAGE 1

“AMP is tackling a major challenge in drug development, on an unprecedented level,” said NIH director Dr. Francis Collins. “As you know, amp is a unit of current, and we’re all amped up this morning about the promise of this new consortium.”

“The good news is that recent dramatic advances in basic research are opening new windows of opportunity for therapeutics. But this challenge is beyond the scope of any one of us and it’s time to work together in new ways to increase our collective odds of success.”

Unveiling AMP at the National Press Club downtown, Collins continued, “It means we are going to try to increase the odds of picking the right targets to go after for the next generation of drug development...This landmark partnership will transform the way we develop medicines. And I think no one will be happier to hear that than patients and their loved ones, for whom we really are dedicated in this effort.”

A critical and groundbreaking element of the partnership is the agreement that the data and analyses generated will be made publicly available to the biomedical community. The 3- to

5-year, milestone-driven pilot projects in these disease areas could set the stage for broadening AMP to other diseases and conditions.

“Patients and their caregivers are relying on science to find better and faster ways to detect and treat disease and improve their quality of life,” said Collins. “Currently, we are investing a great deal of money and time in avenues with high failure rates, while patients and their families wait. All sectors of the biomedical enterprise agree that new approaches are sorely needed.

“The good news is that recent dramatic advances in basic research are opening new windows of opportunity for therapeutics,” he continued. “But this challenge is beyond the scope of any one of us and it’s time to work together in new ways to increase our collective odds of success.”



Cynthia Leoro (l), a translator and type 2 diabetes patient on hand at the AMP event, speaks with Dr. Satwant Narula, vice president of immunoscience and fibrotic diseases, discovery science and biologics at Bristol-Myers Squibb, one of the AMP partners.



With Collins for the historic partnership announcement is former NIH'er Dr. Maria Freire, president of FNIH. The foundation is one of several non-profit partners involved with AMP.

PHOTOS: BILL BRANSON



Another NIH alum, Dr. Gary Nabel (r), now chief scientific officer for global research and development at Sanofi, was present at the briefing.

As a result of revolutions in genomics, imaging and more, researchers have been able to identify many changes in genes, proteins and other molecules that predispose to disease and influence disease progression, Collins explained. While researchers have identified thousands of such changes that hold promise as biomarkers and drug targets, only a small number have been pursued. Choosing the wrong target can result in failures late in the development process, costing time, money and, ultimately, lives.

Currently, developing a drug from early discovery through Food and Drug Administration approval takes well over a decade and has a failure rate of more than 95 percent. As a consequence, each success costs more than \$1 billion.

AMP has been more than 2 years in the making, with intense interactions between scientists in the public and private sectors, progressive refinement of the goals, strategy development support from the Boston Consulting Group and scientific project and partnership management by FNIH.

Through this effort, AMP partners have developed research plans and are sharing costs, expertise and resources in an integrated governance structure that enables the best informed contributions to science from all participants.

More information about the program can be found at www.nih.gov/amp. 

'End of AIDS' Is Topic of LaMontagne Lecture, Mar. 13 in Lipsett

Considerable progress has been made in the global fight against HIV/AIDS, but a sustained, comprehensive approach is needed to end the pandemic, according to Dr. Salim S. Abdool Karim, a leading South African clinical infectious diseases epidemiologist and HIV prevention and treatment researcher.

Abdool Karim will discuss how the global community is positioned to strengthen and reinvigorate the AIDS response during the 2014 John Ring LaMontagne Memorial Lecture titled, "Envisioning 'The End of AIDS': Challenges and Prospects," at 3 p.m. on Thursday, Mar. 13 in Lipsett Amphitheater, Bldg. 10.



Dr. Salim S. Abdool Karim

Abdool Karim is president of the South African Medical Research Council and director of the Centre for the AIDS Programme of Research in South Africa (CAPRISA). A long-time HIV prevention researcher, he was the co-principal investigator of the landmark CAPRISA 004 clinical trial, which provided proof-of-concept that antiretroviral-based vaginal gels can prevent sexually transmitted HIV infection and herpes simplex virus type 2 in women. Additionally, his research on HIV and tuberculosis co-infection has helped shape international treatment guidelines.

