



GETTING A FEEL FOR STRUCTURE 3-D Printing, Virtual Reality Offer New Ways to Experience Molecules

BY CARLA GARNETT

Scientists have known for some time that influenza is a weed in the lawn of life. Shaped very much like dandelions, new hemagglutinin (HA) proteins that decorate the surface of flu viruses crop up every year—persistent, hardy and unwanted. What’s more, the molecules show an uncanny ability to change annually, outwitting the previous year’s vaccine. That’s why we have to get a new flu shot every year, to fight off the HA molecule’s new look.

Since January, scientists in NIAID’s



VRC deputy director Dr. Barney Graham (r) shows 3-D model to Bill Gates at recent visit.

PHOTO: CHIA-CHI CHARLIE CHANG

Vaccine Research Center have used several advanced tech tools to study flu’s structure, to see how it latches onto our body’s cells and figure out the weak spots where a vaccine could best attack and destroy the molecule.

Three-dimensional printing capability places detailed models of flu HA molecules in

researchers’ hands. Virtual reality technology lets scientists walk into a molecule and view it from the inside out. These fresh ways of seeing viruses open intriguing new opportunities for research.

Please, Pass the Flu

For several years, VRC deputy director Dr. Barney Graham, a physician and virologist, has kept models of two conformations of the RSV F protein, from respiratory syncytial virus, atop his desk. Graham, in collaboration with Dr. Peter Kwong, a VRC structural biologist, solved the structure of the pre-fusion form of F and designed the models; NLM printed them in 3-D. Graham refers to them often, reminding other VRC scientists that the models help him figure out spatial relationships for vaccine design.

“I hold these models in my hands almost every day to put new data on antibody binding or protein stability into context of

SEE **VIRTUAL REALITY**, PAGE 6



Program enriches high school seniors; see p. 5.

ALSO THIS ISSUE

- Briefs 2
- Cell Press Editor Outlines Tips for Publication Success 3
- Internship Program Benefits Rising High School Seniors 5
- Milestones 9
- Kansas Sen. Moran Visits 10
- Digest 11
- HHS’s Bardis Pays Call 12



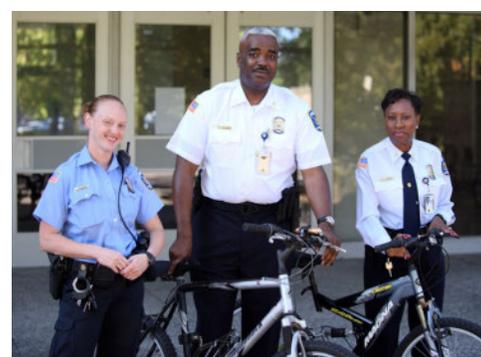
Panel moderator JoAnne Keatley of UCSF

LGBT Health Data Collection Still Needs Work

BY ERIC BOCK

Members of the federal government came together recently in Bldg. 40 to discuss ways to improve and analyze the collection of lesbian, gay, bisexual and transgender (LGBT) health data during a panel discussion called “Making Our Stories Count.”

SEE **LGBT HEALTH**, PAGE 4



Handling the donation of bikes from NIH are (from l) Cpl. Christine Fedorisko, Deputy Chief Leslie Campbell and Maj. Patricia Haynes.

CUTTING THE CHAINS NIH Police Donate Abandoned Bicycles

BY DANA TALESNIK

For the many NIH’ers who enjoy biking to work, it just got a little easier to find a spot at a campus bike rack. In recent months, the NIH Police began clamping down on

SEE **BIKE DONATION**, PAGE 8

Former Surgeon General Murthy To Speak On Stress, Sept. 7

Dr. Vivek Murthy, the 19th U.S. surgeon general, will visit NIH on Thursday, Sept. 7 to discuss “A Nation Under Pressure: The Public Health Consequences of Stress in America.” The event, a conversation with NIH director Dr. Francis Collins, will take place in Masur Auditorium, Bldg. 10 from 11 a.m. to noon and be streamed live via NIH Videocast (videocast.nih.gov) and Facebook Live (facebook.com/nih, facebook.com/nih.nccih). Murthy’s talk is the 2017 Stephen E. Straus Distinguished Lecture in Complementary Therapies, part of a series honoring the founding director of NCCIH.



During their discussion, Murthy and Collins will address what research is revealing about the health effects of stress and approaches people can incorporate into their lives to help reduce stress, such as regular exercise, social connection and

contemplative practices, including meditation. They will also examine how improvements in mental and emotional well-being can have a positive impact on the lives of individuals and communities and explore how models of successful interventions might be scaled to reach larger communities.

The lecture is being supported by the Foundation for the National Institutes of Health. For more information, visit nccih.nih.gov/news/events/lectures/SES17.

NSF Director To Speak at NLM, Sept. 11

National Science Foundation director Dr. France Anne-Dominic Córdoba will deliver the second annual Donald Lindberg and Donald West King Lecture, cosponsored by the Friends of the



National Library of Medicine (NLM) and the American Medical Informatics Association, on Monday, Sept. 11 at 1 p.m. in Lister Hill Center Auditorium, Bldg. 38A.

The lecture, which honors recently retired NLM director Lindberg and former NLM deputy

director of research and education King, is titled, “Computation and Biomedicine: New Possibilities for Longstanding Challenges.”

Córdoba is an American astrophysicist and the 14th director of the National Science Foundation, the

only government agency charged with advancing all fields of scientific discovery, technology innovation, and science, technology, engineering and mathematics education. Previously, she was the eleventh president of Purdue University and served as NASA’s chief scientist. The program will also be videocast.

Light refreshments sponsored by FNLM will follow the lecture.

Institute Challenge Relay, Sept. 28

The 34th NIH Institute Challenge Relay will be held Thursday, Sept. 28 at 11:30 a.m. The NIH Recreation and Welfare Association, members of the original NIH Health’s Angels running club and the ORS Division of Amenities and Transportation Services are sponsoring this year’s relay. Last year, a record 112 teams and 560 runners participated.

The relay consists of teams of 5 runners, each of whom runs a half-mile course (yet to be determined, due to construction around Bldg. 1). All institutes, centers, divisions and contractors are invited to enter as many teams as they wish. Each team must have men and women runners, with at least two runners of the same sex.

Creative team names are a signature of the event. Examples from last year include Champ Ions, Chlor-Ride Like the Wind, Dashing Dendrites, Flossed and Furious and The Hyper Tensions.

