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FISHING FOR THERAPEUTICS

Marine Microorganisms Show Promise as New Cancer Drugs

BY DANA TALESNIK

Admit it—everyone harbors a secret hope that the cure for cancer is obscured only by the ocean depths, and that some day, science will find a way to harvest nature's undersea pharmacopeia.

The ocean was once thought to be too deep, dangerous and difficult to explore, but marine scientists now have the tools to reel in and analyze some of the vast, previously untapped potential of marine microorganisms. It turns out that the ocean contains a plethora of dynamic molecules that have shown great potential as cancer drugs and new antibiotics.

Marine chemist Dr. William Fenical addresses an NIH audience.

"Over the last 60 years, microbes have provided a massive source for antibiotics and for cancer drugs; the first statins came from microbial sources," said marine chemist Dr. William Fenical, director, Center for Marine Biotechnology & Biomedicine of the Scripps Institution of Oceanography at UCSD, who delivered the John Daly Memorial Lecture recently in Masur Auditorium. "It really was based on the fact that microorganisms are diverse, unique and the chemistry of the products produced by them tends to be highly bioactive."

If Alexander Fleming could discover penicillin from a fungus, what medicines might lurk inside tiny organisms in the ocean? There's a great deal we still don't know. So far, scientists have found a variety of molecules, including thousands of bacteria strains—notably cultured marine actinomycetes—the source of many of our antibiotics, said Fenical, who started his NIH-funded research into therapeutic marine organisms 25 years ago. Some of the greatest potential,

SEE **FENICAL**, PAGE 4

Cybathlon pilot Michael McClellan takes a practice ride in a Cleveland park.

Olympic-Style Competition To Showcase Use of Advanced Assistive Devices

BY RAYMOND MACDOUGALL

While much of the world's attention this past summer was on the Olympic Games in Rio de Janeiro, a small team from Cleveland has had their eyes set on a fundamentally different kind of athletic competition for

SEE **CYBATHLON**, PAGE 8

Hospital Harnesses Power Of Science, Technology to Improve Surgery for Kids

BY MARGOT KERN

On the sixth floor of Children's National Health System in Washington, D.C., engineers, scientists and clinicians develop technologies to make pediatric surgery more precise, less invasive and pain-free. They make up the Sheikh Zayed Institute for Pediatric Surgical Innovation, one of the few research institutes in the country housed directly in a children's hospital.

"Being physically located within the hospital enables daily communication between multiple specialties," said Dr. Kevin Cleary, technical director of bioengineering at the institute. "Our scientists and engineers are able to shadow physicians within the medical environment to ensure that solutions developed are clinically relevant. Similarly, physician innovators

SEE **SURGERY**, PAGE 6

Rolling stones come to NIH. See p. 2.

ALSO THIS ISSUE

GORMLEY TO DELIVER KEYNOTE

National Disability Employment Awareness Month Kicks Off at NIH

Dr. Maureen Gormley, NINDS deputy director for management, will deliver the keynote address at the National Disability Employment Awareness Month kickoff on Wednesday, Oct. 5 from 11:30 a.m. to 12:30 p.m. in Wilson Hall, Bldg. 1.

Dr. Maureen Gormley

In her talk, "Workplace Stigma Toward Employees with Intellectual Disability," she will present findings from a study demonstrating that coworker perceptions toward employees with intellectual disabilities change with prolonged organizational contact. She completed the study in the context of Project SEARCH, a school-to-work transition program that has successfully trained and hired youth with intellectual disabilities into the mainstream NIH workforce. Gormley led Project SEARCH at NIH for 6 years and became a strong champion of the program, expanding it across NIH and helping to start programs at the Smithsonian Institution and Montgomery County government.

Gormley, who has spent her career at NIH, has a passion for creating a diverse and inclusive workforce. She holds an undergraduate degree in nursing from Boston College, an M.P.H. from Yale University and a doctoral degree from Fielding in human and organizational systems.

Other kickoff highlights include remarks by Debra Chew, director of the Office of Equity, Diversity, and Inclusion, and the first in a series of "Lightning Round Speakers" spotlighting how #InclusionWorks in the workplace. Three people with a disability will talk for 3-5 minutes each about a contribution they've made to NIH's mission.

Sponsored by EDI's disability engagement committee and ORS's Division of Amenities and Transportation Services, the kickoff will highlight other events focused on disability awareness happening throughout October. For more information, visit http://edi.nih.gov/people/sep/pwd/about.

APAO Solicits Award Nominations

By Oct. 18

The NIH Asian & Pacific Islander American Organization (APAO) will continue its tradition of honoring employees in the NIH Asian Pacific American community for their excellence. Nominations are being solicited in four award categories: Scientific Achievement—for scientists/researchers who have made significant accomplishments in biomedical research; Leadership Excellence—for non-scientists and scientists who exemplify leadership excellence by example, mentorship and empowerment of Asian and Pacific Americans to promote diversity and support the overall mission of NIH; Young Investigator—recognizes achievements by visiting fellows, clinical fellows and research fellows who have spent fewer than 7 years at NIH; and Kuan-Teh Jeang Distinguished Service—recognizes an APAO member who has made an outstanding contribution or demonstrated continual high quality service to the NIH Asian Pacific American community.

Nominees must work or previously have worked (within the past year) at NIH. Awardees will be honored at the NIH APAO Awards holiday luncheon on Dec. 7 in Wilson Hall, Bldg. 1.

To nominate, submit a 1-page narrative/statement to support why you think an individual is deserving of recognition and include a CV of the nominee. A review committee composed of APAO members, non-members representing several ICs and former award recipients will evaluate nominations. Submit nominations electronically no later than COB Tuesday, Oct. 18 to Dr. Shioko Kimura at kimuras@mail.nih.gov. For details, ask for the 2-page Award Nomination Manual.

'Minerals in Medicine' Exhibit at CC

The Clinical Center is featuring a "Minerals in Medicine" exhibit as part of a collaboration with the Smithsonian Institution's National Museum of Natural History's department of mineral sciences and its National Gem and Mineral Collection. While the objects were being unpacked, Clinical Center director Dr. John Gallin (second from l) marveled at one of the exhibit's stones presented by Smithsonian geologist Dr. Michael A. Wise (l). Looking on with amusement are Dr. Frederick Ognibene (second from r), Clinical Center deputy director for educational affairs and strategic partnerships, and Dr. Jeffrey E. Post (r), chairman, department of mineral sciences and curator, National Gem and Mineral Collection. The exhibit highlights the essential role minerals and metals play in medicine, medical devices and in the normal functioning of the human body. Under the loan agreement, the items will be displayed in the Clinical Center's admissions area for 18 months.

