NIH RECORD

October 5, 2018
Vol. LXX, No. 20

19-Ton Magnet Augments NIH MRI Facility

BY RICH MCMANUS

Lowered through a hatch in the roof of the NIH MRI Research Facility (NMRF) on Aug. 25—with only an inch to spare on each side—was the ninth and newest member of a family of huge magnets used to conduct magnetic resonance imaging studies in humans. The 7-Tesla, 19-ton behemoth required a 600-ton capacity crane, buttressed by a 75-ton support crane, to swing the magnet 170 feet from a flatbed truck parked on South Dr. to its new home in Bldg. 10 NMR Center, Rm. B1D305.

"It took 19 tractor-trailers to deliver the cranes and magnet to campus, but all went smoothly that sunny Saturday morning," said Dr. Joelle Sarlls, a staff scientist in the NMRF. The sizeable effort was coordinated by Daniel Lid, a project officer in the Office of Research Facilities.

Magnet weighing 38,000 pounds lifts off from South Drive.

The NMRF is a trans-NIH facility within the In Vivo NMR (nuclear magnetic resonance) Center, which first opened in 1987 as an appendage to the southwest side of Bldg. 10. Presently, the center boasts active research programs from NIMH, NINDS, NIAAA, NHLBI and the Clinical Center's radiology department, as well as the NMRF and another trans-NIH facility, the Mouse Imaging Facility.

In 1987, NIH hosted its first human research MRI magnet, a 1.5-Tesla machine made by GE. Because the field generated

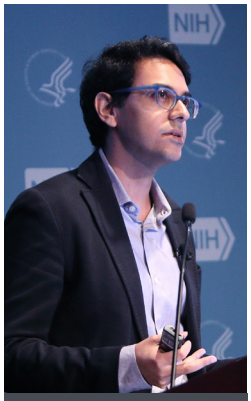
SEE **MAGNET**, PAGE 6

Can you type in the key of A? See story, p. 12.

ALSO THIS ISSUE

Wachtel Awardees Discuss Advances in Cancer Genomics

BY DANA TALESNIK



Dr. Neville Sanjana

It's an exciting time to be a young scientist, as new technology keeps opening new doors to scientific discovery. Two NIH early-career investigators recently discussed their research on cancer genomics, made possible by the latest genetic and analytic tools.

"Early-career investigators are the future of our institution and of biomedical research," said Dr. Tom Misteli, director of NCI's Center for Cancer Research, at

SEE **GENOMICS**, PAGE 4

Gassmann Lectures on High-Altitude Physiology

BY ERIC BOCK

Dr. Max Gassmann

People are naturally adapted to live at or close to sea level, where the body's oxygenation is more optimal than in higher-altitude environments, said Dr. Max Gassmann in a lecture at the Clinical Center's FAES Education and Conference Suite recently. But for those who do not, acclimatization is possible.

"Every single cell in your body is able to sense reduced oxygen supply," explained

SEE **GASSMANN**, PAGE 8

Stetten Lecture Focuses on Regeneration

Within a span of 2 weeks, a small worm can accomplish a feat no human has ever achieved. The worm, known as a planarian, can regrow any severed body part—including its head. For the past 20 years, Dr. Alejandro Sánchez Alvarado has tried to figure out how this happens. In June, his team at Stowers Institute for Medical Research disclosed what they believe is the long-sought source of planarians' remarkable regenerative abilities.

Dr. Alejandro Sánchez Alvarado

Sánchez Alvarado will explain the findings during this year's DeWitt Stetten Jr. Lecture. His talk, titled "Understanding the Source of Regenerative Ability in Animals," will occur on Wednesday, Oct. 10 at 3 p.m. in Masur Auditorium, Bldg. 10. It is sponsored by NIGMS and is part of the NIH Director's Wednesday Afternoon Lecture Series.

A videocast of the lecture (live or later) will be available at http://videocast.nih.gov. For reasonable accommodation during the lecture, contact Jacqueline Roberts at Jacqueline.Roberts@nih.gov or (301) 594-6747.

NEI Symposium on Future of Vision Research, Oct. 18

All are invited to the symposium "The Future of Vision Research," the fourth in a series celebrating the National Eye Institute's 50th anniversary. The event will feature new and emerging methodologies in vision research.

Presentations will include research into the brain's processing of visual information, new retinal imaging and image analysis technologies and the development of novel prosthetic devices and transplantable retina tissue.

The event will be held Thursday, Oct. 18 from 9 a.m. to 3:15 p.m. in Lipsett Amphitheater, Bldg. 10. For more information and to register, visit https://www.nei.nih.gov/nei-50th-anniversary-symposium-future-vision-research.

For more information about NEI 50th anniversary events, including the symposium series, visit https://nei.nih.gov/neiat50.

New Policy Promotes Employee Health

Most of us at NIH invest a great deal of mental and emotional energy each day helping to improve the health of the nation. But how many of us invest in our own health during the work day?

Inn Audience Enjoys 'Hamilton' Tunes

On Aug. 28, the NIH *a cappella* group Nerds in Harmony performed tunes from the popular musical *Hamilton* for an audience of children and families at the Children's Inn at NIH, who listened while enjoying a lunch catered by volunteers. Dr. Diana Bianchi, (r) director of the National Institute of Child Health and Human Development and an ardent *Hamilton* fan, introduced the performers and led a fun history lesson about the founding father. For a video clip, visit https://www.facebook.com/TheChildrensInn/videos/260679861226077/.

PHOTO: SONJA LUECKE

We can infer from the results of the 2017 Federal Employee Viewpoint Survey (FEVS) that it's a low number, with only 16.3 percent of NIH respondents indicating they participate in "health and wellness programs," including exercise and medical screenings. The government-wide FEVS response to that question was 10 percentage points higher than the NIH response.

However, this may soon change for the better with publication of the first NIH policy to address employee wellness. Finalized last summer, the NIH Workplace Wellness Policy aims to empower employees to work with their supervisors to make use of scheduling flexibilities to engage in a wide range of wellness activities.

"As the nation's premier biomedical research agency, the NIH recognizes that our organizational effectiveness relies upon the well-being of our employees," said Dr. Alfred Johnson, NIH deputy director for management. "The new policy demonstrates NIH's commitment to promoting the health and productivity of our workforce."

The workplace wellness policy, one of several achievements of the NIH health & wellness council (HWC) since its inception in 2010, provides guidance on the use of scheduling flexibilities for work-day participation in exercise, wellness lectures, visits to the Employee Assistance Program and/or other approved activities that support health and well-being.