The registration fee is \$15 per team. To sign up, visit <http://govemployee.com/nih/2017/06/28/time-to-start-training-the-institute-relay-is-september-28th/>, where race site information will also be included in early September. To be a race volunteer or for more information, contact the R&W office at (301) 496-6061.

WHO Director-General Consults with NIH On U.S. Tour

NIH has a friend at the helm of the World Health Organization in Geneva, now that Dr. Tedros Adhanom Ghebreyesus has taken up his position as director-general. Known as “Dr. Tedros,” he previously served as health and foreign minister of Ethiopia, where he got to know NIH and Fogarty while collaborating on a Medical Education Partnership Award.

In preparation for assuming office on July 1, Ghebreyesus spent 5 days in the U.S., visiting the leadership of the Bill & Melinda Gates Foundation, World Bank, UN, State Department, HHS, CDC and NIH. While in Bethesda, he met with NIH director Dr. Francis Collins and Fogarty director Dr. Roger Glass, among others.

In his initial address to staff, Ghebreyesus pledged a commitment to global health equity, noting that without health, people have nothing. “This is our collective vision: a world where everyone can achieve healthy and productive lives, no matter who they are or where they live.”

He listed four priorities: universal health coverage;



NIH director Dr. Francis Collins (l) and Fogarty director Dr. Roger Glass (r) met with incoming WHO director-general Dr. Tedros Adhanom Ghebreyesus during his recent visit to the U.S.

health emergencies; women’s, children’s and adolescents’ health; and health impacts of climate and environmental change. He has also emphasized the importance of continuing efforts to turn WHO into a more effective, transparent and accountable agency, serving as “the best possible” partner for global health.

“WHO’s work is about serving people, about serving humanity,” Ghebreyesus said. “Most importantly, it’s about fighting to ensure the health of people as a basic human right.”

Webinar on Automating Machine Learning For Prevention Research

Dr. Jason Moore, director of the Institute for Biomedical Informatics at the Perelman School of Medicine at the University of Pennsylvania, will present the next Medicine: Mind the Gap webinar on “Automating Machine Learning for Prevention Research” on Tuesday, Aug. 29 from 11 a.m. to noon. The event is sponsored by the NIH Office of Disease Prevention.

Successful disease prevention will depend on modeling human health as a complex system that is dynamic in time and space and driven by biomolecular and physiologic interactions. Machine learning holds promise for embracing this complexity in Big Data.

Moore came to the University of Pennsylvania in 2015 from Dartmouth College, where he was director of the Institute for Quantitative Biomedical Sciences.

Register at <https://nih.webex.com/nih/onstage/g.php?MTID=e5fa19ad830ca29df663ef1f4d6cc2b72>.

Moore will accept questions during his webinar via WebEx and on Twitter with #NIHMtG.



Cell Press Editor Outlines Tips for Publication Success

BY CAROL TORGAN

Dr. Deborah Sweet has served as an editor on a variety of Cell Press journals for more than a decade. She's seen a lot during this time, including cover letters inquiring about submission that list the wrong journal name and authors who provide a suggested list of manuscript reviewers that reads, "nobody from Boston can review my paper." Sweet highlighted publishing tips and insights for scientists during a keynote address, "Navigating Your Way to Publication Success," at the NIAMS intramural research program's recent annual scientific training event.

Sweet is editor-in-chief of *Cell Stem Cell* and has held editorial positions at *Cell*, *Molecular Cell* and *Developmental Cell*. She is also a publishing director at Cell Press, playing a role in overall strategic development and operational management.

"The process of successful publishing starts a long time before you ever get anywhere near your computer and start typing," Sweet explained to researchers. She emphasized that the process involves thinking about the logic of what you're going to say and the experiments that are needed to make the key points. She advised the audience to ask themselves, "What's the point I'm going to make and how am I going to make it?"

Sweet stressed the importance of clear and concise writing. "When writing your paper, give it to somebody who doesn't work in your field, such as a colleague down the corridor who works on something completely different," she suggested. "Make sure that when they read your paper, they get out of it what you're hoping to say. If they don't understand it, the chances are that someone else reading it—even the editor—won't get it either."

Sweet acknowledged that she gets lots of questions about whether pre-submission inquiries are useful or necessary. Such pre-submissions are optional at Cell Press, but can be a good way to get advice and feedback on whether a paper is a good fit for the journal, before going through the work of formatting it, she said. *Cell Stem Cell* provides an online form, which asks for information such as the abstract and a brief description of results.

The cover letter is a critical part of the submission, Sweet advised. "Explain to me what you think is interesting about your paper and where it fits in the broader context—the things that you can't put in the abstract—and why you chose to submit it to the journal. It's an opportunity to talk about what your paper is contributing." Cover letters shouldn't be more than 2 pages, she said.

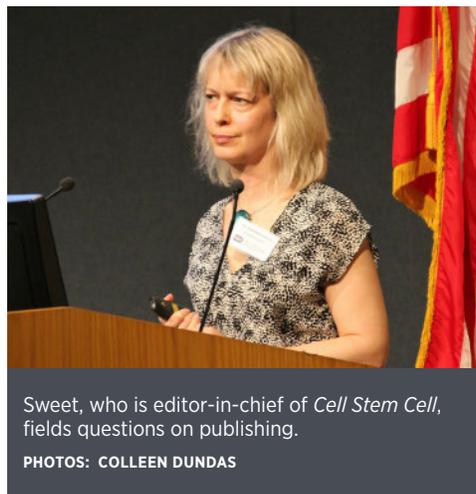
Sweet highlighted three key points that editors consider when reviewing a paper: Does the paper



Dr. Vittorio Sartorelli, co-chair of the NIAMS intramural research program's scientific training event and NIAMS IRP deputy scientific director, welcomes keynote speaker Dr. Deborah Sweet of Cell Press.

fit within the subject scope of the journal? Is the question it addresses interesting and important? Is there a clear advance above what's already published? The last point is the most significant, she said. "What is the conceptual advance beyond the existing literature? How far does the paper take our thinking forward?"

Once the paper is submitted, it's assigned to an editor who reads the paper in detail and then



Sweet, who is editor-in-chief of *Cell Stem Cell*, fields questions on publishing.