PHOTO: ERNIE BRANSON

NHLBI Holds Vascular Symposium

Registration is now open for the 2016 National Heart, Lung, and Blood Institute symposium "Unraveling Vascular Inflammation: From Immunology to Imaging," the first of its kind to focus on vascular inflammation emerging research as it relates to immunology, systemic inflammation and multi-modal imaging.

The Oct. 24-25 symposium, to be held at the Natcher Conference Center, will bring together the world's most renowned experts in the field, providing a forum for international collaboration across disciplines to speed discoveries, fill gaps in existing knowledge and potentially lead to critical breakthroughs in ways to understand vascular inflammation as it relates to future cardiovascular disease events. Keynote speakers include Dr. Frank Nestle, King's College London; Dr. Paul Ridker, Brigham and Women's Hospital; and Dr. David Newby, University of Edinburgh.

Fast-paced presentations will facilitate exchange of ideas on critical topics, including translational studies involving cardiovascular imagery and quantification and the immunology of inflammation. A poster session, including a competition and cash award, will enable evaluation and discussion of additional research and guidance to early career researchers.

Symposium registration is free. To register, submit an abstract or learn more, visit https://www.nhlbi.nih.gov/news/events/unraveling-vascular-inflammation-immunology-imaging-2016. R

Bianchi Named NICHD Director

Dr. Diana W. Bianchi has been named director of the National Institute of Child Health and Human Development. She is expected to join NIH on Oct. 31.

"Diana's accomplishments as a prenatal geneticist, along with her leadership, clinical and research experience in both pediatrics and obstetrics, make her ideally suited to lead NICHD," said NIH director Dr. Francis Collins, who made the appointment. "We are excited to have her join our team and lead this important area of research."

Bianchi will oversee research on pediatric health and development, maternal health, medical rehabilitation, population dynamics, reproductive health and intellectual and developmental disabilities. With an annual budget of about $1.3 billion, NICHD supports research grants and contracts at universities and other institutions across the country and overseas and an intramural research program of scientists working at NIH.

She will join NIH from the Floating Hospital for Children and Tufts Medical Center in Boston, where she serves as founding executive director of the Mother Infant Research Institute and vice chair for pediatric research. She is also the Natalie V. Zucker professor of pediatrics and obstetrics and gynecology at Tufts University School of Medicine and editor-in-chief of the international journal *Prenatal Diagnosis*.

A practicing medical geneticist with expertise in reproductive genetics, Bianchi studies prenatal genomics with the goal of advancing noninvasive prenatal DNA screening and diagnosis to develop new therapies for genetic disorders that can be administered prenatally. She spoke at NIH last year on this topic (see https://nihrecord.nih.gov/newsletters/2015/03_13_2015/story2.htm).

Dr. Diana W. Bianchi

Bianchi earned her M.D. from Stanford University School of Medicine and completed her residency training in pediatrics at Boston Children's Hospital and her postdoctoral fellowship training in medical genetics and neonatal-perinatal medicine at Harvard Medical School. She is board-certified in all three specialties.

From 2011 to 2015, she served on NICHD's national advisory council and is a past president of the International Society for Prenatal Diagnosis and the Perinatal Research Society. Bianchi is a former member of the board of directors of the American Society for Human Genetics and a former council member on both the Society for Pediatric Research and the American Pediatric Society. She was elected to membership in the Institute of Medicine (now National Academy of Medicine) in 2013.

Bianchi recently received two major lifetime achievement awards: the Landmark Award in 2015 from the American Academy of Pediatrics in recognition of her research and contributions to genetics and newborn care and the Maureen Andrew Award for Mentoring in 2016 by the Society for Pediatric Research, which recognized her commitment to mentoring the next generation of clinician-scientists.

"I want to recognize and thank Dr. Catherine Spong, who served ably as acting director of NICHD over the past year," noted Collins. "Cathy showed much commitment, dedication and leadership in this role. She is an incredible asset to the NIH community." R

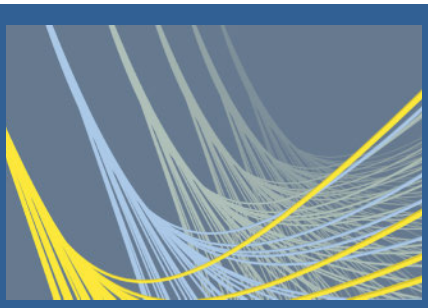
International Opportunities Expo Scheduled

OCT. 20

The 10th International Opportunities Expo, sponsored by the visiting fellows subcommittee of the NIH fellows committee (FelCom), is scheduled for Thursday, Oct. 20 from noon to 4:30 p.m. in the NIH FAES Education Center, Bldg. 10.

The event focuses on opportunities for postdoctoral fellows and graduate students interested in pursuing international science careers. Representatives from embassies, funding agencies and globally minded science and health organizations will be on hand to answer questions and promote their programs and resources.

Whether you are in the job market or at the beginning of your training, the expo offers the opportunity to gather information to consider an international career. To find out more, visit https://www.training.nih.gov/for_expo_exhibitors_and_speakers.



ON THE COVER: *Visual interpretation of spinal cord injury and modern warfare, from a 2012 NIMH lecture poster*

IMAGE: NIH MEDICAL ARTS

The NIH Record

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National Institutes of Health
Turning Discovery Into Health

Fenical's team has discovered two drugs that are currently in clinical trials for cancer treatment.

PHOTOS: ERNIE BRANSON

Fenical

CONTINUED FROM PAGE 1

he noted, may lie in the deep ocean, where sediments have a billion bacterial cells per cubic centimeter.

"These marine bacteria are producing metabolites we haven't seen before," Fenical said. "They're unprecedented; a lot of them have very interesting bioactivities including in the areas we need them now—cancer and infectious diseases."

Scientists can isolate the sediments and cultivate the samples in large scale. The initial challenge was bringing them to shore. To reach ocean bottom, researchers developed powerful fishing reels with snapping or coring devices that can freefall thousands of meters then collect and bring up samples.

Fenical's team discovered two drugs derived from marine microorganisms that are currently in clinical trials for cancer treatment. Marizomib first showed successful results in targeting multiple myeloma and lymphomas when investigators determined another promising sign—the drug passes the blood-brain barrier. Now it's in phase 2 trials for treating glioblastoma, among other cancers. Another drug they found, Plinibulin, is in phase 3 trials for lung cancer.