"The primary reason we created the policy," said NIDA's Quandra Blackeney, HWC workplace wellness policy committee chair, "was to promote a culture of wellness at NIH. And the place to start was by strongly encouraging supervisors to actually initiate the discussions and offer employees the option."

Much research shows that many chronic medical conditions can be prevented or better managed by daily healthy lifestyle choices related to how we eat, handle stress, manage our finances, exercise, socialize and sleep. "We have to help employees see that making lifestyle changes can optimize their health and also be part of their work day, and this policy sets out to do both," Blackeney noted.

To access the new policy, go to https://policymanual.nih.gov/1481. For tips on Creating Healthy Habits, go to https://newsinhealth.nih.gov/2018/03/creating-healthy-habits.

For more information about the HWC and the range of wellness offerings that support employee well-being, visit https://wellnessatnih.nih.gov/Pages/About.aspx.—**Sophia Glezos Voit**

Walk/Run Marks NEI's 50th Anniversary

The National Eye Institute will host a 5K walk/run on Oct. 24 in commemoration of its 50th anniversary. The course goes around the perimeter of the NIH campus (total distance of 3.25 miles). Participants will require their PIV card to re-enter the campus.

The start/finish line is in front of Bldg. 1. Festivities and a group warm-up kick off at 11:30 a.m. with the first start at 12:15 p.m. Get your vision screened and try out the new NEI virtual reality eye disease simulator. Food will be available for purchase truck-side. To register, go to https://forum.nei.nih.gov/5kfor50. Questions? Contact Lilly Sadler at sadlerla@mail.nih.gov or (301) 451-8007.

PIONEER IN MEDICINE

Braunwald Recalls His Early Days at NIH

BY COURTNEY COOMBES

Dr. Eugene Braunwald, a cardiologist and distinguished Hersey professor of medicine at Harvard Medical School, has seen his field come a long way since starting his career in the early 1950s at NIH. At that time, the outcomes for patients were bleak. Without the life-saving strategies that Braunwald and his peers would later develop, there was little to be done for patients after a heart attack (or myocardial infarction) and many died within a year.

Dr. Eugene Braunwald gives NHLBI 70th Anniversary Lecture.

PHOTO: CHIA-CHI CHARLIE CHANG

Cardiovascular death rates were 3 times what they are today. There were no sophisticated tools like the modern echocardiogram to diagnose patients. Where others might just see challenges and obstacles, young Braunwald saw opportunity. He spent a lifetime moving the field of cardiology further, particularly by developing new, less invasive ways to monitor the heart and by advancing cardiac surgery.

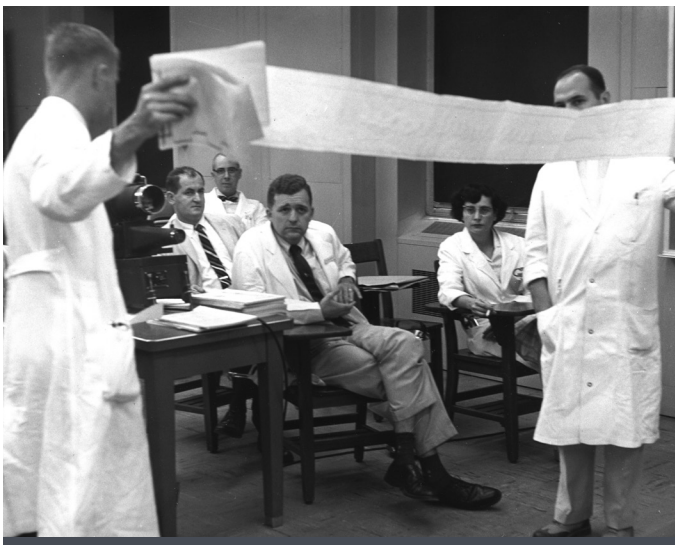
Those were the themes of Braunwald's career, which he described at his recent lecture "Clinical Cardiovascular Research Inspired by the NHLBI: A Personal Odyssey." It was a special occasion to celebrate the 70th anniversary of the National Heart, Lung, and Blood Institute, where Braunwald became a research fellow in 1954 and later served as clinical director from 1959 to 1968.

He was introduced by NHLBI director Dr. Gary Gibbons and NHLBI scientific director Dr. Robert Balaban. Gibbons, who remembers presenting cases to Braunwald during his morning report as an intern at Brigham and Women's Hospital, described him as an "American master" of biomedicine who is both humbling and inspiring.

During his time at NHLBI, Braunwald, with his colleagues and mentors, performed what are now considered classical studies in blood flow mechanics and heart function. At the time, he said, there were no clinical trials and no evidence-based medicine in cardiology. But there were also three Nobel Prize winners walking the halls of the Clinical Center, one of whom was Dr. Andres Cournard, honored in 1956 for the development of cardiac catheterization—threading a tube through a blood vessel to measure blood flow and pressure within the heart. Cournard became Braunwald's mentor and helped him understand the importance of hypothesis-driven research and how studying a disease intervention can provide a deeper understanding of the disease.

Braunwald also extended his mentor's work to develop an important tool called left-heart catheterization. Although Cournard and others had successfully "cathed" the right side of the heart, the left side—"where the action is"—had yet to be measured. Braunwald developed a safe and effective way to collect this vital measurement.

His studies of heart attack—done in collaboration with his wife, the first board-certified female heart surgeon in the U.S., Dr. Nina Starr Braunwald—helped establish that opening clogged vessels to the heart could help prevent damage to cardiac muscle. That work led to earlier and more aggressive intervention for heart attack patients, which has greatly improved long-term survival rates. (To see more about Nina Starr Braunwald's contributions to cardiology, check out the exhibit "Innovation and Invention: NIH and Prosthetic Heart Valves" in the Clinical Center south lobby.)



Drs. Eugene (l) and Nina Starr Braunwald (r) study an EKG printout, circa 1963.

PHOTO: JERRY HECHT

Braunwald left NHLBI in 1968, but throughout his career, he has maintained a close affinity with the institute, including serving as founding chair of the NHLBI-funded thrombolysis in myocardial infarction group, which conducts trials that have led to some of the most commonly used medications to treat and prevent heart attacks. (Thrombolysis refers to breaking apart the blood clots that can cause myocardial infarction.)