PHOTOS: COLLEEN DUNDAS

discusses it during a team meeting. A decision is then made about whether to send it out for peer review. Selecting reviewers is a crucial step. "We think about getting the subject balance right, getting a good balance of experience and trying to introduce new reviewers. Technical coverage is very important," Sweet explained. "We also think about consistency. If we've had another paper on a very similar topic, we'll try to send it to the same reviewers so it gets the same consideration."

Authors can provide names of suggested reviewers, as well as reviewers to exclude. "We want your paper to be reviewed fairly. If there are people who are not going to do that, please feel free to tell us," Sweet said. "We ask you to keep it to three people. If you exclude absolutely everyone who knows

about your topic, then we'll have a really hard time finding qualified reviewers," she said to laughter.

Sweet advised authors to wait at least 24 hours before responding to feedback from reviewers. "Read the reviews carefully, let your emotions subside, focus on the science and think about what you can do to address what's going on," she said. "Balance the time and effort involved in revising a paper compared to publishing someplace else and moving on to a new project."

Sweet concluded her talk by offering a glimpse into the future of publishing. Cell Press recently introduced the STAR (Structured, Transparent, Accessible Reporting) Methods format, which is designed to increase the clarity and completeness of methods to promote rigor and reproducibility. In a nod to the growing interest in preprints, Sweet noted that some Cell Press journals recently started accepting submissions by direct transfer from bioRxiv, an online service for unpublished preprints in the life sciences. **R**



ON THE COVER: *The locust is a valuable model system for investigating basic questions about neural function. NICHD's Stopher Lab uses locusts to study how populations of neurons work together to process information about sensory stimuli.*

IMAGE: NICHD/S. DAFFRON, M. STOPHER

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National Institutes of Health
Turning Discovery Into Health

LGBT Health

CONTINUED FROM PAGE 1

The event, held in recognition of Pride Month, was presented by NIH's Office of Equity, Diversity and Inclusion and the Sexual and Gender Minority Research Office. JoAnne Keatley of the Center of Excellence for Transgender Health at the University of California, San Francisco, moderated the panel.

Before the discussion began, the senior advisor for LGBT health at HHS, Elliot Kennedy, summarized efforts to collect data for LGBT research. In 2011, the Institute of Medicine released the LGBT health report. It confirmed anecdotal accounts that this population has worse health outcomes compared to other populations. The report also found researchers know little about the population.

"We need to know more about the people that we're working with in order to effectively meet their needs," said Kennedy.

Three panelists—Alexandra Chandler, a senior intelligence operations specialist in the Office of the Undersecretary of Defense for Intelligence; Phil Crehan, a researcher at the World Bank who studies the socioeconomic impact of discrimination and violence towards the LGBT community; and Mahri Monson, a management and policy analyst in the Environmental Protection Agency's Office of General Counsel—gave brief presentations about themselves and their work before they took part in the question-and-answer session.

Chandler described her experience as a transgender woman in the intelligence community. She called her story a "case study" of what can happen in the absence of data. She joined the intelligence community as a closeted transgender woman after the attacks on Sept. 11, 2001. After she joined, she decided to transition and was prepared to leave her job to do it. Her superiors, however, were supportive of her decision and figured out a process that met her needs.

A few years later, she joined her field's LGBT group after reading a newspaper article about another analyst's isolating experience during transition. Since then, Chandler has supported the group's development of data collection methods that will allow employees to self-identify their sexual orientation and gender.

"We are not doing the American people a



Panelists at the Pride Month event included (clockwise, from upper l) Mahri Monson, Alexandra Chandler, Elliott Kennedy and Phil Crehan.

PHOTOS: ANDREW PROPP

service unless we're using the entirety of our force," she explained.

Crehan detailed his efforts to quantify LGBT discrimination in countries where the World Bank operates. He said one survey of Thailand's LGBT population found 45 percent of them were denied jobs due to their orientation and over half experienced emotional problems.

He also surveyed employees at the World Bank. That study found, on average, lesbian, gay and bisexual employees felt they were treated with respect and saw an improvement in the climate. Not enough transgender people responded to be included in the sample.

"We also found a large part of the population is still hiding their identity in the workplace," Crehan added.

Finally, Monson spoke about her role leading EPA's pilot voluntary survey of sexual orientation and gender identity data. Right now, all federal agencies with at least 500 employees are mandated to collect demographic data on their workers. She wants sexual orientation and gender identity information to be included.

"The goal of the entire pilot is to get it to a point where we have the data we need to look at in the equal employment opportunity process," Monson explained.

Audience members then asked questions. One advised the panel to be aware of variables such as age or where a respondent lives and how these could influence the data. Monson agreed and said the EPA has 10 regional offices across the U.S.; where employees are geographically affects how they self-identify. Crehan noted that younger respondents were more likely to self-identify as LGBT in data from the Thailand study.

Another participant wanted to know how to ask relevant questions that are statistically meaningful. In response, Chandler said the intelligence community holds an annual LGTA—the "A" stands for allies—summit to build partnerships for agencies to share best practices and challenges and how to continually adapt to reach different populations. Monson added that sharing personal experiences is a good way "to help folks get comfortable with the language and have the opportunity to ask" about terminology.

Keatley cautioned it's not enough to survey people who already work in government. More must be done to create better opportunities for LGBT people to be hired and to combat transphobia and homophobia.

"We need to address those. Until we do that, we're just touching the surface," she concluded. **R**



Dr. Steven Brooks (l), postdoctoral fellow, NHLBI and Pamela Aluvale, HiSTEP

'LIKE SPONGES'

Internship Program Benefits High School Students

BY KATHERINE LEE

This summer, 25 of NIH's youngest interns spent 6 weeks exploring their dreams in science and preparing for their future under the guidance of the Office of Intramural Training and Education (OITE). The interns, all rising high school seniors, were part of the third annual HiSTEP (High School Scientific Training and Enrichment Program), which invites students from financially disadvantaged local public schools to experience science in both classroom and laboratory settings while also receiving college advice and mentoring.



Jarrett Jackson (front, r), post-baccalaureate fellow, NHLBI Sickle Cell Branch, joins a meeting of NIH'ers and the HiSTEP group.

One of the program's activities was a networking session on July 25, where each student was assigned three NIH professionals, including investigators, program directors, science administrators and other experts. The event took on a speed-dating style, with students speaking to each professional for 30 minutes then rotating on to the next mentor. The students also visited different labs throughout the week, donning colorful lab coats and joining researchers in their day-to-day routines.