"In cancer research, today's challenge is really to find ways to discover treatments—new drugs—that are highly selective...to specific types of cancer—something that is selective for melanoma, selective for breast cancer—so that you minimize the side effects of these drugs," said Fenical.

As his team set out to find marine molecules that would target new biochemical pathways and proteins specific to cancer cells, they developed an approach to label and tag the proteins using immunofluorescent probes and confocal microscopy. They screen all microbial collections against cancer cell lines, exploit only the molecules showing specific cell selectivity and label inhibitors with fluorescent tags that show exactly where the protein binds in the cell.

Using this approach, they found a bacterium in shallow waters in the Bahamas that contains 2 unusual metabolites—ammosamides A and B—found to be effective against several neuroblastoma cell lines. When they incubated ammosamide B with colon carcinoma, it glowed, an intense blue fluorescence exclusively in the cytoplasm. Then they found their target: the large protein myosin, which transports tubulin and other proteins in the cell and might be a target for a tubulin inhibitory drug.

Another example is seriniquinone, a bright orange gram-positive bacterium collected in shallow waters off of Palau, which showed excellent selectivity against melanoma. When seriniquinone was introduced to melanoma cells, said Fenical, the cells began to die within hours. They also found their protein target, dermcidin, which is overexpressed in advanced melanoma.

A strain of *Streptomyces*, extracted from deep waters off of southern California, yielded 2 compounds—chlorizidines A and B, which target enolase, an enzyme present in all living cells that seems to regulate production of several proto-oncogenes. Further study is needed to uncover the potential of enolase as a cancer target. "There are targets that people don't think are of any use, however they result in rapid cell kill and offer some new opportunities," said Fenical.

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"In cancer research, today's challenge is really to find ways to discover treatments—new drugs—that are highly selective...to specific types of cancer...so that you minimize the side effects of these drugs."

-DR. WILLIAM FENICAL

★ ★ ★

"Chlorizidines are structurally unprecedented types of molecules, which is what we hope to find all the time," said Fenical. "[We look for] things that are new, that offer opportunities not only in biomedical discovery but also open up opportunities for more effective patenting and more effective drug development, giving the pharmaceutical industry confidence that they have effective [intellectual property]."

PRAT Fellows Find Success Through Support

BY ERIN ROSS

Finding mentors, peer companions and future funding are all challenges current postdoctoral fellows face. About 20 recent Ph.D.s in labs across NIH are finding support through NIGMS' Postdoctoral Research Associate (PRAT) program. The 3-year training experience culminates with a symposium where the fellows share their findings.

Shown with NIGMS director Dr. Jon Lorsch (fourth from l) and PRAT program director Dr. Jessica Faupel-Badger (third from l) are (from l) Carrie House, Alicia Pickrell, Julia Lemos and Alex Valm.

PHOTO: BILL BRANSON

"This symposium is like our capstone," said PRAT program director Dr. Jessica Faupel-Badger of NIGMS.

This year, four of the PRAT fellows finished the program. Drs. Carrie House, Julia Lemos, Alicia Pickrell and Alex Valm presented their research on subjects ranging from organelle interactions to ovarian cancer to an audience of PRAT alumni, mentors and other NIH staff.

"It was a really upbeat and positive day," said Faupel-Badger. "It was terrific to see all that the PRAT fellows have accomplished with their research projects and to draw inspiration from the keynote speaker, NCATS director Dr. Chris Austin."

For the fellows, PRAT is more than a funding opportunity. This year's class cited the support and extra coaching they received as major benefits of the program. Throughout the fellowship, the postdocs practiced presenting their research to each other. They received training in public speaking, gave "elevator speeches" and even answered questions from high school students during NIGMS' annual online web chat focused on cells and research careers. The fellows learned about early career funding opportunities from NIH program directors. Guest speakers discussed their career trajectories and offered advice and guidance to fellows.

"It was very beneficial to hear how other scientists obtained their positions in academia, industry, government or the private sector," said Pickrell.

Fellows received leadership training, too, which Lemos said was "extremely helpful in training us as future managers of a team of people." All of this year's fellows hope to pursue careers in academia and one day lead labs of their own.

The fellows unanimously agreed that some of the best parts of the program aren't advertised on the PRAT web page. Faupel-Badger calls these PRAT's "hidden gems." One of them is a sense of community.

"Unlike graduate school, where you have a distinct cohort, postdocs come in as individuals and can sometimes feel very isolated," said Lemos. "The PRAT program creates a cohort of postdocs each year that you end up becoming very close to."

Other fellows agreed.

"One thing I enjoyed that was unexpected was the camaraderie that came with the PRAT fellowship," said House. "There are no other postdocs in my lab, so it has been great to have a group of peers I can reach out to. I received a lot of insightful comments and questions from the non-cancer researchers in my program. It prompted me to think more broadly about my work and to look at it from different perspectives."

If you asked the fellows, they would say another hidden gem is Faupel-Badger herself. House said they receive "an extra level of support and encouragement" from Faupel-Badger and program analyst Chrissy Shaw. Valm said their presence was "invaluable."

Faupel-Badger sees the guidance they provide coming back to the program in turn. Past fellows, for instance, work at NIGMS and other NIH institutes and others are current NIGMS grantees.

Several of this year's postdocs were encouraged to apply by program alumni.

"The alumni are an excellent resource and an instant network," said Faupel-Badger. "Current and past fellows feel comfortable cold-emailing each other. Alums have shared tips about grant applications, offered career advice and mentored each other."

Valm, for one, hopes to give back to the program. "I'm honored to call myself an alum and I look forward to helping out future PRAT fellows in any fashion."

PRAT is accepting applications until Oct. 3. For details, see www.nigms.nih.gov/Training/Pages/PRAT.aspx.

Ransohoff To Deliver the Next 'Mind the Gap' Seminar

Dr. David Ransohoff, professor of medicine at the University of North Carolina, Chapel Hill, will present "Making Guidelines for Colon Cancer Screening: Evidence, Policy and Politics" at the next Medicine: Mind the Gap Seminar on Tuesday, Sept. 27 from 11 a.m. to noon via NIH VideoCast, http://videocast.nih.gov/. This seminar is the first of a three-part series on disease prevention screening.