"Mathematical models show that available interventions have the potential to reduce HIV incidence to a level that it no longer represents a public health threat," says Abdool Karim. But, he warns, "Ending AIDS will not be an easy task and will require much more than political commitment or biomedical tools."

Abdool Karim will highlight the need for a more detailed understanding of HIV transmission at the local level along with an increased effort to address ongoing transmission and develop effective interventions tailored to fit a given community. He will also discuss the need to address gender inequalities, violence against women, stigma and discrimination to lessen the HIV/AIDS burden among at-risk populations, while strengthening health systems and programs for HIV testing, prevention and treatment. Further, he will discuss the need to bolster research for an effective HIV vaccine and cure.

The NIAID-sponsored lecture honors LaMontagne's contributions to NIH and public health during his 30-year career with the institute. He earned international recognition and widespread admiration for his distinguished leadership and accomplishments in fighting emerging and re-emerging infectious diseases. He served as NIAID deputy director from 1998 until his untimely death in 2004.



LANGER

CONTINUED FROM PAGE 1

Above:

Langer (c) is joined by NIH deputy director for intramural research Dr. Michael Gottesman (l) and NIBIB director Dr. Roderic Pettigrew.

PHOTOS: KATE EGAN

offers, 4 from Exxon alone. It wasn't like I was that great, they just had a lot of job openings."

Despite the wealth of opportunity, Langer craved more from a career than pursuit of profit. In an attempt to transition into academia based on his graduate experience developing chemistry curricula, he sent more than 40 application letters to local universities with potential assistant professorships. Not one replied.

"I guess I wasn't in the right box, the chemistry education box," he recalls. "So that wasn't going real well. Starting to think how else I could use my chemical engineering background to help people, I thought about medicine. I wrote to a lot of hospitals and medical schools and they didn't write back either."

Langer finally landed a spot in noted cancer researcher Dr. Judah Folkman's lab at Massachusetts General Hospital. There, he began to work on isolating large molecules capable of inhibiting the growth of blood vessels and developing degradable polymer scaffolds to control the release of such inhibitors.

The stakes were high; if successful, the findings could become a viable treatment for cancer and help reduce deaths due to metastases, the leading cause of cancer mortality. But Folkman's hypothesis of angiogenesis-driven tumor growth was still unproven at the time and had many detractors.

So even after achieving some career stability, Langer continued to face rejection. The one company at the time doing similar work, for which Folkman served as a scientific advisor, refused to help because the proposed approach

was deemed as likely as a person walking through a wall.

Describing the audience reaction to his first scientific presentation on achieving a constant rate of medication release with specially engineered microspheres, Langer said: "I stepped off the podium and a bunch of people came up and said, 'We don't believe anything you just said.'"

Around the same time, Langer had also started filing for patents, hoping to entice private industry to help translate some of his findings from bench to bedside. A skeptical patent examiner repeatedly turned him down until Langer was able to obtain affidavits from researchers affirming their by-then years'-old acknowledgment of the promise and novelty of his work.

In all, 28 years would pass from publication in *Science* of the initial, *in vivo* proof-of-concept study to FDA approval of the first angiogenesis inhibitor, bevacizumab (Avastin), in 2004. During that time, Langer continued to tackle tough questions in biomedical technology such as designing novel drug delivery systems and biomaterials.

Still, reviewers claimed the projects he proposed were impossible and still Langer refused to be deterred. Instead, he accepted each challenge, faced every claim of impossibility and turned the research world on its head—in the process, fostering the careers of some of the most lauded engineers, educators and innovators today.

That the veritable flood of discoveries that have come to define Langer's place in the scientific pantheon was fed by a wellspring of rejection and incredulity speaks to a theory put forth by the late Sir Arthur C. Clarke: "Every revolutionary idea seems to evoke three stages of reaction. They may be summed up by the phrases: It's completely impossible. It's possible, but it's not worth doing. I said it was a good idea all along."

The videocast of Langer's talk, "Biomaterials and Biotechnology: From the Discovery of Angiogenesis Inhibitors to the Development of Drug Delivery Systems and the Foundation of Tissue Engineering," can be viewed at <http://videocast.nih.gov/summary.asp?Live=13563>. ●

digest



An NCI study found that women who take aspirin daily may reduce their risk of ovarian cancer by 20 percent.