"Dr. Meredith Fox [of NIMH's Office of Science Policy, Planning and Communications] told me, whenever you're given an opportunity, never to let go. Take them because you never know where they'll take you," said HiSTEP participant Stephany Carrasco. "The experience is giving me a broader view of what science really is. I never knew there were so many different jobs in science, it's incredible."

"We email researchers about participating in the informational interviews and they volunteer their time," said Dr. Sharolyn Kawakami-Schulz, one of the directors of HiSTEP. "Within the NIH community, we know that training is important. There are many people who have benefited from mentorship and training who are very willing to give back."

Nathan Phillips, a rising senior at James Hubert Blake High School, took the advice he received to think about creative career options for his interest in sports medicine and kinesiology.

"I want to go into sports medicine, but I also want to do TV production and combine the two and make a show where they talk about different athletes and how they got through their injuries," he said.

Along with introducing students to numerous opportunities in science, technology, engineering and mathematics (STEM) fields, HiSTEP teaches them how to apply for college and interact with experts who might be able to help them.

in touch with program directors Dr. Sharolyn Kawakami-Schulz and Dr. Natasha Lugo-Escobar, who continued to advise her as she applied for colleges. That year, she was accepted to the University of Maryland.

Lema subsequently returned for a second year at NIH, as part of a program called HiSTEP 2.0. Through version 2.0, OITE prepares students for life in college, giving each youngster an opportunity to work in labs while teaching them about the importance of wellness, time management and stress management on campus.

Lema also met her college roommate at the first HiSTEP.

"I feel like I've met a lot of lifelong friends," she said. "We came from the



In the physiology section of NHLBI's Sickle Cell Branch are (from l) Aluvale; Brooks; Kathleen Dang; Majed Almashjary, Ph.D candidate, NIH GPP program with Catholic University; Dr. Yu Yang, biologist, NHLBI; Kavisha Chandrawarakalage; Nathan Phillips; Olamide Alabi; Dr. Hans Ackerman, principal investigator, NHLBI; Dr. Dongying Ma, research fellow, NHLBI; and Carlos Carhuas, NIH summer student, University of Maryland. PHOTOS: MARLEEN VAN DEN NESTE

Dr. Kristen Zukosky, who advises HiSTEP students on researching and applying to college, said the application process could be especially overwhelming for students whose high schools or families did not have the resources or knowledge to weigh a diversity of college options. Zukosky has been helping students think about what to look for in a college experience, allowing them to navigate the characteristics of each school without paying sole attention to school rankings.

"I'm constantly impressed by their thirst for knowledge and their passion and devotion for STEM fields," Zukosky said. "They're like sponges the whole 6 weeks."

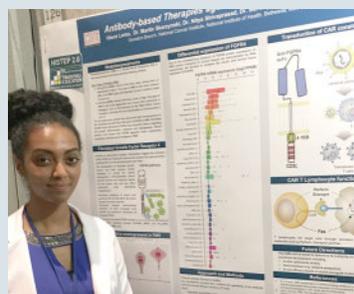
"I thought the program was just going to be about science, science, science," said Tooba Malik, a rising senior at Eleanor Roosevelt High School. "But they have lectures on how to have informational interviews, how to write good emails, basic communications skills that I kind of didn't know about. My emails are way better than I used to write them."

back for her third year, this time having been selected for the highly competitive NCI summer internship program.

"I really like doing research. I never thought I would. I thought I would be more clinical, but I don't know, it just opened my life to impact human lives in other ways," Lema said. "NIH is the medicine of tomorrow, and people come here when they have no other options. It's very exciting for me."

The 2017 HiSTEP program concluded Aug. 10, with a Poster Day where students presented the lessons and experiments they found most impressive.

For a video of the HiSTEP program, visit <https://www.training.nih.gov/oite-yt/histep>.



Hiwot Lema at NIH Summer Poster Day in 2016

PHOTO: NATASHA LUGO-ESCOBAR

same backgrounds, and I definitely met a lot of people that I can relate to not only academically but socially as well."

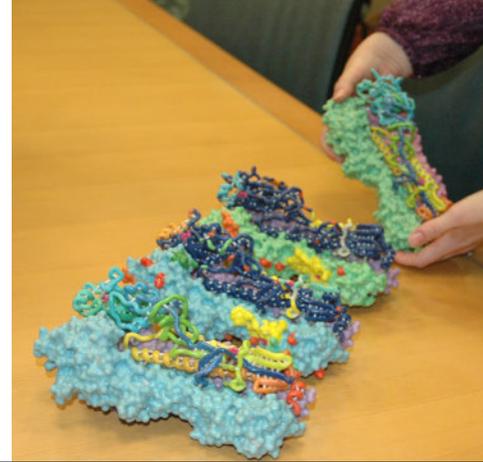
After spending two rigorous high school summers at NIH, Lema came

HiSTEP Alumnus Offers Testimony

Hiwot Lema is an alumnus of the first HiSTEP class in 2015. Lema, who has always wanted to be a doctor, first heard about the program through her high school AP biology teacher, who also worked at NIH.

"Coming to NIH and being at a place where you're manipulating the mechanisms of your body and solving problems really opened my eyes," Lema said. "I wasn't just learning what naturally happens. I was learning what doesn't usually happen and how we're trying to fix that. It was bringing the books to life, and it really fascinated me."

Lema completed her HiSTEP program and throughout senior year stayed



At left, Dr. Phil Cruz uses a laptop to get the VR model set up on screen as Dr. Michelle Crank prepares to don the headset. Center, now virtually walking inside the flu molecule, Crank manipulates elements of her journey—she can zoom in, pan around and even flip her environment. James Tyrwhitt-Drake input the molecule's coordinates according to scientists' specifications. At right, several HA molecules printed in 3-D provide different information about the way flu behaves and where it might be vulnerable to a vaccine.

PHOTOS: CARLA GARNETT

Virtual Reality

CONTINUED FROM PAGE 1

the 3-D structure,” says Graham, chief of the VRC's Viral Pathogenesis Laboratory.

And his enthusiasm for 3-D printing has infected his whole team.

Imagine the flu molecule is shaped like a flowering weed. As Dr. Michelle Crank, head of the translational sciences core in the Viral Pathogenesis Laboratory, and head of the flu program under Graham, explains, scientists want to cut off the top of the molecule (the part that changes and adapts to evade the immune system every season) and address the constant part—the molecule's “stem”—that stays much the same from strain to strain.