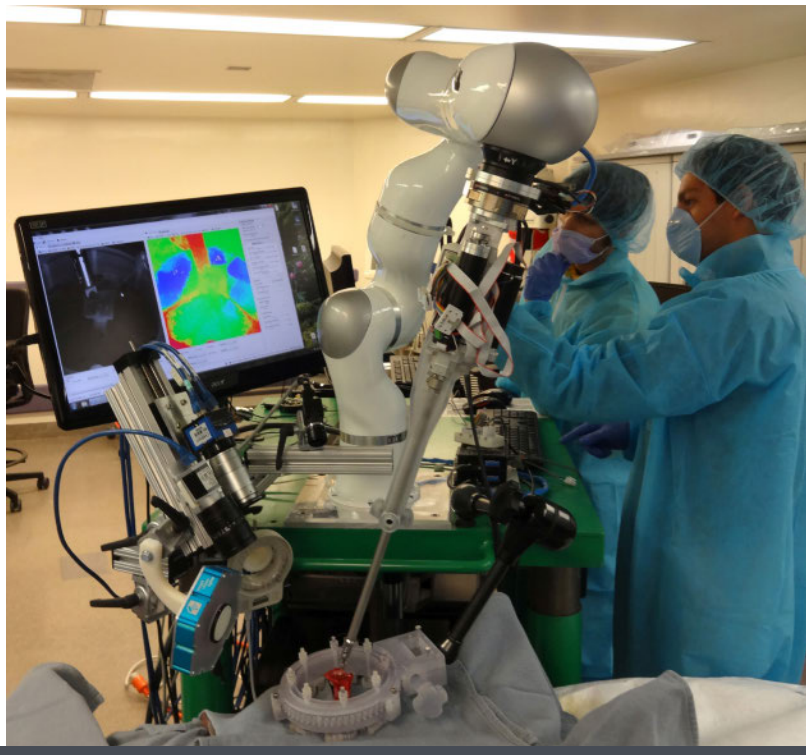
A major goal of clinical practice guidelines is to maximize benefit and minimize harm for patients. Yet many guidelines are made by many organizations and often they conflict on the same topic. As a result, Congress commissioned the Institute of Medicine to write a report about how to identify "guidelines you can trust." This seminar will illustrate challenges and practical realities in guidelines-making by describing the evolution of evidence and of guidelines for colon cancer screening.

Dr. David Ransohoff

As one of the first clinical epidemiologists trained at Yale University with Alvan Feinstein, Sr., Ransohoff has written extensively about how to improve research methods used to evaluate diagnostic tests, with seminal publications in major journals. Also trained in gastroenterology at the University of Chicago, he was one of the first clinical epidemiologists in a subspecialty field and has widely published on colon cancer screenings, including colonoscopies, fecal occult blood testing, sigmoidoscopies and virtual colonoscopies, as well as clinical practice guidelines and policy.

Ransohoff will accept questions before and during his presentation via email at prevention@mail.nih.gov and on Twitter with #NIHMtG.

Registration, although not required, is encouraged for planning purposes. You can do so at https://prevention.nih.gov/programs-events/medicine-mind-the-gap/registration.



At left, prototype of an imaging headset that could be used to help determine whether verbal and non-verbal children are in pain, and to what degree, based on brain activity. At right, surgeons look at a display showing the view from a surgical robot that can stitch soft tissues all by itself. The robot is equipped with 3-D and infrared cameras to keep track of the tissues' position.

PHOTOS: CHILDREN'S NATIONAL HEALTH SYSTEM

Surgery

CONTINUED FROM PAGE 1

can bounce an idea by the engineers to assess initial feasibility and collaborate on validated concepts."

Recently, NIBIB staff had the opportunity to tour the unique institute and get a behind-the-scenes look at some of the projects currently under way, many of which are NIH-funded.

One example of a successful collaboration between an engineer and a surgeon was the development of a surgical robot that can suture tissues all by itself. While robots are commonplace in today's operating rooms, their movements are almost always directed by a surgeon. In contrast, this robot uses special cameras to track tissue as it shifts or bends while being stitched so that the robot can proceed autonomously.

The researchers' current goal is to automate a common but complex and delicate task called anastomosis, which is the stitching together of tubular structures in the body, such as arteries or intestines. Dr. Axel Krieger, lead engineer on the project, says the robot can make smaller, more precise stitches than surgeons are able to, lessening the likelihood of leakages, which are a common complication of anastomoses.

The idea for the robot came from Dr. Peter Kim, vice president of the institute and a pediatric thoracic surgeon in the hospital. Kim, who specializes in minimally invasive surgeries, believes a suturing robot could be particularly helpful for use in children.

"Many pediatric surgical procedures require precision, gentleness, maneuverability and fine dexterity," he said. "Having precise and intelligent tools—including robots that can provide better vision, intelligence and cognition—would be highly beneficial."

He added that robots in the surgical suite could standardize and improve care for the pediatric population at large by making the best surgical techniques available to all children.

Other exciting projects included a strategy for treating painful bone tumors using magnetic resonance-guided high-intensity focused ultrasound; an imaging headset that could help doctors determine the extent to which very young children are in pain based on activity patterns in their brain; and software for planning difficult surgeries on children with skull abnormalities.

Throughout the tour, researchers stressed many of the unique challenges associated with developing surgical technologies and devices for children. For example, pediatric

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"Having precise and intelligent tools—including robots that can provide better vision, intelligence and cognition—would be highly beneficial."

-DR. PETER KIM

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The tip of a surgical robot makes a stitch while sewing two pieces of tissue together.

devices often stay in the body longer and, therefore, need to be more durable. Devices also need to adapt as children grow to avoid repeat surgeries. In addition, a number of surgical robots are being developed that would enable surgeons to operate on children inside an MRI scanner. This would lessen their exposure to radiation generated by CT and fluoroscopy, imaging modalities currently used by surgeons to visualize tissues during an operation.

"What struck me was the breadth of technologies being developed," said Dr. Steven Krosnick, a program director at NIBIB. "To me, it demonstrates the power of bringing together clinicians, engineers and scientists to solve complex challenges in medicine. Surgeons often have a sense that if only they had a specific tool or imaging technology, they could do their job better, faster, safer. The problem is they don't generally have the time or the expertise to develop it. It's the collaboration with the engineers and scientists that can turn those ideas into reality." R

Study Seeks Healthy Older Adults

Healthy older adults, ages 55-75, are invited to participate in an outpatient research study investigating the benefits of omega-3 oil and blackcurrant supplements on vascular health. The goal of the study is to determine whether the supplements improve blood flow and blood vessel function that can affect your heart. Eligible participants must be medication-free and in good general health. The study will be carried out in an outpatient clinic and includes 4 visits over 6 months. Compensation is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 14-NR-0034.