Study Finds Regular Aspirin Use May Reduce Ovarian Cancer Risk

Women who take aspirin daily may reduce their risk of ovarian cancer by 20 percent, according to a study by scientists at NCI. However, further research is needed before clinical recommendations can be made.

The study was published Feb. 6 in the *Journal of the National Cancer Institute*.

It is estimated that over 20,000 women in the United States will be diagnosed with ovarian cancer in 2014, and more than 14,000 will die from the disease. Early-stage ovarian cancer may be successfully treated. However, symptoms associated with this disease can mimic more common conditions, such as digestive and bladder disorders, so for this reason and others, it is often not diagnosed until it has reached advanced stages.

Late-stage ovarian cancer leaves women with limited treatment options and poor prognoses, making preventive strategies potentially important for controlling this disease.

Chronic or persistent inflammation has been shown to increase the risk of cancer and other diseases. Previous studies have suggested that the anti-inflammatory properties of aspirin and non-aspirin NSAIDs (non-steroidal anti-inflammatory drugs) may reduce cancer risk overall. However, studies examining whether use of these agents may influence ovarian cancer risk have been largely inconclusive.

This is the largest study to date to assess the relationship between these drugs and ovarian cancer risk.

This study adds to a growing list of malignancies, such as colorectal and other cancers, that appear to be potentially preventable by aspirin usage.

Adverse side effects of daily aspirin use include upper gastrointestinal bleeding and hemorrhagic stroke. Therefore, a daily aspirin regimen should only be undertaken with a doctor's approval, caution the scientists.

Study Seeks to Improve Asthma Therapy for African Americans

Researchers will enroll around 500 African-American children and adults who have asthma in a multi-center clinical trial to assess how they react to therapies and to explore the role of genetics in determining the response to asthma treatment. This new clinical study, which will take place at 30 sites in 14 states, is aimed at understanding the best approach to asthma management in African Americans, who suffer much higher rates of serious asthma attacks, hospitalizations and asthma-related deaths than whites.

The Best African-American Response to Asthma Drugs (BARD) study is under the auspices of NHLBI.

"This large-scale clinical effort is expected to provide new insights into how health care professionals can better manage asthma in African Americans to improve outcomes," said NHLBI director Dr. Gary Gibbons.

"BARD reinforces the institute's commitment to understand, reduce and ultimately even eliminate the disparities in asthma outcomes observed in the African-American population compared to other Americans with asthma," added Dr. James Kiley, director of NHLBI's Division of Lung Diseases.

Study Offers Insight into Why Cancer Incidence Increases with Age

The accumulation of age-associated changes in a biochemical process that helps control genes may be responsible for some of the increased risk of cancer seen in older people, according to an NIH study.

Scientists have known for years that age is a leading risk factor for the development of many types of cancer, but why aging increases cancer risk remains unclear. Researchers suspect that DNA methylation, or the binding of chemical tags, called methyl groups, onto DNA, may be involved. Methyl groups activate or silence genes by affecting interactions between DNA and the cell's protein-making machinery.

Drs. Zongli Xu and Jack Taylor, researchers from NIEHS, identified DNA methylation sites across the human genome that changed with age. They demonstrated that a subset of those sites—the ones that become increasingly methylated with advancing age—are also disproportionately methylated in a variety of human cancers. Their findings were published online in the journal *Carcinogenesis*.

"You can think of methylation as dust settling on an unused switch, which then prevents the cell from turning on certain genes," Taylor said. "If a cell can no longer turn on critical developmental programs, it might be easier for it to become a cancer cell."

milestones

Still Plans to Volunteer

Medical Arts' Brown Retires After 48 Years

By Rich McManus

Linda Brown, who for decades assured that NIH's world-class science was represented by world-class art—including lecture, event and



Linda Brown, who for the past 17 years was creative services director in what is now the Division of Medical Arts, retired Jan. 31 after 48 years at NIH.

PHOTO: ERNIE BRANSON

campaign posters that both won awards and became collectors' items—retired Jan. 31 after a 48-year NIH career.

And, with her signature sense of humor and warmth, she announced her plans to return to NIH the following Monday to serve as a volunteer.

Brown joined NIH's Medical Arts and Photography Branch as a general illustrator fresh out of the University of Kansas in 1966; she had majored in design.