“The head is the part that the immune system sees best,” Crank says. “To make a universal vaccine—to protect against more than one strain or for more than one year—researchers want to get rid of the head. We hope if we remove it, the immune system will attack the stem.”

That way, a universal vaccine might be developed to attack all strains and save us from getting the yearly shot.

3-D printed models mean the scientists no longer have to imagine molecule shape; they now get a better feel for how the proteins covering the virus move and behave by holding them in their hands.

“When you cut off or change part of a big molecule, what's left doesn't just stay in the same shape or fit together the same way on its own,” Crank explains. “Any 3-D model like this might help our eyes find subtle relationships and changes between strains of HA that could give us clues for how to stabilize the stem across all the strains.”

Viruses and their surface molecules are

miniscule, far too small to be seen with the naked eye. In fact, most of the molecules scientists study are many thousands of times smaller than a strand of hair. The benefits of a handheld model are obvious.

Sizing, Scaling

“The flu molecule we are working on is absolutely tiny—about 13 nanometers in the longest dimension,” notes James Tyrwhitt-Drake, a scientific visualization specialist in the Bioinformatics and Computational Bioscience Branch of NIAID's Office of Cyberinfrastructure and Computational Biology. “It's important to scale the model of the molecule in a deliberate way, so

comparisons can be made. The software we use will convert each ångström [0.1 nanometer] in the molecule to a millimeter in the printed object, which is a magnification of precisely 10 million times. However, if the model has delicate features, I will print it larger—15 million or 20 million times—so that they will not break during printing.”

If the molecule is “large” like a whole virus, Tyrwhitt-Drake says, he'll scale it down to 1 million times, so it will fit in the volume of the printer.

“Not only can you look at it and hold it in your hand,” Crank says, “but if you also have an antibody [model], you can have that

‘COOL’ FACTOR A BONUS

Explore with NIH's 3-D Print Exchange

In 2007, Dr. Darrell Hurt, head of the computational biology section in NIAID's Bioinformatics and Computational Biosciences Branch (BCBB), began experimenting with 3-D printing for molecular visualization. He started by taking raw molecular structure data and putting it in a 3-D-printable form.

“There's so much more you can learn when you have it in your hands, rather than looking at it on a 2-D screen or even with 3-D glasses,” explains Dr. Meghan McCarthy, program lead for BCBB's 3-D Printing and Biovisualization Program.

BCBB provides data analysis consultation and custom software development services to NIAID researchers and wanted to make 3-D printing more accessible to the public. As a solution, the branch created the NIH 3-D Print Exchange (<https://3dprint.nih.gov>), an online resource where people can find models and share their own models as well as web tools that eliminate skills barriers.

“We developed automated tools that are free. Anyone around the globe can use them,” says

McCarthy, who manages the exchange under BCBB's larger program for 3-D printing and biovisualization.

The exchange is owned and maintained by NIAID, but was initially created in partnership with NICHD and the National Library of Medicine with support from the 2013 HHS Ignite and 2014 HHS Ventures initiatives. Team members were recognized with an HHS Innovates award in 2015.

BCBB has processed more than 100 scientific 3-D printing requests over the last 10 years, reports BCBB Scientific Visualization Specialist James Tyrwhitt-Drake. “However, each request may



Dr. Meghan McCarthy holds a model brain produced by the 3-D Print Exchange.



Carrying the flu. With the virtual flu molecule on screen behind them, Cruz, Tyrwhitt-Drake, Crank and McCarthy each hold a 3-D print version. At right, scientists compare the complexity of a flu molecule's structure to that of a dandelion.

antibody come in and bind at a particular binding site or see relationships between the different components.”

First Impressions

All sorts of uses emerged for the 3-D models, which also have become popular props at lectures.

“This molecule is heavier than I

include multiple different models or copies of the same model,” he says.

“Color printing of scientific models requires a considerable amount of preparation and processing time, so we primarily limit the service to requests from NIAID staff that have scientific utility. Production is limited by the physical complexity of the model, consumption of materials and occasionally troubleshooting mechanical or software issues with the printer.”

Over the years, as technology advanced, BCBB's capabilities and responsibilities expanded to include other 3-D technologies, including virtual and augmented reality.

Tyrwhitt-Drake, along with team member and structural biologist Dr. Phil Cruz, also produces the virtual reality models that allow investigators to walk inside a molecule and have a look around its structure.

Use of virtual reality has “really taken off, especially in the last year,” McCarthy points out. “Anyone that we've ever put into the 3-D goggles—even people who have worked on a particular molecule for 10 or 15 years as part of their career—says they see something different, that they didn't see before.”

Both 3-D printing and VR are useful applications

expected!” says Dr. Jeffrey Boyington, a structural biologist in VRC director Dr. John Mascola's Laboratory of Virology and lead designer of the headless HA stem vaccines, recalling his initial reaction to holding the printed HA molecule in his hand. “One of the first things I noticed is that these are great teaching and discussion tools for one-on-one or small group settings. You can easily point



Other models designed and printed by James Tyrwhitt-Drake for the exchange's collection include (clockwise, from top right) Zika virus capsid, bacteriophage, Cas9 from CRISPR, papilloma virus, nucleosome and HIV capsid.

for learning, sharing and education, as well as research, McCarthy notes. In addition to exploring their work from a unique perspective, researchers also seem to enjoy the “cool” factor.

“Most people think of gaming and entertainment when they think of VR,” McCarthy concludes, “but we really like that we've been able to bring this scientific value to it.”

to a critical region and others in the room see exactly see what you are referring to in 3 dimensions with the added perspective of seeing the whole molecule.”

New Views Reviewed

When Bill Gates came to call at NIH this past spring, VRC scientists were tapped to give him a demo of some of their latest gadgetry. In addition to literally passing around the flu strains, the cyberinfrastructure team set Gates up with a virtual reality headset and let him take a stroll through an HA molecule.

Noting that the experience was similar to video gaming, Gates wanted to know how an admittedly sophisticated toy could help scientists in the global fight against viruses. Researchers then described the potential impact of their new views.

“When you get inside the goggles,” Crank explains, “you can actually stand in that space and look around at all the side chains coming off of the protein, pointing at you, and you can see how big the space is.