Nondrug Approaches Effective for Treatment of Common Pain Conditions

Data from a review of U.S.-based clinical trials published Sept. 1 in *Mayo Clinic Proceedings* suggest that some of the most popular complementary health approaches—such as yoga, tai chi and acupuncture—appear to be effective tools for helping to manage common pain conditions. The review was conducted by a group of scientists from the National Center for Complementary and Integrative Health.

Some popular complementary health approaches appear to be effective tools for helping to manage common pain conditions.

Millions of Americans suffer from persistent pain that may not be fully relieved by medications. They often turn to complementary health approaches to help, yet primary care providers have lacked a robust evidence base to guide recommendations on complementary approaches as practiced and available in the United States. The new review gives primary care providers—who frequently see patients with chronic pain—tools to inform decision-making on how to help manage that pain.

"For many Americans who suffer from chronic pain, medications may not completely relieve pain and can produce unwanted side effects," said Dr. Richard Nahin, NCCIH's lead epidemiologist and lead author of the analysis. "As a result, many people may turn to nondrug approaches to help manage their pain. Our goal for this study was to provide relevant, high-quality information for primary care providers and for patients who suffer from chronic pain."

Extreme Temperatures Could Increase Preterm Birth Risk

Extreme hot or cold temperatures during pregnancy may increase the risk of preterm birth, according to a study published in *Environmental Health Perspectives* by NIH researchers.

Study authors found that extremes of hot and cold during the first 7 weeks of pregnancy were associated with early delivery. Women exposed to extreme heat for the majority of their pregnancies also were more likely to deliver early.

The researchers found more consistent associations with early delivery after exposure to extreme heat than to extreme cold weather. They theorized that, during cold spells, people are more likely to seek shelter and so could more easily escape the cold's effects. But during extreme heatwaves, people are more likely to endure the temperature, particularly when the cost of or access to air conditioning is an impediment.

Extreme hot or cold temperatures during pregnancy may increase the risk of preterm birth, according to a study by NIH researchers.

"Our findings indicate that it may well be prudent to minimize the exposure of pregnant women to extremes in temperature," said study senior author Dr. Pauline Mendola, an epidemiologist at the National Institute of Child Health and Human Development.

A pregnancy is considered full term at between 39 and 40 weeks. Preterm birth occurs before 37 weeks of pregnancy and increases the risk for infant death and long-term disability. It is unknown why extremes of hot or cold might influence preterm birth risk. However, the researchers theorize that the stress of temperature extremes could hinder the development of the placenta or alter blood flow to the uterus, both of which could potentially lead to early labor.

Cybathlon

CONTINUED FROM PAGE 1

human-machine teams. This first-of-its-kind event, the international Cybathlon, features contests for people with disabilities using assistive technologies and will take place Oct. 8 in Zurich, Switzerland. Team Cleveland has entered the functional electrical stimulation bike race.

Though paralyzed by a spinal cord injury, the Team Cleveland cyclist will use power generated by his own leg muscles to pedal for gold around a 750-meter oval course. He will control a system that activates his muscles using electronic pulses. Researchers developed the implanted stimulation system with support from the National Institute of Biomedical Imaging and Bioengineering. This bionic system will enable the cyclist to pilot a three-wheeled recumbent cycle in the race.

The Cybathlon consists of six disciplines, including the functional electronic stimulation cycle competition and other events that feature brain-computer interfaces, powered-arm and powered-leg prostheses, powered exoskeletons and powered wheelchairs. Each of the disciplines showcases different disabilities and technical capabilities, enabling a wide range of pilots and technologists to participate.

Team Cleveland includes a volunteer crew of engineers, scientists and medical experts led by Dr. Ron Triolo, Case Western Reserve University professor of orthopedics and biomedical engineering and executive director of the Advanced Platform Technology Center at the Louis Stokes Cleveland VA Medical Center.

For the past 20 years, Triolo's research team has developed motor system neural prostheses for people immobilized by spinal cord injuries. The neural stimulators have enabled study volunteers to stand, step and control their seated posture and balance. Recumbent cycling is an added activity that Triolo has offered to selected implant recipients as recreation and to improve their muscle tone. The team has provided implanted systems to 39 recipients over the years, 27 of which could function for cycling, according to Triolo.

Cybathlon pilot Mark Muhn rides the indoor track in a Cleveland arena.

"The main reason I entered the competition was to raise awareness about the advantages of this implanted technology," Triolo said, noting that Team Cleveland is the only competitor in the functional electrical stimulation race whose pilot will be using implanted technology. The other 11 teams use skin-surface, or transcutaneous, systems, which are attached to the surface of the pilot's legs.

"Every other team uses electrodes that you stick to the surface of the skin and they try to inject charge down to the nerve from outside the body," Triolo said. "With the implanted electrodes, the responses tend to be stronger and more specific."

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"Every one of our subjects who has tried biking just loves it. It gives them a sense of freedom and independence that you don't get from standing and walking..."

-DR. RON TRIOLO

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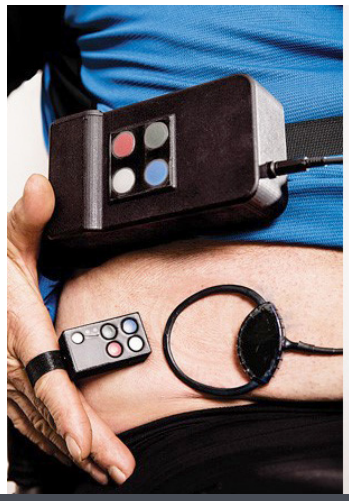
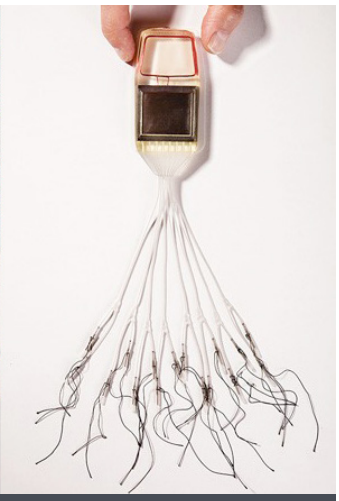
During Team Cleveland's Cybathlon Trials earlier this summer, 5 volunteers with spinal cord injuries—4 men and 1 woman—vied for the opportunity to travel with the team to Zurich. Two volunteers earned spots as cycle pilots: Michael McClellan of Rocklin, Calif., who sustained a spinal cord injury in 2009 and has used an implanted neural stimulation system for 5 years; and Mark Muhn of Morgan Hill, Calif., who was injured in 2008 and has used his neural stimulation system for 4 years. Both are training for the event, but just one will ultimately pilot the Team Cleveland recumbent cycle at the Cybathlon.