The group's first study found that the clot-busting drug tissue plasminogen activator was far more effective for acute heart attacks than the previous standard of care. The group was also the first to show that angiotensin-converting enzyme inhibitors could preserve heart function and reduce mortality after a heart attack.

Braunwald ended the lecture with his thoughts and predictions for the future of his field. "There are now many cardiologies," he said, explaining that it will be important to understand how cardiology interfaces with other fields of medicine such as pulmonology, diabetes and oncology. For example, he noted that the second most common cause of death for breast cancer patients is heart failure, and that it will be critical for cardiologists and oncologists to work together on improving patient outcomes.

Braunwald also noted the potential for genomic research and big data to bring new precision medicine approaches to his field. Going forward, "it will be important for cardiology to move into the molecular age using big data and new tools," he concluded.

ON THE COVER: *Microneedle flu vaccine patch application. The microneedles dissolve within minutes after insertion into skin to release encapsulated drug or vaccine.*

IMAGE: ROB FELT, GEORGIA TECH

The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email editor or phone (301) 496-2125.

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NIH National Institutes of Health
Turning Discovery Into Health

Genomics

CONTINUED FROM PAGE 1

the recent CCR Grand Rounds in Lipsett Amphitheater. "We have reached a point where we actually do understand many of the basic principles and mechanisms [underlying cancer] with sufficient detail, so we can use that knowledge to translate it to the clinic."

Misteli introduced the two researchers who recently received the Martin & Rose Wachtel Cancer Research Award, splitting the $25,000 prize from the Wachtel endowment. Dr. Neville Sanjana of New York University and the New York Genome Center and Dr. Omer Yilmaz of the Koch Institute for Integrated Cancer Research at MIT, who both teach biology, described their findings at the AAAS-sponsored Wachtel Lecture, co-hosted by NCI.

Sanjana's lab is using gene-editing technologies to pinpoint genetic variants that contribute to cancer growth and therapeutic resistance.

"How do we take the human genome, with its 3 billion bases, and find that needle in a haystack?" he asked. "As we get this huge number of variants from tumor sequencing, it's becoming more and more difficult to understand which of these variants cause the disease, which ones drive tumor evolution and drug resistance and which ones might just be passengers along for the ride."

In analyzing cancer mutations, much attention is focused on protein-coding genes of the genome. But they make up only a small fraction of the entire human genome — less than 2 percent. Sanjana is particularly interested in the noncoding regions, which comprise 98 percent of the genome. Using CRISPR nucleases like Cas9, his lab is able to knock out thousands of genes and noncoding regions to help find mutations that drive drug resistance in melanoma. His gene-editing approach using pooled screens does not rely on making a single mutation at a time but instead harnesses libraries that can test thousands of mutations in parallel.

BRAF is the most commonly mutated gene in melanoma and a common treatment for BRAF-mutant melanoma is the FDA-approved drug vemurafenib. Most melanoma patients go into remission for a time after receiving the drug, but then resistance sets in and the prognosis worsens. By

Dr. Omer Yilmaz

PHOTOS: CHIA-CHI CHARLIE CHANG

editing human melanoma cells and exposing them to the drug or a placebo, Sanjana and his colleagues have identified novel genes and noncoding regions of the genome that drive vemurafenib resistance.

"Even though we already have all these assays of noncoding function," said Sanjana, "the functional screens add another layer on top of those assays that's directly connected with an important phenotype, the drug resistance itself that we see in patients."

Another study in Sanjana's lab is identifying mutations that prevent immunotherapy from working. This collaborative work with NCI's [Dr. Nicholas] Restifo's lab uses genome-wide screens to pinpoint tumor mutations that result in immunotherapy failure across genetically diverse melanomas and also other cancers where immunotherapy is currently being deployed in the clinic.

One gene they identified, the apelin receptor, hadn't previously been associated with immunotherapy response. But in a mouse melanoma model, tumor cells without the apelin receptor significantly decreased the efficacy of immunotherapy in terms of tumor volume and survival.

Said Sanjana, "We're moving slowly toward a future with precision medicine where we could, in advance of a patient receiving a T-cell immunotherapy, be able to predict whether their tumor is a good candidate for this kind of therapy or whether it should be [used in combination with, or in lieu of] another therapy."

The second Wachtel awardee, Yilmaz, discussed dietary origins of intestinal cancer. In many cases, low-calorie diets delay the incidence and inhibit the progression of different cancers, he said, whereas high-fat diets and obesity are found to accelerate cancers.

"Many tissues in the body are maintained by stem cells that integrate environmental cues like different types of nutrients and circulating hormones to coordinate tissue homeostasis and regeneration," said Yilmaz.

Adult intestinal stem cells (ISCs) respond to these cues by interacting with their microenvironment, made up of support or "niche" cells, which include Paneth cells. Under normal dietary conditions, Yilmaz explained, ISCs are adjacent to their Paneth cell niche. But in a high-fat diet, ISCs proliferate and become uncoupled from this niche. It is possible that these changes enhance intestinal tumor formation in high-fat diets.

In one study, mice were fed an extremely high-fat diet for 18 months and became obese. These mice had at least triple the risk of developing spontaneous intestinal cancers, Yilmaz reported.

"Obesity is a modifiable risk factor for cancer," he said. "Human patients with a body mass index of more than 30 have a modest, but significant, likelihood of developing and dying from colorectal cancer."

RNA sequencing revealed a pathway called PPAR-delta that drives a fatty acid oxidation program enabling cells to utilize fat as an energy source. Interestingly, synthetic activation of the PPAR-delta pathway emulates many aspects that a high-fat diet has on intestinal stem cells: ISCs become uncoupled from their Paneth niche and these ISCs and their more differentiated daughter cells are better able to initiate intestinal tumors.

"We believe this high-fat diet PPAR-delta program contributes to intestinal tumorigenesis," said Yilmaz.

Currently, his lab is studying reversibility, that is, the effects of a person quitting a high-fat diet and returning to a healthier diet and weight. They're also studying whether fatty oxidation helps restore stem cell functionality and what other mechanisms might contribute to tumorigenesis.

Ultimately, Yilmaz hopes to create diet-based interventions that improve regenerative function while minimizing the risk of developing cancer. Sanjana looks forward to the next wave of analytic tools to help understand how tumor mutations affect cancer progression as well as therapeutic resistance. Then, he concludes in a recent article in *Science Translational Medicine*, we might "precisely tailor treatments from which cancers cannot escape."