“Not being a structural biologist, I have not spent a lot of time using molecular graphics programs on a computer, so seeing inside the molecule and looking out was a totally new perspective for me,” she adds. “Appreciating the gaps inside a 3-D structure like the HA molecule is something you cannot do from the printed models, since you cannot see ‘through’ to the inside. And sometimes it's understanding that inner structure that can reveal helpful relationships for designing ways to stabilize vaccine immunogens that utilize only part of the whole molecule, but still need to present an authentic or accurate shape to the immune system.”

Of course, no matter how advanced, technology alone won't produce effective vaccines overnight, scientists acknowledge. Having more up-close and personal interactions with viruses, however, will help researchers better understand what we're up against.

“We will still be using desktop molecular graphics programs for most of our work,” concludes Boyington, “but as we periodically examine the 3-D print models or walk through VR in the coming months, we might have some eureka moments of insight since these views give us a slightly different perspective than we are used to.” **R**



At left, Harriet Fermaa Sekyere of Ghana uses her bike to carry twice as much water in a quarter the time it took on foot. PHOTO: VILLAGE BICYCLE PROJECT, GHANA

Above, students in the Philippines who are part of a project aimed at preventing kids from dropping out of school show off donated bike helmets. PHOTO: BIKES FOR THE PHILIPPINES

Bike Donation

CONTINUED FROM PAGE 1

abandoned bicycles, removing dozens of them so far and sending unclaimed bikes out to a good cause.

“A lot of people had complaints about not being able to park their bikes on campus due to the bike racks being full,” said Cpl. Christine Fedorisko, community police coordinator. “Some of these bikes had been sitting abandoned for years.”



“We’re trying to get the police department to have a more positive impact on the community.”

-CPL. CHRISTINE FEDORISKO



So she and her NIH Police colleagues took action. They began putting a 5-day warning notice on abandoned bikes; if nobody claimed them, the police cut the locks and wheeled them over to a storage facility where they sat for a couple of months, giving their owners another chance to claim them.

“I realized I was cutting a lot of bikes,” said Fedorisko, “and these bikes were in good condition—basically some flat tires, some rusty chains, some seat wear and tear.”

Who would abandon such nice bikes? Fedorisko learned that many trainees who brought bikes to get around campus were

unable to travel home with them. She also heard stories of lost bike lock keys and flat tires or minor damage that remained unfixed.

It seemed a shame to send these usable bikes to recycling centers, as was done in the past when the NIH Police periodically removed abandoned bikes. So NIH Police Chief Alvin Hinton suggested donating the bikes and Fedorisko set out to find a suitable recipient.

She picked up 43 abandoned bikes over the past 2 months. After sending an NIH-wide last-chance-to-retrieve-your-bike email, she reports that 3 were claimed and the remaining 40 were donated to Bikes for the World, a nonprofit that sends bikes and bike parts to lower-income people in the United States and abroad. This shipment went to Village Bicycle Projects in Ghana and Sierra Leone.

The NIH Police coordinated the effort with the NIH Bicycle Commuter Club, which has a longstanding relationship with Bikes for the World. For nearly a decade, the NIHBCB has helped collect unwanted bikes and donated them to this organization.

Bikes for the World donates most bikes to countries in Africa and Central America as well as to youth projects in Barbados and the Philippines. Others get donated to disadvantaged

communities locally. The organization takes any bike with at least some workable parts, bike accessories and even old parts that are a little worn or rusty.

“Before you replace a part, consider donating it,” said Yvette Hess, outreach coordinator at Bikes for the World. “It may have too much wear for you, but it still has value to others, especially overseas.”

Fedorisko, who aims to get the NIH Police more actively involved in community projects, said this is the first time the police have ever made this type of donation.

“People see the police department right now as parking tickets and traffic enforcement,” she said. Many are unaware of the force’s host of community activities, such as the Coffee with a Cop program at the Children’s Inn, facility tours, details



Fedorisko and Cpl. Marcus Gray help load up bikes going out for donation.

PHOTO: CHIA-CHI CHARLIE CHANG

downtown, safety initiatives and Take Your Child to Work Day and Bike to Work Day events.

“We’re trying to get the police department to have a more positive impact on the community,” said Fedorisko. “Yes, we have to get out there and write tickets; that’s important. Parking is a huge issue. But I don’t want [people’s perceptions of us] to be all negative.”

Another bike-related service the police provide is registration. When none of the abandoned bikes in the storage facility had an NIH or even a county decal, Fedorisko put the pedal to the metal encouraging all NIH’ers to register their bikes.

“You’d be surprised how many people don’t even know where the serial number is on their bike,” she said.

In the past month, Fedorisko registered some 400 bikes on campus. “I was able to get out there and show people the best locks to use—the U-lock is the best—and I warned them about the racks by the Medical Center Metro station, which is a high theft area right now.”

There are covered and uncovered bike racks behind most buildings on campus and more are being built. Fedorisko has noticed some NIH’ers leaving their bikes by fences or railings, or trying to bring them into their offices, but these are violations for which you can get cited. “The only proper place to park your bike is at a bike rack or in a storage locker,” she said.

And don’t forget basic bike safety. Wear a helmet and high-visibility clothing; have reflectors on your bike and perhaps a bell or horn; use hand signals and be aware of pedestrians and drivers. It’s also a good idea not to have earbuds in, said Fedorisko, to help stay more aware of your surroundings.

“When I came to NIH, I realized what a parking shortage we have on this campus,” she said. “We want more people taking Metro and biking.”

Have a bike or bike parts to donate? Contact Ellen Condon, NIHBCA administrator, who can facilitate the donation. Or, call Bikes for the World at (703) 740-7856. Their warehouse is located in Rockville and they’re always in need of volunteers.

Want to register your bike with NIH or report an abandoned bike you’ve seen on campus? Call (301) 496-3020 or email Christine.fedorisko@nih.gov. 

Machiela Named Stadtman Investigator

BY VICTORIA FISHER

Dr. Mitchell Machiela was recently appointed Earl Stadtman tenure-track investigator in NCI’s Laboratory of Genetic Susceptibility (LGS). Machiela studies the role of germline variation and somatic mosaicism in cancer risk. He joined the Laboratory of Translational Genomics as a postdoctoral fellow in 2012, transitioned to LGS in 2015, and was promoted to research fellow in 2016.