"Once you are paralyzed, you just don't have good ways to use those large lower extremity muscles that are essentially along for the ride when you are in your wheelchair," Triolo said. "Every one of our subjects who has tried biking just loves it. It gives them a sense of freedom and independence that you don't get from standing and walking, which has been the focus of our research studies for the past 20 or so years."

"By technologically bridging the gap between the spinal cord and muscles, neural stimulation can help people with spinal cord injuries regain movement and function that was thought to be unrecoverable," said Dr. Michael Wolfson, director of the NIBIB program in implantable and assistive medical devices. "The restorative power of this approach serves not only to provide rehabilitation, independence and recreation, but also an unheard of seamlessness and reliability."

The road to the Cybathlon has been a herculean volunteer effort on the part of the pilots and from the APTC engineers and medical crew. Kevin Foglyano, a biomedical engineer, tunes the stimulation patterns for each pilot and makes sure all the electronics work. Lisa Lombardo, a physical therapist, ensures pilot safety and that they are exercising appropriately in the recumbent tricycles. Stephanie Nogan Bailey, an





At left, Cybathlon pilot McClellan is surrounded by members of Team Cleveland (from l) John McDaniel, Vi Huynh, Kevin Foglyano, Lisa Lombardo, Joonhyuk Lee, Jeremy Reynoso, Stephanie Nogan Bailey, Ron Triolo, Paul Marasco and Musa Audu. At right is the functional electronic stimulation system. The stimulator's patterns are selected using external controllers and its programming is changed via an external transmitter (l). The implanted pulse generator sends current through thin wires that stimulate the nerves (r).

PHOTOS: NATHANIEL WELCH

engineer, is in charge of laboratory and team logistics. Dr. Paul Marasco, a sensory neuroscientist, is also a certified bike mechanic. He has made custom modifications to the cycles and keeps the mechanical components in working order. "If somebody blows a tire or jumps a sprocket, he'll be there with his tools," Triolo said.

Over the years, the neural prostheses used by Triolo's team have been enhanced so that the implanted electrodes are now "radically different" from the original design. The original circular nerve cuffs had a limited number of electrodes that could be placed against the nerve. Since then, the team has developed oval cuffs, which gently reshape the nerve and create a larger surface area and enable substantially more electrodes.

"We can have a high-density array of electrical contacts around the nerve, which gives us the added ability to pick off and activate isolated groups of fibers within a large nerve to control individual muscle groups or portions of muscles from a single surgical site," Triolo said. "The geometry of our electrodes, their contact density and selectivity are much improved—and all in a structure that is almost mechanically invisible to the tissue and doesn't penetrate the nerve."

The neural stimulator system Triolo's team is using has no batteries, relying instead on an external controller to transmit power and command signals to the implant via an antenna taped to the cyclist's skin above the implanted pulse generator. The patterns of muscle activity, which are customized for each individual, are preprogrammed into the external controller. By selecting one of these preprogrammed patterns, users are able to control the kind and rate of leg motion.

Cyclist McClellan is implanted with a system that has 16 channels of stimulation, while Muhn's system has 24 channels. "That's higher capacity than any transcutaneous system can put out right now," Triolo said. "Just in terms of the strength and the repeatability of the muscle contractions, our guys are going to be really competitive."

When spinal-cord-injured candidates elect to receive the implant, it is assumed by Triolo's team that they will keep the system for life. Occasionally, people will choose to have their implant removed if it's not part of their lifestyle anymore; infrequently, removal is required for medical reasons. But Triolo says that there is 90 percent reliability on the part of the stimulators themselves, and the nerve cuffs "just don't fail." This is in stark contrast to transcutaneous systems, which are affected by sweat, alignment and a need to be reapplied on a regular basis.

In a recent retrospective study, Triolo's group contacted more than 20 implant recipients who have had their systems close to 7 years on average. Those who responded were still using their systems about 4 times a week.

"The systems are still operational and it's up to individuals to choose how and when to use it once they are home," Triolo said. "It does appear people are finding it valuable and are choosing to incorporate it into their lives."

Triolo's program has expanded from implants for volunteers with lower-extremity paralysis due to spinal cord injury to other populations with motor impairments due to central nervous system injury or disease, such as stroke survivors and patients with multiple sclerosis.

Also, the team at Case Western is now working to develop a system that expands the number of output channels. Triolo also is principal investigator on a number of grants funded by the National Institute of Neurological Disorders and Stroke.

With preparations for the Cybathlon trip in full swing, Triolo has high expectations for the success of Team Cleveland. "We're relatively new to this game and only started cycling when they announced the competition 2 years ago," he said. "I want to be competitive and I think our chances are as good as anyone's to win this thing. We'll celebrate by getting everyone ready for the next Cybathlon with even better neurotechnology 4 years from now."

A second Cybathlon is being planned for 2020 in Tokyo, host of the Summer Olympic Games.

For more about the Cybathlon, go to www.cybathlon.ethz.ch/en/.

Dr. Linda Birnbaum has received the 2016 North Carolina Award.

PHOTO: STEVE MCCAW

Birnbaum Honored by North Carolina

NIEHS and National Toxicology Program director Dr. Linda Birnbaum has received the 2016 North Carolina Award, the state's highest civilian honor. The awards are presented each year in the fields of science, literature, fine arts and public service.

"It is an honor to pay tribute to these remarkable individuals who have made North Carolina better by their extraordinary involvement in this state," said Susan Kluttz, secretary of the North Carolina department of natural and cultural resources. "Each has enriched the lives of our citizens and propelled North Carolina onto the national and world stages."

The award cites Birnbaum's international recognition in the fields of environmental health and toxicology and her position as the first woman to lead NIEHS, which is celebrating its 50th anniversary this year. Before coming to NIEHS, she directed the experimental toxicology division at the Environmental Protection Agency.

"Her work exploring the effects of dioxins, asbestos, flame retardants and Agent Orange has impacted practices and health outcomes worldwide," the award read in part. "Birnbaum was a trailblazing woman in the science lab as a student in the 1960s. She was encouraged by her high school cheerleading coach who also taught science, making it cool for girls in science."

Birnbaum received the award from Gov. Pat McCrory at a Sept. 22 banquet and ceremony. Other honorees in the field of science this year are NIEHS grantee Dr. Aziz Sancar and Dr. Paul Modrich, who shared the 2015 Nobel Prize in chemistry with Dr. Tomas Lindahl, for work on DNA repair.—**Kelly Lenox**

New NCAB Members, Chair Appointed

Six new members have been named to the National Cancer Advisory Board and Dr. Elizabeth Jaffee has been appointed as NCAB chair.