"I did not expect to be here 48 years later," she confides. "The plan was to spend a little time on the East Coast, a little time on the West Coast... but that didn't happen," she laughs. "NIH is a wonderful place to work."

Born and reared in the vicinity of Kansas City, Mo., Brown, 71, grew up at the height of counterculture ascendancy in the U.S. and embraced its imagination, openness and sense of adventure, while cultivating a Midwesterner's bedrock accountability. When scientists brought their ideas to her, they found someone whose mind was often as agile as theirs and absolutely dedicated to delivering a project that would delight everyone.

"I have enjoyed my clients," she says. "Gosh, we've got the greatest clients you could imagine."

Brown describes herself as "very old-school. Everything we do should be quality-driven. That's what medical arts always was for me... when you can point with pride to what you do, you feel good about work."

Although she began as an illustrator, Brown was for years chief of the design section in medical arts, where she hand-picked a stable of artists

she considered the equal of any design house in the private sector.

"I have really worked with some wonderful people," she said. "I've been lucky. These are people I consider friends. But it's beyond that—it's family."

For the past 17 years, she has been creative services director in what is now the Division of Medical Arts. "I slid out of the drawing-board phase," she recalls, "but I did keep some projects for myself."

In recent years she interviewed clients in DMA's front office and assembled the most appropriate teams to tackle the work. "I like to play matchmaker," she said, "passing out work, taking it to the right section head. I managed the more complicated projects, arranging all the pieces."

When an astonished coworker discovered that Brown could detect which contractor worked on a project, based simply on the smell of the printer's ink, Brown could only reply, "It's just stuff you pick up."

That kind of dedication, however, is becoming rare, she said. "Times have changed and people tend to move around more. Medical arts has been my career for so long, it's really the only business I know. I'm afraid that retirement will be like leaving home, so I'm turning right around as a volunteer. It's the social interactions and the people I'm going to miss."

She took particular satisfaction in establishing rapport with clients, many of whom became friends.

A number of corridors at NIH are decorated with her branch's art. "I remember all of those," she says. "It's fun to walk around NIH and see posters hanging up on the walls. I know the backstory of every one, who planned the event, etc. I met the greatest people and got to invent how their event was going to be branded. It was really fun to work with people."

She jokes, "I'm counting on NIH to save my memory—that's why I support NIH. Save my happy memories!"

Brown also treasured mentoring newcomers, a role she assumed easily. "I like working with the new or young employees," she said. "Passing out the work and monitoring it in progress is not the same reward as doing it all yourself, but it is a great reward to watch others take off and succeed. I have been very lucky to work with such talented people."

Starting Feb. 3, Brown returned to her desk to wrap up projects already in progress and com-

plete some committee assignments. “I’m not ready to give those up,” she said. “Once you’ve had the management hat on, it’s really hard to take off.”

She also intends to help the archivists at NIH’s history office: “I plan to sit at the feet of the historians and do what they want me to do,” Brown said.

“I could never picture myself not working,” she admitted, and once relished a reputation among the many contractors with whom she worked as never mentioning retirement, even though she could have done so years ago. “But your interests do shift,” she said. “I thought they never would. But I’m backing out slowly. Maybe I will have more time for middle school science projects and closet organization.”

She laughs, “Isn’t that what every retiree says? I’m going to clean out that closet!”

NIDCD Audiologist Brewer Honored



Dr. Carmen Brewer of the National Institute on Deafness and Other Communication Disorders has been honored by the American Academy of Audiology with its distinguished achievement award. The honor was given in acknowledgement of her “dedication to the profession of audiology for almost 40 years as an innovator in clinical teaching and mentoring, a pioneer in the area of delivery of clinical services and a translational researcher whose body of work has impacted generations of audiologists.”

For the past 11 years, Brewer has served as a research audiologist and chief of NIDCD’s audiology unit. The unit functions as both a research and clinical laboratory and conducts studies and has current collaborations with more than 30 intramural research protocols from various institutes and centers.

Brewer’s current position was preceded by a 28-year tenure at Washington Hospital Center, where she began her professional career as a clinical fellow and rose to director of hearing and speech and administrative director of oral surgery and otolaryngology.