Nobel laureate Dr. Michael W. Young

Nobel Laureate Addresses Sleep, Circadian Rhythms, Oct. 17

If you enjoyed hearing about the Nobel Prizes this week, don't miss the upcoming lecture by 2017 Nobel laureate in physiology or medicine Dr. Michael W. Young.

Together with two other NIH grantees, Young, a geneticist at Rockefeller University, was honored for discovering molecular processes that control the daily biological rhythms of virtually all organisms.

These roughly 24-hour cycles, known as circadian rhythms, control our waking and sleeping patterns; the rise and fall of body temperature and blood pressure; the ebb and flow of hormones; learning, memory, digestion, immunity…essentially, almost every activity in our bodies.

Young will present the NIGMS-sponsored lecture "Genes Controlling Sleep and Circadian Rhythms" on Wednesday, Oct. 17 at 3 p.m. in Masur Auditorium, Bldg. 10.

As with all NIH Director's Wednesday Afternoon Lectures, you can watch the presentation live or later at http://videocast.nih.gov. For reasonable accommodation during the lecture, contact Jacqueline Roberts at Jacqueline.Roberts@nih.gov or (301) 594-6747.

Physical Therapy Month Events

The physical therapy section of the Clinical Center rehabilitation medicine department will be celebrating PT month in October by hosting booths at the Work Life Event in the south lobby of Bldg. 10 on Oct. 16 and at NEI's 5K walk/run on Oct. 24 at noon in front of Bldg. 1. Drop by to learn more about physical therapy and how it can help you achieve your goals.

PILLAR OF HEALTH

Workshop Examines Role of Sleep in Health Disparities

The National Institute on Minority Health and Health Disparities, the National Heart, Lung and Blood Institute and the Office of Behavioral and Social Sciences Research recently convened a 2-day workshop examining the role of sleep in health disparities. It brought together a diverse group of academic researchers from two fields—sleep and health disparities—to strategize how to integrate research to understand the causes of sleep disparities and how to intervene.

Dr. Michael Twery, director of the National Center on Sleep Disorders Research at NHLBI, emphasized the role of sleep as a potential mediator/moderator on pathways such as oxidative stress, metabolism and brain function connecting behavioral and social determinants. Keynote speaker Dr. Margarita Alegria of Harvard Medical School discussed how to apply health disparities research frameworks to sleep disparities.

Over the past 50 years, the literature has shown that poor sleep quantity and quality correlates with higher incidence and mortality of many diseases. Sleep affects every organ system; insufficient or poor sleep has been linked to weight gain, depression, a higher risk of heart disease and diabetes, poor concentration, higher infection rates and myriad other health conditions.

Like diet and exercise, sleep is increasingly understood as a pillar of health. Differences in sleep are just beginning to be studied with health disparities populations. For example, African Americans and Latinos are more likely than whites to suffer from a lack of sleep across all ages and even within the same socioeconomic class. African Americans are also more likely to report daytime sleepiness, which is strongly correlated with a poorer quality of life and a higher risk of accidental injury.

Underlying social, cultural, environmental and biological factors have been shown to contribute to sleep deficiencies among minority and health disparity populations; these sleep deficiencies may lead to disparities in health outcomes. Sleep is often regarded as "unproductive time" in society and is thus not seen as a health priority. Research has shown that sleep patterns begin as early as in the womb and change through adulthood. Biological differences arising from sleep deprivation can cause people to react differently to triggers, such as noise and light exposure, interpersonal stressors and food choices and meal timing.

Participants discussed multi-level interventions to reduce sleep disparities, especially how clinicians, communities and policymakers can play a role to reduce disparities in sleep health. Focusing on modifiable behaviors and surrounding influences, interventions can start with educating parents and youth on the value of sleep and how to improve sleep environments. Advancing multi-level interventions that can integrate sleep as a socially patterned behavior and embracing "circadian health" will be important. Community and policy interventions must tackle external influences, such as neighborhood safety and noise pollution.

Breakout sessions facilitated discussion and development of recommendations for both understanding the causes and consequences of sleep disparities and interventions. For example, participants prioritized verifying the relationship between racism and discrimination as a driver of sleep disparities and developing population-level, culturally and developmentally sensitive interventions to promote sleep health across the life course.

The final session covered strategies to integrate the sciences of sleep and health disparities research. Life course models emphasize that, because of vulnerable developmental periods, the right intervention needs to be delivered at the right age to be effective. Holistic models that include genomic, behavioral, clinical, sociodemographic and built-environment assessments will be important to advance sleep disparities research.

Participants in the workshop "The Role of Sleep in Health Disparities: Causes and Health Consequences"

PHOTO: EDGAR DEWS

The 7T magnet eases through a roof hatch, with an inch to spare on each side. There are also bay doors in the side of the facility that can admit magnets.

PHOTOS: CHIA-CHI CHARLIE CHANG

Magnet

CONTINUED FROM PAGE 1

by the magnet was so large, GE designed an add-on to Bldg. 10 that has grown into the present NMR Center. The location outside of the main part of Bldg. 10 shielded the machine from harming any metal-bearing neighbors, said Dr. Alan Koretsky, NMRF director for the past 19 years who has recently stepped out of his role as NINDS scientific director.

The new 7T magnet is self-shielded, as are most new-generation magnets, so that the large center—initially pioneered by first Office of Research Services director (and NIDDK scientist) Dr. Ted Becker—can continue to accommodate more and stronger MRI fields without having to grow physically. Despite the continuous improvement in magnet technology, the NMR Center has expanded four times during its 31-year lifespan to meet the growing need for research MRI by more and more institutes within the Intramural Research Program.

The tesla is a unit of magnetic field strength, adopted internationally in 1960 in honor of Nikola Tesla, a Serbian American inventor. One T equals 10,000 gauss. One talks T only at industrial-grade, or research, applications; a strong refrigerator magnet is about 100 gauss.

The higher the field strength of an MRI magnet, the sharper the resolution of images of interest to researchers, of whom several hundred work under the umbrella of the In Vivo NMR Center. "It's like a whole institute of activity, with hundreds of researchers using the resources," notes Koretsky.

The NMRF was the first of what are now 7 trans-NIH facilities that are overseen by NIH deputy director for intramural research Dr. Michael Gottesman and the scientific directors; they make special resources available to NIH scientists. The In Vivo NMR Center was also a model for how to integrate the research of multiple institutes, Koretsky added. "The Porter Neuroscience Research Center is the most recent example of integrating research across multiple institutes that was influenced by the NMR Center—but the NMRF and In Vivo NMR Center was once unique."