Jaffee is deputy director of the Sidney Kimmel Comprehensive Cancer Center, the Dana and Albert "Cubby" Broccoli professor of oncology and co-director of the Skip Viragh Center for Pancreas Cancer at Johns Hopkins University. She has focused her scientific career on the pre-clinical and clinical development of vaccines for the treatment of cancer.

Dr. Francis Ali-Osman is the Margaret Harris & David Silverman professor of neuro-oncology research and professor of surgery and pathology at Duke University School of Medicine. He is a world leader in experimental oncology, cancer therapeutics and pharmacology and cancer-drug resistance.

Lawrence Gostin is university professor, faculty director and founding Linda D. and Timothy J. O'Neill professor in global health law at the O'Neill Institute for National and Global Health, Georgetown University. Gostin has extensive expertise in legal issues in health care, including the issues of national and global health, human rights, HIV testing and reporting, privacy, disability and discrimination.

Dr. Scott Hiebert is the Hortense B. Ingram chair in cancer research and professor of biochemistry in the department of biochemistry at Vanderbilt University School of Medicine. He has research specialty in the molecular mechanisms of acute leukemia, cell cycle control and the action of tumor suppressors and co-repressors.

Dr. Electra Paskett is the Marion N. Rowley professor of cancer research and director of the division of cancer prevention and control in the department of internal medicine at the School of Medicine, Ohio State University. She is nationally recognized for studying cancer health disparities and work in intervention research directed at cancer prevention, early detection and survivorship issues.

Dr. Nancy Raab-Traub is a professor in the department of microbiology and immunology at the School of Medicine, Lineberger Comprehensive Cancer Center at the University of North Carolina, Chapel Hill. She specializes in the role of Epstein-Barr virus in the etiology of human disease and has identified the genes that are expressed in nasopharyngeal carcinoma by cloning and sequencing cDNAs directly from tumor tissue.

Dr. Margaret Spitz is professor at the Dan L. Duncan Comprehensive Cancer Center at Baylor College of Medicine. She has a longstanding interest in genetic susceptibility to lung cancer and has developed a lung cancer risk prediction model.

Koretsky Joins NIGMS's Scientific Review Office

Dr. Tracy Koretsky recently joined NIGMS as a scientific review officer in its Office of Scientific Review. Her responsibilities include managing the review of research, training and capacity-building grant applications. Koretsky initially came to NIGMS as a contractor after having served as a special volunteer at CSR. Prior to that, she was a research specialist at NICHD and an assistant professor at Carnegie Mellon University. Koretsky earned a B.S. in cell and molecular biology from San Francisco State University and a Ph.D. in biology from Carnegie Mellon University. She conducted postdoctoral research at the Massachusetts Institute of Technology.

Dr. Tracy Koretsky

Acting NCI director Dr. Doug Lowy (l) welcomes new NCAB members (from l) Lawrence Gostin and Drs. Nancy Raab-Traub, Electra Paskett, Margaret Spitz, Francis Ali-Osman, Scott Hiebert and Elizabeth Jaffee.

The current Council of Councils members are (back row, from l) John Postlethwait, Terry Magnuson, Norbert Pelc, Marlene Belfort, Philip Alderson, DPCPSI Director James Anderson, David Holtzman (not a member), Jorge L. Contreras, Sharon Anderson, Joseph Buckwalter (not a member); (middle row, from l) Vivian Lee, Kimberly Leslie, Lila Gierasch, Gail Yokote, J. Leslie Winston, King Holmes, Nsedu Obot Witherspoon, Terry Jernigan; (front row, from l) Jonathon Epstein, Melissa Brown, Ana Cuervo, Mary Carnes, Hakon Heimer. Not shown are Eric Boerwinkle, Judy Garber, Norma Sue Kenyon, Guillermina Lozano and Keith Reimann.

Eight Named to Council of Councils

The Division of Program Coordination, Planning and Strategic Initiatives in the Office of the Director, NIH, recently welcomed 8 new advisory members to the Council of Councils who will advise on DPCPSI policy and programs.

The new members are:

Dr. Eric Boerwinkle, professor and director of the Institute of Molecular Medicine Center for Human Genetics, the University of Texas Health Science Center at Houston. His research interests encompass the genetic analysis of common chronic diseases in humans, including coronary artery disease, hypertension and non-insulin dependent (type II) diabetes.

Dr. Melissa Brown, professor of ophthalmology at Thomas Jefferson University and president and CEO for the Center for Value-Based Medicine in Pennsylvania. She is lead author of *Evidence-Based to Value-Based Medicine*, an acclaimed text published by the AMA Press (2005) that defines the field of value-based medicine and its application to the clinical setting.

Jorge Contreras, associate professor at the University of Utah and senior policy fellow at American University Washington College of Law, with an adjunct faculty appointment in human genetics at the University of Utah School of Medicine. He has written extensively on the institutional structures of intellectual property, technical standardization and biomedical research, particularly in the areas of genomics and genetics.

Dr. Jonathan Epstein, professor of cell and developmental biology and executive vice dean and chief scientific officer of the Perelman School of Medicine and the William Wikoff Smith professor of medicine at the University of Pennsylvania. His research focuses on the molecular mechanisms of cardiovascular development and understanding and treating human disease.

Dr. John Postlethwait, professor of biology at the Institute of Neuroscience, University of Oregon. He developed mutational models for Fanconi anemia in zebrafish via conducting a small molecule screen for compounds to rescue zebrafish Fanconi anemia mutants as a way to identify potential therapeutics for human Fanconi anemia patients and to understand disease mechanisms.

Dr. J. Leslie Winston, associate director of the Global Oral Care Professional and Scientific Relations Health Care Research Center at Procter & Gamble Co. She is responsible for representing Crest Oral-B science and products to the dental and research communities, dental professional organizations and opinion leaders and has experience in clinical trials research and technology development.

Nsedu Obot Witherspoon, executive director of the Children's Environmental Health Network, Washington, D.C. As a leader in the field of children's environmental health, she has conducted nationwide presentations and lectures on children's vulnerabilities and the need to protect them.

Gail Yokote, librarian emeritus, University of California, Davis. She chaired the National Library of Medicine's board of regents and has served on several NLM and other NIH study section panels associated with informatics or library special services and operations.