Machiela leads studies of large-scale genetic mosaicism to investigate the causes of acquired mosaic alterations and their impact on cancer risk. Genetic mosaicism results from a DNA mutation that is present in some of the body’s cells but not in others. A person with mosaicism has a mixture of normal and mutated cells.

“Mosaicism is a somatic event, meaning a mutation occurs sometime in life after fertilization. It is not an inherited genetic variant,” said Machiela. “We define mosaicism quite broadly; it can be limited to a one base pair change in your genome different from what you inherited. Or, it can be as large as an entire chromosome that is lost or duplicated.”

Machiela and collaborators have published a number of studies estimating the frequency and distribution of mosaicism in existing genotyped collections of blood and buccal DNA. Now, he is utilizing an unparallel set of genotype data—200,000 DCEG samples, 500,000 genotyped samples from the UK Biobank and a merged international mosaicism consortium of over 1 million samples—to expand the size and scope of his research on mosaicism and cancer risk.

In addition, he is developing improved approaches for detecting genetic mosaicism.

“Previous studies have focused on detecting mosaic events larger than 2 megabases in size and affecting cellular proportions of 10 percent or greater,” he said. “This is a conservative threshold to ensure detected events have a high true positive rate. We are now exploring ways to use haplotype data to improve the array-based detection of events affecting a smaller proportion of cells.”

In recent studies, he and colleagues found evidence to suggest that mosaicism increases cancer risk for hematologic malignancies and select solid tumor subtypes. He is expanding this work to examine the influence of mosaicism on cancer risk in various populations and tissue types.

Machiela is also the creator of a web-based tool LDlink, which interactively explores linkage disequilibrium across population groups from the 1000 Genomes Project. LDlink is tailored for investigators interested in mapping disease susceptibility loci by generating output linking correlated alleles and highlighting putative functional variants.



Dr. Mitchell Machiela

‘BE INSPIRED’ SERIES

EDI Presents Morgan Stanley’s Harris

Part of the Office of Equity, Diversity and Inclusion’s “Be Inspired” series is to highlight remarkable women who continue to defy the odds, shatter glass ceilings and influence others to maximize their potential. With that aim, EDI will welcome guest speaker Carla Harris, Morgan Stanley vice chair for global wealth management and senior client advisor, to share “Tools for Maximizing Your Success” on Thursday, Sept. 7 at 10 a.m. in Lipsett Amphitheater, Bldg. 10.



A respected thought leader and author, Harris has appeared on television shows, including the *Today Show with Kathie Lee & Hoda*, with strategies to “win” in the workplace. Recently she was featured on CNBC discussing the importance of diversity in business. Harris is a *magna cum laude* graduate of Harvard Business School and author of *Strategize to Win*. She is also a gifted Carnegie Hall gospel singer.

In 2013, President Obama appointed Harris to chair the National Women’s Business Council.

Harris’s presentations provide practical insights on communication, bouncing back after a misstep and building “relationship currency.” Whether you are repositioning yourself in the workplace, new to your career or looking to move up or move on, you may benefit from her talk.

For details about the event, contact Joy Gaines at joy.gaines@nih.gov or call (301) 496-6301.



At left, U.S. Sen. Jerry Moran (R-KS, l) takes a tour of the Porter Neuroscience Research Center led by NIH director Dr. Francis Collins (r). At right, Collins and several other NIH leaders join the Kansas contingent for a briefing on Alzheimer's.

PHOTOS: CHIA-CHI CHARLIE CHANG

Kansas Sen. Moran, KU Chancellor Visit NIH

U.S. Sen. Jerry Moran (R-KS), a member of the Senate appropriations subcommittee on Labor, Health and Human Services, Education and related agencies, visited NIH on July 11, accompanied by University of Kansas chancellor Dr. Douglas Girod and other university officials.

The senator, members of his staff, along with Girod, a medical doctor, and a couple of KU scientists involved in Alzheimer's disease research were greeted at the Porter Neuroscience Research Center by NIH director Dr. Francis Collins and principal deputy director Dr. Lawrence Tabak.

NIA grantee Dr. Jeffrey Burns, director of the Alzheimer and Memory Program, professor in the department of neurology at the University of

Kansas Medical Center and assistant director of the General Clinical Research Center, Dr. Russell Swerdlow, director of the KU Alzheimer's Disease Center and the KUMC Neurodegenerative Disorders Program, and KU Director of Federal Relations Jack Cline were among those touring the PNRC.

There the group met with NIMH director Dr. Joshua Gordon, NIA director Dr. Richard Hodes and NINDS director Dr. Walter Koroshetz. The BRAIN Initiative and Alzheimer's were among topics discussed, before the group embarked on a laboratory tour spotlighting the genetics of neurodegenerative diseases.

Dr. Sonja Scholz, assistant clinical investigator in the neurodegenerative diseases research unit of NINDS's Neurogenetics Branch, and NIA senior investigator Dr. Mark Cookson in the Laboratory of Neurogenetics also participated in the tour.

At a roundtable discussion on Alzheimer's, Hodes and Koroshetz were joined by Dr. Eliezer Masliah, director of NIA's Division of Neuroscience.

The group heard about advances in genetics and biomarkers converging on new-generation early intervention trials and new initiatives and programs for AD research and took in an Alzheimer's imaging presentation by Dr. Susan Resnick, a senior investigator in NIA's Laboratory of Behavioral Neuroscience. She discussed how PET scans for the amyloid and tau proteins are being used to track disease at the earliest stages of AD and to select patients for tests of new medications.



The group hears from Dr. Sonja Scholz (r), assistant clinical investigator in the neurodegenerative diseases research unit of NINDS's Neurogenetics Branch.



Above, the senator chats with Dr. Michiyo Iba (c) and Dr. Changyoun Kim, both of NIA's Laboratory of Neurogenetics; below, NINDS director Dr. Walter Koroshetz talks with Moran in front of NIH's exhibit on "father of neuroscience" Santiago Ramon y Cajal.





Experimental Treatment for Niemann-Pick Disease Type C1 Appears Safe, Effective

An experimental drug appears to slow the progression of Niemann-Pick disease type C1 (NPC1), a fatal neurological disease, according to results of a clinical study led by researchers at NIH. The study appears in *The Lancet*.

NPC1 is a rare genetic disorder that primarily affects children and adolescents, causing a progressive decline in neurological and cognitive functions. The Food and Drug Administration has not approved any treatments for the condition.