Begun as a joint effort of NINDS, NIAAA, NHLBI (Laboratory of Cardiac Energetics, headed by Dr. Robert Balaban), NCRR and CC radiology (Laboratory of Diagnostic Radiology Research, headed by Dr. Joseph Frank), the In Vivo NMR Center has added research partners over the years, including NIMH, NCCIH, NEI and NCI. The users of the NMRF paid for the new 7T, helped by the NIH Director's Challenge Innovation Award Program.

"It is very rare to find that many institutes that contribute to a single endeavor because they want to," said Koretsky. "Sometimes 2 or 3 ICs will do things, but to get 5 or 6 so readily aligned is unusual."

In addition to the new 7T magnet, which cost about $6.5 million, the center has had two other 7Ts. The first was very developmental—funded by NINDS and NIMH—and

It took two cranes to hoist the magnet. In the foreground is the 600-ton capacity crane and at rear is the 75-ton support crane.

The team involved in the 7T magnet renovation and installation project included (from l) Mesfin Medhin, construction management personnel mechanical inspector; Aaron Burroughs, facility operations and maintenance staff; Dr. Joelle Sarrls, NMRF staff scientist; Seung Yang, project manager, Healthcare Design Builders; Chip Gavin, senior project manager, Siemens Healthineers; Joellyn Stolinski, NMRF MRI technologist; Dave Sweeney, director of operations, Healthcare Design Builders; and Daniel Lid, ORF project officer.

few could use it due to the early-stage nature of the project, Koretsky said. The first 7T was replaced with a second-generation 7T MRI that has found widespread use by investigators in NIMH and NINDS as part of the joint NIMH/NINDS Functional MRI Facility in the NMR Center. The center also has 7 3-Tesla magnets. An 11.7T magnet is on order for delivery later this year; the biggest magnet currently in use for human studies is 10.5T, at the University of Minnesota.

Institutes with major research programs in the NMR Center accommodate research partners not only at NIH, but also at Suburban Hospital, Children's National Medical Center and Washington Hospital Center, Koretsky noted.

"MRI images with improved signal-to-noise ratio and/or resolution can be obtained with scanners operating at higher field strengths," explained Dr. S. Lalith Talagala, NMRF technical director. "Therefore, the new 7-Tesla scanner will allow investigation and understanding of anatomical and functional changes due to brain abnormalities at finer detail than possible with 3-Tesla scanners. The new scanner represents the third generation of 7-Tesla scanners and has been approved by the FDA. Therefore, the new scanner will be more robust and easy to use."

NIH is one of the world's cradles of NMR expertise, making not only scientific and clinical advances, but also technical developments in the MRI systems themselves, said Koretsky. "There are only a handful of places in the world that have as much NMR expertise as we do."

Fifteen years ago, NIH got the third 7T magnet ever made. This first-generation machine, made by GE, required 300 tons of steel shielding.

"Interesting results with [the first-generation machine] led to the development of a second-generation 7T," said Koretsky. "This work demonstrated the need for another 7T for the broader NIH community."

The new machine, built by Siemens, represents the third-generation of 7T magnets. It is expected to perform in the proud tradition of its smaller, lower-field forbears: NIH acquired one of the first 4T MRI machines in the world when it debuted and pioneered GE's first 3T machine years ago. 3T MRI is now a standard around the world.

"We fully expect 7T will find widespread use and hopefully the same will happen at 11.7T," Koretsky said.

"We have CRADAs [cooperative research and development agreements] with all three major vendors of MRI machines—Siemens, Philips and GE," he continued. "These are critical for a large number of applications. MS [multiple sclerosis] trials have been pioneered at the NMR Center, as well as important functional imaging work—watching the brain work, for example. We have an innovative NHLBI heart-imaging program right now. A lot of fundamental things have been pioneered here...I'm honored to be a part of it. We know we're in a special place."

Koretsky says he recently stepped aside as NINDS scientific director to pursue more research as a principal investigator: "All these cool new magnets are coming—I want to get back to science."

The new 7T machine should be ready for users before the end of the year, said Sarlls.

"Initially, the institutes that contributed to the purchase of the scanner will have access to it," noted Talagala. "However, any NIH investigator will be able to request time to use the new scanner for suitable protocols."

Asked if the new magnet was attracting enthusiasm in the research community, Sarlls replied, "Oh, definitely." R

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"There are only a handful of places in the world that have as much NMR expertise as we do."

–DR ALAN KORETSKY

• • •

Hughes-Halbert To Give NCI Seminar

Dr. Chanita Hughes-Halbert is the featured guest speaker for the next lecture in NCI's Center to Reduce Cancer Health Disparities' Continuing Umbrella of Research Experiences (CURE) Distinguished Scholars Seminar series on Wednesday, Oct. 17, 1-2:30 p.m. at the NCI Shady Grove Campus, Rm. TE110. The title of her talk is "Translational Issues in Cancer Health Disparities."

Hughes-Halbert is a professor in the department of psychiatry and behavioral sciences and AT&T distinguished endowed chair for cancer equity at the Hollings Cancer Center at the Medical University of South Carolina (MUSC). She is also associate dean for assessment, evaluation and quality improvement in the College of Medicine at MUSC and the first of three MUSC SmartState endowed chairs in the Center for Cancer Disparities who are addressing cancer equity issues.

A nationally recognized expert in disparities research and behavioral science, Hughes-Halbert focuses on understanding barriers to clinical trial participation in underserved communities and developing population-based interventions to reduce disparities in local settings.

Visit https://bit.ly/2OLQLlq to register for the seminar via WebEx. For reasonable accommodation, call (301) 402-1366 or the Federal Relay (1-800-877-8339).

Gassmann

CONTINUED FROM PAGE 1

Gassmann, chairman of the University of Zurich's Institute of Veterinary Physiology and the Zurich Center for Integrative Human Physiology in Switzerland.

Usually, a person can acclimate to higher-altitude conditions, but it can take up to 10 days to do so. Ideally, a person should begin his or her ascent to higher altitudes at 2,500 meters.

Gassmann advised that each day, one should climb 500 meters, descend 200 meters and then go to sleep. It's difficult to slowly acclimate because it takes time and money. Additionally, there might not be a good place to pitch a tent on a steep mountainside.