NIAMS Program Trains New Generation of Scientists

This summer, 18 students from all regions of the United States spent 8 weeks in the NIAMS Summer Research Program. They received career mentoring from senior researchers, participated in poster sessions, attended lectures and symposia and engaged in basic and clinical research.

The valuable experience they gained at NIH will help them achieve their career goals in biomedical research and academic medicine. "I feel honored to have had this experience, as it allowed me to learn lab techniques and think like a scientist under the guidance of helpful mentors," said one intern. "I absolutely recommend this program to all individuals who are looking to do world-renowned biomedical research," said another student.

The NIAMS Summer Research Program provides outstanding training opportunities for high school, undergraduate, graduate and medical students. Students can apply online at https://www.training.nih.gov/programs/sip. The application for summer 2017 will be available in mid-November.

2016 summer students with Dr. Robert Walker (center, back row), chief of the NIAMS Career Development and Outreach Branch, and Dr. Stephanie Mathews (third from left, back row), scientific program manager

Flu Vaccine Clinic for Staff Begins Oct. 3

The Office of Research Services and the Clinical Center will provide free flu shots to staff with a valid NIH identification badge from Oct. 3 through Nov. 10.

The best way to reduce the risk of getting the flu is to get the flu shot every year. By getting the flu shot, health care personnel can also reduce the risk of exposing patients to the influenza virus. All staff who have patient contact, including employees and contractors, are required to get the flu vaccine each year. For all other NIH staff, immunization with the flu vaccine is encouraged, but not required.

Opening early in the morning, the flu clinic will be located on the east side of the 7th floor of the Clinical Research Center. Employees intending to receive a flu shot must wear clothing that does not restrict access to the upper arm. Changing areas will not be available.

Starting Oct. 13, there will also be off-campus sites providing free flu shots. Shady Grove, Bayview, Poolesville, Neuroscience Center, Fishers Lane and Rockledge locations are included on the schedule.

NIH ordered both high-dose and the regular quadrivalent vaccines for all flu shot sites. Staff ages 65 and older can receive the high-dose vaccine. A limited number of egg-free doses have been ordered and will only be administered to health care personnel with a documented egg allergy.

To learn more about the high-dose flu shot, visit http://go.usa.gov/PAUY. For more information about availability and to find locations, visit foiltheflu.nih.gov or call (301) 496-2209. For directions to the 7th fl. CRC clinic, visit www.takemethere.cc.nih.gov and search "Flu."

Foil the Flu: 2016 Immunization Schedule

NIH employees and contractors are encouraged to participate. NIH photo ID required.

MAIN CAMPUS SITE

Date	Day	Location	Morning	Afternoon/Evening
10/03/16	Monday	10-CRC[1]	8:00 – Noon	Noon – 3:30
10/04/16	Tuesday	10-CRC	8:00 – Noon	Noon – 3:30
10/05/16	Wednesday	10-CRC	8:00 – Noon	Noon – 3:30
10/06/16	Thursday	10-CRC	6:00 – Noon	Noon – 7:00
10/07/16	Friday	10-CRC	8:00 – Noon	Noon – 3:30
10/10/16	Monday	10-CRC	Closed	Closed
10/11/16	Tuesday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/12/16	Wednesday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/13/16	Thursday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/14/16	Friday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/21/16	Friday	10-CRC	8:30 – 11:30	12:30 – 3:30
10/31/16	Monday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/01/16	Tuesday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/02/16	Wednesday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/03/16	Thursday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/04/16	Friday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/07/16	Monday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/08/16	Tuesday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/09/16	Wednesday	10-CRC	6:00 – 11:30	12:30 – 7:00
11/10/16	Thursday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/11/16	Friday	10-CRC	Closed	Closed

WEEKEND HOURS (10-CRC) - SATURDAY 11/05/16

Open to All Employees • 6:30a – 8:00a and 6:30p – 8:00p

OFF CAMPUS SITES

Date	Day	Location	Morning	Afternoon/Evening
10/13/16	Thursday	BRC[2]	8:30 – Noon	Noon – 3:30
10/14/16	Friday	BRC	8:30 – 11:30	Harbor Hospital 12:30 – 2:00
10/17/16	Monday	Fishers Lane[3]	8:30 – Noon	Noon – 3:00
10/18/16	Tuesday	Fishers Lane	8:30 – Noon	Noon – 3:00
10/19/16	Wednesday	NSC[4]	8:30 – Noon	Noon – 3:00
10/19/16	Wednesday	Poolesville[5]	8:30 – 11:00	11:30a – 2:00
10/20/16	Thursday	NSC	8:30 – Noon	Noon – 3:00
10/24/16	Monday	RKL[6]	8:30 – Noon	Noon – 3:00
10/25/16	Tuesday	RKL	8:30 – Noon	Noon – 3:00
10/26/16	Wednesday	Shady Grove[7]	8:30 – Noon	Noon – 3:00
10/27/16	Thursday	Shady Grove	8:30 – Noon	Noon – 3:00
10/28/16	Friday	Shady Grove	8:30 – 11:30	12:30 – 3:30

For questions, please contact OMS at 301-496-4411.

[1]Main Campus: Building 10, CRC 7th Floor Atrium, East Side

[2]BRC: 251 Bayview Boulevard, Baltimore, MD 3rd Floor Atrium Lobby

[3]Fishers Lane: 5601 Fishers Lane, Rockville, MD Rooms LD 20 A&B

[4]Neuroscience Center: 6001 Executive Boulevard 1st Floor Room D&E

[5]Poolesville: Building 103 (am)/ Building 110 (pm)

[6]Rockledge II: 6701 Rockledge Drive, Bethesda, MD – Room 6191

[7]Shady Grove: 9609 Medical Center Drive, Rockville, MD Seminar Room 110 - Terrace Level East Tower

NIDDK's Felsenfeld Receives Horwitz Prize

Dr. Gary Felsenfeld, NIDDK senior investigator and NIH distinguished investigator, is a 2016 recipient of the Louisa Gross Horwitz Prize. Columbia University gives the award to recognize outstanding basic research in biology or biochemistry. Since the prize was first awarded in 1967, 43 awardees have gone on to win Nobel Prizes.

Dr. Gary Felsenfeld

Felsenfeld's research has focused on how chromatin proteins regulate the biochemical behavior and structure of DNA within the cell's nucleus, including the processes of cellular differentiation and how embryos develop.

Understanding the changes in chromatin structure and function associated with both normal and abnormal growth and development is essential to advancing progress in diseases such as cancer and diabetes. Felsenfeld's work helped lead to the formation of the epigenetics field.