“Through her clinical, scientific and training leadership, Dr. Brewer has raised the profile of NIH audiology into an internationally recognized center with unparalleled expertise in

the auditory and vestibular phenotypes of rare diseases,” said NIDCD scientific director Dr. Andrew Griffith. “Her expertise is reflected in the referral of dozens of visiting audiology doctoral candidates from a variety of institutions across the U.S. for clinical and research mentorship in the NIH audiology unit.”

The award will be presented at AAA’s annual meeting Mar. 27 in Orlando.



NIMH Scientist Emeritus Mudd Mourned

NIMH scientist emeritus Dr. S. Harvey Mudd, 86, died of pneumonia Jan. 21, following heart surgery. His family reported that he was having them read him emails about patients and attempting to answer them up until the day before he died. Throughout his final month he was discussing the details of his treatment with his physicians and nurses.

Born in Bryn Mawr, Pa., Mudd graduated from Harvard University in 1949, completed his M.D. at Harvard in 1953 and his internship at Massachusetts General Hospital in 1954. He worked as a National Science Foundation research fellow in biochemistry for 2 years at MGH. He then came to NIMH’s Laboratory of General and Comparative Biochemistry headed by Dr. Giulio Cantoni in 1957.

He became chief of the section on alkaloid biosynthesis in that lab from 1961-1987, during which time he also served as a commissioned officer in the Public Health Service. He received the Distinguished Service Medal in 1988, when he retired.

Mudd studied methionine metabolism over the next several decades with special emphasis on the pathway by which methionine is synthesized by plants—the ultimate source of dietary methionine for mammals.

He wrote almost 200 papers (his latest review was published in November 2013), many of which were highly influential. He was widely considered the “father of methionine metabolism.” He collaborated across the globe and was methodical in his pursuit of understanding how best to treat patients with these inborn errors of metabolism.

Dr. William Gahl, NHGRI clinical director, noted, “We have lost a generation of biochemistry in a single man. His work improved the lives of hundreds of homocystinuria patients over the years and nurtured the minds of scores of scientists.”

Mudd and his wife Marion, who survives him, were avid bird watchers and hikers. Other survivors include Mudd’s sister Emily, brother John, children Susan, Lincoln and Dan, 6 grandchildren, sisters-in-law and many nieces, nephews, grandnieces and grandnephews. 🍷



NIH Hosts Two Congressional Visits, Feb. 3

NIH hosted two special visitors from Congress on Feb. 3—Sen. Richard Durbin (D-IL) and staff, and Rep. Joe Pitts (R-PA) and his staff. Pitts is chair of the energy and commerce health subcommittee. Durbin is assistant majority leader in the Senate.

Durbin met with NIH director Dr. Francis Collins and several institute/center leaders, including NHLBI director Dr. Gary Gibbons, NINDS director Dr. Story Landis and NCI director Dr. Harold Varmus. The senator also heard presentations on traumatic brain injury and MRI-procedures in the heart.

In addition to chats with Collins and CC director Dr. John Gallin, Pitts went on a tour of the clinical movement analysis lab led by Dr. Diane Damiano, chief of the CC's functional and applied biomechanics section.

More congressional visits are expected this spring.



Sen. Richard Durbin, flanked by his health legislative assistant Binta Beard (l) and legislative director Dena Morris, confers with NIH leaders. They include (from l) NINDS director Dr. Story Landis, NHLBI director Dr. Gary Gibbons, NIH director Dr. Francis Collins and NCI director Dr. Harold Varmus. Gibbons is explaining current research in the area of heart disease.



Durbin (l) listens to a presentation on the development of image-guided MRI procedures in the heart given by NHLBI scientific director Dr. Robert Balaban. Sitting next to him is CC director Dr. John Gallin. At right, Durbin (l) is briefed on recent findings in humans with traumatic brain injury by Dr. Dorian McGavern, chief of the viral immunology and intravital imaging section, NINDS.



Clockwise, from above:

Gallin (l) shows Rep. Joe Pitts (R-PA) a model of the Clinical Research Center.

Collins greets Pitts, who visited the NIH campus with his staff on Monday, Feb. 3 to learn more about NIH's mission.

Pitts gets a tour of the clinical movement analysis lab led by Dr. Diane Damiano, chief of the CC's functional and applied biomechanics section.

PHOTOS: ERNIE BRANSON, LISA HELFERT