During the adaptation period, red blood cell production increases. In places where oxygenation is reduced, a person's kidneys will secrete the hormone erythropoietin. The hormone travels through the bloodstream to the bone marrow, where it spurs production of red blood cells. Gassmann noted that this process requires iron. Most iron in the body is found in hemoglobin, a protein that transports oxygen. Hemoglobin is contained in red blood cells. The protein binds oxygen in high-oxygen areas, such as the lungs, and releases it in low-oxygen tissues. When abundant, iron is stored in the liver.

Iron is an essential nutrient, at the right levels. Too little causes anemia, while too much causes hemochromatosis. People with anemia do not transport enough oxygen in the blood. As a result, they feel tired and weak. According to the World Health Organization, anemia affects almost a quarter of the world's population.

Hemochromatosis is a condition where a person absorbs too much iron from food, Gassmann said. If severe, symptoms include fatigue, weight loss and joint pain. Treatment includes removing blood from the body (usually via blood donation), chelation therapy and low-iron diets.

To ensure the correct amount of iron enters the bloodstream, the liver produces hepcidin, a protein that regulates the entry of iron into the circulatory system. When hepcidin is suppressed, more iron is released from the liver and directed to the bone marrow. The intestines also release higher levels of iron from food passing into the circulation.

Failing to acclimate increases the risk of developing acute mountain sickness, which begins to occur at 2,500 meters above sea level. Symptoms include headache, nausea and fatigue. Gassmann said the condition is like "somebody is squeezing your brain." When someone experiences acute mountain sickness, it's important to get him or her to lower altitudes as soon as possible.

There are a few populations around the world who have adapted to higher altitudes, including Andeans and Tibetans. Each population has a different mechanism that allows them to function.

Populations that live in the Andes of South America adapt by producing more red blood cells to transport oxygen. However, this adaptation can lead to chronic mountain sickness. One of the classic symptoms of chronic mountain sickness is polycythemia, a condition where bone marrow produces far too many red blood cells. Blood becomes thicker and doesn't travel through blood vessels easily.

Polycythemia increases the risk of heart attack and stroke. Affected individuals also suffer from pulmonary hypertension. Treatment involves moving patients to lower altitudes, which many don't want to do for family reasons, Gassmann noted.

Tibetans, on the other hand, have a mutation that reduces the biological response to low oxygen supply. They present with higher lung capacity and use energy as efficiently as possible. He noted their ancestors have lived on the Tibetan plateau—which, on average, is 4,000 meters above sea level— in isolation for 3,500 years already. Thus, evolution has had enough time to proceed. Tibetans don't get chronic mountain sickness.

Even though these populations can live at high altitude, others will never be able to live in or even visit there.

"Training doesn't mean you'll reach a summit even if you're in the best physical condition," Gassmann cautioned. "Some people will never get acclimatized to high altitudes."

Gassmann explains that the air at high altitude does not contain less oxygen compared to the air we breathe at sea level. The air's oxygen concentration always stays at 21 percent. What happens at high altitude is that the air pressure becomes lower, which reduces air (and oxygen) uptake in the lungs.

PHOTOS: CHIA-CHI CHARLIE CHANG

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"Training doesn't mean you'll reach a summit, even if you're in the best physical condition. Some people will never get acclimatized to high altitudes."

-DR. MAX GASSMANN

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NIH Learns How to Use Naloxone, Save Lives

Public Health Service officers at NIH have trained more than 150 officers and others at NIH in opioid overdose response and use of naloxone.

In response to the nationwide epidemic of opioid overdoses and death, Surgeon General Jerome Adams issued an advisory in April urging more Americans to carry the lifesaving medication naloxone, which can reverse the effects of an opioid overdose. A dozen PHS Commissioned Corps officers from eight ICs answered the call by forming a working group to develop a program to train others at NIH and in the community.

Recently, 45 NIH officers were trained and certified as opioid response trainers by Dr. Al Romanosky, medical director/state emergency preparedness coordinator of the Maryland department of health's Office of Preparedness and Response.

These NIH PHS officers then held a marathon training session a few weeks later at Stone House. Four 90-minute training sessions were held throughout the day. Trainees were briefed on the current opioid crisis, how to recognize the signs and symptoms of an opioid overdose, how naloxone works and how to administer the medication. Following the lecture, attendees were divided into small groups for hands-on skill training. In the break-out groups, trainees were given scenarios to assess their ability to recognize signs and symptoms of an opioid overdose and given test kits to administer the naloxone in three different available forms. By the end of the day, 153 individuals were trained in administering naloxone; 34 of them were also trained and certified as trainers.

Cmdr. Daniel Goldstein and Lt. Cmdr. Raven McGlotten lead a hands-on training session at Stone House.

PHOTO: PETER KILMARX

Attendees included staff from the NIH fire and police departments and interest extended beyond NIH's walls with participants from the Food and Drug Administration, the Centers for Medicare and Medicaid Services, the Department of Defense, the Health Resources and Services Administration and the Office of the Secretary.

"The response by the NIH PHS officers has been outstanding," said Radm. Peter Kilmarx, FIC's deputy director, who helped lead the training initiative. "We're proud to have a meaningful and visible role in responding to the surgeon general's advisory and are planning to extend the training to others at NIH and in the community."

Romanosky noted, "We're very pleased with this relationship with the PHS officers. I was truly impressed by their dedication and drive and see this as a model of collaboration."

Opioids are a class of drugs that include prescription pain relievers, heroin and synthetic opioids such as fentanyl. Naloxone is an opioid antagonist that is used to temporarily reverse the effects of an opioid overdose and can potentially save a life. More than 2 million people in the U.S. struggle with an opioid use disorder. Rates of opioid drug deaths are rapidly increasing, reaching 49,000 in 2017. R

At EDI's recent Open House on anti-retaliation, staffers gather to welcome attendees.

Anti-Retaliation Campaign Educates NIH Community

NIH recently rolled out its first-ever Anti-Retaliation Campaign to educate and inform employees, managers and supervisors so they are aware what retaliation is, why it's illegal and not tolerated at NIH and how to find anti-retaliation resources from the Office of Equity, Diversity and Inclusion (EDI).

Retaliation occurs when employers treat applicants, employees, former employees—or people closely associated with these individuals—less favorably than others because the person:

• Reports discrimination;

• Participates in a discrimination investigation or lawsuit (for example, serving as a witness);

• Opposes discrimination (for example, threatening to file a charge or complaint of discrimination).

In an agency-wide email message, NIH director Dr. Francis Collins said, "We are committed to preventing victimization and other retaliatory behavior" toward any person raising Equal Employment Opportunity or unlawful practice concerns.

The campaign also included a 4-week blog series of information and tips: "NIH is Serious About Anti-Retaliation," "Educating Managers: Avoid These Dangers," "Educating Managers: 10 Interpersonal Skills to Prevent Retaliation" and "Words Matter: Chilling Effect of Retaliation."

EDI's Resolution and Equity Division staffers took to the streets with various activities throughout the month and personally engaged with the NIH community in Bldgs. 31 and 10 to share information on protections against retaliation and discrimination.

In anti-retaliation training for managers, EDI's Eric Hebron explained, "Retaliation appears to be a function of human nature and how people react when there are allegations of wrong-doing. It is expected that a supervisor who learns that an employee has complained concerning the supervisor's behavior will have difficulty treating the subordinate as if no complaint was made. However, that is what the law requires."

At a subsequent session, Hebron explained to employees, "You should consider asking questions, seeking clarification and eliminating assumptions, if you feel you have been retaliated against."

Future sessions of anti-retaliation training will be posted on EDI's website.

EDI also hosted an Open House in Bldg. 2, where about 60 attendees learned about the EEO complaint process while mingling with EDI staff.

To wrap up the campaign, Gary M. Gilbert, president of Gilbert Employment Law and former administrative judge for the Equal Employment Opportunity Commission, briefed NIH'ers on the different types of protected activities, what constitutes a claim of retaliation and employee rights for participating in protected EEO activity.

To learn more, check out the EDI training site.

Gebo Joins 'All of Us' Research Program

Dr. Kelly Gebo

Dr. Kelly Gebo has joined the All of Us Research Program as chief medical and scientific officer.

She will work with health care professionals and researchers, participants and national and community-based organizations to lead the program's scientific agenda, with a special focus on populations that have been historically underrepresented in research.

"Kelly has the right combination of research skills, leadership experience and passion for personalized medicine for the job," said Eric Dishman, director of the program. "I'm delighted to have her join our team in this new position."

Gebo has clinical, research and educational experience in the health care and higher education sectors. She is a professor of medicine at Johns Hopkins University and an expert in HIV health services research and clinical outcomes of persons with HIV. She has served as co-principal investigator of the HIV Research Network, an 18-year clinical cohort study of high-volume HIV sites caring for more than 20,000 persons with HIV across the country. Her research has been funded through NIH, the Agency for Healthcare Research and Quality and the Health Resources and Services Administration.

Gebo has authored more than 150 peer-reviewed publications, is an elected member of the American Society for Clinical Investigation and has received numerous national awards for her research and teaching.

She is also a leader in higher education, previously serving as an American Council on Education fellow at the University of Pennsylvania and as vice provost for education at Johns Hopkins.

Gebo holds a doctorate in medicine from Johns Hopkins University School of Medicine and a master's in public health from the Johns Hopkins Bloomberg School of Public Health. She did her internal medicine residency at Johns Hopkins and completed fellowship training in both the Robert Wood Johnson Foundation Clinical Scholars program and in the infectious diseases fellowship training program at Johns Hopkins.

Gebo will maintain her faculty appointment at Johns Hopkins concurrent with her NIH role.

NEI's Redmond Receives Vision Science Award

Dr. T. Michael Redmond, chief of the NEI Laboratory of Retinal Cell and Molecular Biology, was honored with the 2018 António Champalimaud Vision Award on Sept. 4 in Lisbon, Portugal.

This year's award, shared by Redmond and six other researchers, recognizes scientific contributions that led to the development of the first gene therapy to successfully treat a human disease. Collectively, their achievements led to the development and 2017 approval of voretigene neparvovec-rzyl (Luxturna) for treating Leber congenital amaurosis (LCA), an inherited disorder that causes childhood blindness.

In his 35 years at NEI, Redmond has made foundational scientific discoveries about the molecular biology of the retina, the light-sensing tissue at the back of the eye. Since the early 1990s, he has led research efforts to clone, sequence and characterize the function of the RPE65 gene. His work deduced how the gene converts dietary

Dr. T. Michael Redmond

vitamin A, from sources such as carrots, into a form of the vitamin that is central to the workings of the visual cycle, the enzymatic processes by which the eye converts light into electrical signals that are sent to the brain.

"We owe much to Michael Redmond for setting a course toward an effective gene therapy for LCA," said NEI director Dr. Paul Sieving.—**Kathryn DeMott**

NINR Welcomes New Advisory Council Members

NINR recently announced the appointment of three new members to its National Advisory Council for Nursing Research.

Dr. Jeffrey A. Kelly is professor of psychiatry and behavioral medicine and director of the Center for AIDS Intervention Research at the Medical College of Wisconsin. His academic career focuses on the application of behavioral science principles to the public health challenge of preventing HIV infection.

Dr. Ida M. (Ki) Moore is the Anne Furrow professor and interim dean at the University of Arizona College of Nursing. For the past 25 years, she has focused on the impact of central nervous system-directed treatment for pediatric acute lymphoblastic leukemia and brain tumors on cognitive outcomes and on mechanisms of tissue injury.

NINR acting director Dr. Ann Cashion (second from l) welcomes new council members (from l) Dr. Jeffrey Kelly, Dr. Nilda (Nena) Peragallo Montano and Dr. Ida M. (Ki) Moore.

Dr. Nilda (Nena) Peragallo Montano became the seventh dean of the School of Nursing at the University of North Carolina at Chapel Hill in January 2017. Formerly dean and professor of the University of Miami School of Nursing and Health Studies, she is an internationally recognized nurse scientist specializing in health disparities and culturally competent interventions with minority populations.

Annual Flu Vaccine Clinic for NIH Staff Open in CRC; Off-Campus Sites Underway Soon

The Office of Research Services and the Clinical Center are providing free flu shots through Nov. 9 to staff who have a valid NIH identification badge.

Getting immunized each year provides the best protection against influenza throughout the flu season. By getting the flu shot, health care personnel can also reduce the risk of exposing patients to the influenza virus. All staff who have face-to-face patient contact, including both 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.

MAIN CAMPUS SITE[1]

Date	Day	Location	Morning	Afternoon/Evening
10/01/18	Monday	10-CRC	8:00 – Noon	Noon – 3:30
10/02/18	Tuesday	10-CRC	8:00 – Noon	Noon – 3:30
10/03/18	Wednesday	10-CRC	8:00 – Noon	Noon – 3:30
10/04/18	Thursday	10-CRC	6:00 – Noon	Noon – 7:00
10/05/18	Friday	10-CRC	8:00 – Noon	Noon – 3:30
10/08/18	Monday	10-CRC	Closed	Closed
10/11/18	Thursday	10-CRC	8:00 – Noon	Noon – 3:30
10/12/18	Friday	10-CRC	8:00 – Noon	Noon – 3:30
10/17/18	Wednesday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/18/18	Thursday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/23/18	Tuesday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/24/18	Wednesday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/29/18	Monday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/30/18	Tuesday	10-CRC	8:00 – 11:30	12:30 – 3:30
10/31/18	Wednesday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/01/18	Thursday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/02/18	Friday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/05/18	Monday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/06/18	Tuesday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/07/18	Wednesday	10-CRC	6:00 – 11:30	12:30 – 7:00
11/08/18	Thursday	10-CRC	8:00 – 11:30	12:30 – 3:30
11/09/18	Friday	10-CRC	8:00 – 11:30	12:30 – 3:30

WEEKEND HOURS

Date	Day	Location	Morning	Afternoon/Evening
11/03/18	Saturday	10-CRC	6:30 - 8:00	6:30 - 8:00

OFF CAMPUS SITES

Date	Day	Location	Morning	Afternoon/Evening
10/09/18	Tuesday	Fishers Lane[2]	8:30 – Noon	Noon – 3:00
10/10/18	Wednesday	Fishers Lane	8:30 – Noon	Noon – 3:00
10/15/18	Monday	NSC[3]	8:30 – Noon	Noon – 3:00
10/16/18	Tuesday	NSC	8:30 – Noon	Noon – 3:00
10/17/18	Wednesday	Poolesville[4]	8:30 – 11:00	Closed
10/19/18	Friday	Shady Grove[5]	8:30 – Noon	Noon – 3:00
10/22/18	Monday	Shady Grove	8:30 – Noon	Noon – 3:00
10/25/18	Thursday	RKL[6]	8:30 – Noon	Noon – 3:00
10/26/18	Friday	RKL	8:30 – Noon	Noon – 3:00
11/01/18	Thursday	BRC[7]	8:30 – Noon	Noon – 3:00
11/02/18	Friday	BRC	8:30 – 11:30	Harbor Hospital 1:00 – 2:00

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

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

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

[3]Neuroscience Center: 6001 Executive Boulevard - 1st Floor Rooms A1/A2

[4]Poolesville: Building 103

[5]Shady Grove: 9609 Medical Center Drive, Rockville, MD Room TE406 - Seminar 110

[6]Rockledge II: 6701 Rockledge Drive, Bethesda, MD Room 3091

[7]Biomedical Research Center: 251 Bayview Boulevard, Baltimore, MD - 3rd Floor Atrium Lobby

Opening early in the morning, the flu clinic will be located on the east side of the 7th floor of the Clinical Research Center.

Starting Oct. 9, off-campus sites will also provide free flu shots. Shady Grove, Bayview, Poolesville, Neuroscience Center, Fishers Lane and Rockledge locations are included on the schedule.

There are several clinics offered specifically for those who work nights and weekends. Clinic hours are scheduled in early mornings, evenings and on Saturdays at the CRC 7th floor atrium. Check the schedule at left for specific dates, times and directions.

The vaccine is administered in the upper arm, so wear short sleeves or clothing that allows for easy exposure of your upper arm/shoulder. There is a high-dose vaccine for workers 65 and older, available upon request.

It takes about 2 weeks after immunization for antibodies to develop in the body and provide protection against influenza virus infection. In the meantime, you are still at risk for getting the flu. That's why it's better to get immunized early in the fall, before the flu season really gets under way.

A flu vaccine is needed every year because flu viruses are constantly changing. The flu vaccine is adjusted each year to keep up with the flu viruses as they change.

Also, multiple studies conducted over different seasons and across vaccine types and influenza virus subtypes have shown that the body's immunity to influenza viruses (acquired either through natural infection or immunization) declines over time.

Getting immunized each year provides the best protection against influenza throughout the flu season. R

VOLUNTEERS

HIV Vaccine Study Needs Subjects

Vaccine Research Center researchers seek persons 18-60 years old who are living with HIV for a research study. The study evaluates an investigational product targeting the HIV virus to determine if it is safe and can generate an immune response. Compensation is provided. For more information, call 1-866-833-5433 or email vaccines@nih.gov. Read more online at https://go.usa.gov/xQGp2. Se habla español.

A Pharmacy You Can Hear. ABOVE: National Symphony Orchestra trombonist David Murray was featured in a selection from Jose Berghmans' *Tableaux forains*. RIGHT: Dr. James Gilman, CEO of the Clinical Center, welcomes patients, staff and guests to the NSO performance.

Eric Shin solos on typewriter in *The Typewriter*, as Steven Reineke, the NSO's principal pops conductor, leads the orchestra. At right, an orchestra member indicates that for the Leroy Anderson piece *The Typewriter*, the typist would play in the key of A.

National Symphony Orchestra Delights CRC Crowd

When you see a semi-trailer pull up in front of the Clinical Research Center, followed by a tour bus, there's a good chance the National Symphony Orchestra is back on campus.

The NSO played a 10-selection concert on Sept. 18 in the CRC atrium as part of its Sound Health Initiative, now in its 6th year.

Patients, staff and visitors crowded not only the atrium floor but also several stories worth of balcony to enjoy the performance.

The concert had a pronounced pharmaceutical effect; it was as though the entire lobby went into a hush to allow the music space to enchant.

"It was an important goal of the architects to design a hospital that was comfortable and welcoming," said Dr. James Gilman, CEO of the hospital, in welcoming remarks. He added that the frequent NSO visits—either as orchestra or smaller ensembles—have promoted "tranquility, healing and wellness."

Selections at the concert ranged from Beethoven, whose compositions both began and ended the show, to Aaron Copland, Ralph Vaughan Williams and Bryce Dessner, a modern American composer perhaps best known as a member of the rock group The National.

The concert also featured Leroy Anderson's *The Typewriter*, a whimsical piece featuring Eric Shin on, yes, an old Royal manual typewriter.

The performance was sponsored by the Foundation for Advanced Education in the Sciences, Inc.—**Rich McManus**

The NSO as seen from the upper floors of the CRC. Part of its Sound Health Initiative, the group's frequent visits—either as orchestra or smaller ensembles—have promoted "tranquility, healing and wellness," says hospital CEO Gilman.

PHOTOS: MARLEEN VAN DEN NESTE