The drug, 2-hydroxypropyl-beta-cyclodextrin (VTS-270), is being tested under a cooperative research and development agreement between NIH and Sucampo Pharmaceuticals, Inc. In April 2017, Sucampo acquired Vtesse Inc., which previously had been developing VTS-270.

“The results are very encouraging and support continued development of VTS-270 for treating NPC1,” said Dr. Forbes Porter, clinical director at NICHD and the study’s senior author. “Compared to untreated patients we followed in an earlier study, participants who received VTS-270 scored better on a scale used to evaluate disease severity and progression, including elements such as speech, cognition and mobility.”

The researchers did not observe any serious adverse outcomes related to the drug. However, the participants, most of whom had already experienced hearing loss because of the disease, had additional hearing loss after treatment. Earlier studies had shown that the treatment carries the risk for hearing loss. In the current study, hearing loss was compensated with hearing aids, which enabled participants to go about their daily lives.

NCI Study Identifies Essential Genes for Cancer Immunotherapy

A new study identifies genes that are necessary in cancer cells for immunotherapy to work, addressing the problem of why some tumors don’t respond to immunotherapy or respond initially but then stop as tumor cells develop resistance to immunotherapy.

The study, from the National Cancer Institute, was led by Dr. Nicholas Restifo, a senior investigator

with the Center for Cancer Research, with coauthors from NCI, Georgetown University, the Broad Institute of MIT and Harvard University, New York University and the University of Pennsylvania. It was published online in *Nature* on Aug. 7.

“There is a great deal of interest in cancer immunotherapy, especially for patients who have metastatic cancer,” said Restifo. “The response to immunotherapy can be fantastic, but understanding why some patients don’t respond will help us improve treatments for more patients.”

Cancer immunotherapy relies on T cells, a type of cell in the immune system, to destroy tumors. Restifo and his colleagues have previously shown that the infusion of large numbers of T cells can trigger complete regression of cancer in patients. They and others have also shown that T cells can directly recognize and kill tumor cells.

However, some tumor cells are resistant to the destruction unleashed by T cells. To investigate the basis for this resistance, the researchers sought to identify the genes in cancer cells that are necessary for them to be killed by T cells.



Midlife Cardiovascular Risk Factors May Increase Chances of Dementia

A large, long-term study suggests that middle-aged Americans who have vascular health risk factors—including diabetes, high blood pressure and smoking—have a greater chance of suffering from dementia later in life. The study, published in *JAMA Neurology*, was funded by NIH.

“With an aging population, dementia is becoming a greater health concern. This study supports the importance of controlling vascular risk factors like high blood pressure early in life in an effort to prevent dementia as we age,” said Dr. Walter Koroshetz, director of the National Institute of Neurological Disorders and Stroke, which partially funded the study. “What’s good for the heart is good for the brain.”

The study was led by Dr. Rebecca Gottesman, professor of neurology at Johns Hopkins University. Her team analyzed the data of 15,744 people who participated in the Atherosclerosis Risk in Communities study, funded by the National Heart, Lung, and Blood Institute. From 1987 to 1989, the participants, who were black or white

and 45-64 years of age, underwent a battery of medical tests during their initial examinations at one of four centers in four different states. Over the next 25 years they were examined four more times. Cognitive tests of memory and thinking were administered during all but the first and third exams.

Her team found that 1,516 participants were diagnosed with dementia during an average of 23 follow-up years. Initially, when they analyzed the influence of factors recorded during the first exams, the researchers found that the chances of dementia increased most strongly with age followed by the presence of APOE4, a gene associated with Alzheimer’s disease. Whites with one copy of the APOE4 gene had a greater chance of dementia than blacks. Other factors included race and education: blacks had a higher chance of dementia than whites; those who did not graduate from high school were also at higher risk.

In agreement with previous studies, an analysis of vascular risk factors showed that participants who had diabetes or high blood pressure, also called hypertension, had a higher chance of developing dementia. In fact, diabetes was almost as strong a predictor of dementia as the presence of the APOE4 gene.

“Our results contribute to a growing body of evidence linking midlife vascular health to dementia,” said Gottesman. “These are modifiable risk factors. Our hope is that by addressing these types of factors early, people can reduce the chances that they will suffer from dementia later in life.”

Breakthrough Method Yields Trove of Neuron Subtypes, Gene Regulators

With funding from the BRAIN Initiative, researchers using a new method they developed have discovered a trove of neuronal subtypes and gene regulators. It allows for the discovery of subtypes based on their unique profiles of molecular switches that regulate gene expression within the cell. This opens the door to potentially discovering changes in such profiles linked to brain disorders, say the researchers.

The new method, described Aug. 10 in *Science*, profiles molecular changes to the DNA (the genetic blueprint) known as epigenetic regulation. This is accomplished by sequencing the neuronal genomes in a way that detects modified DNA, producing a signature called the methylome. It turns out that each cell type has a unique methylome, even though the DNA itself is the same in every cell.

In the frontal cortex, the researchers identified 16 neuronal subtypes in mice and 21 subtypes in humans. Neurons that slow down brain activity were found to share more regulatory elements across mice and humans than neurons that speed up brain activity. Some of the latter excitatory neuron types appear to be unique to humans.



At left, HHS Assistant Secretary for Administration John Bardis meets Wonder Woman (a.k.a. Farrah Mackenzie, a youngster being treated at the Clinical Center), her mom and Dr. David Lang, CC pediatrician. Above, Bardis's visit ends at the Central Utility Plant. Shown after enjoying a cost-savings discussion are (from l) NIH Chief Engineer Tony Clifford, NIH acting chief of staff Dr. Carrie Wolinetz, Bardis and his chief of staff Rasheed Williams.

HHS Assistant Secretary Bardis Visits, Tours

HHS Assistant Secretary for Administration John Bardis and his chief of staff Rasheed Williams visited NIH on July 10.

They were met by NIH principal deputy director Dr. Lawrence Tabak, Clinical Center CEO Dr. James Gilman, NIH deputy director for administration Dr. Alfred Johnson and NIH associate director for science policy and acting chief of staff Dr. Carrie Wolinetz. The group first set out for the CC's pediatric oncology unit to meet with a youngster undergoing treatment there.

After chatting with the patient, Bardis and company headed for a meeting with Dr. Carlos Zarate, chief of NIMH's Experimental Therapeutics & Pathophysiology Branch and section on the neurobiology and treatment of mood disorders. He also introduced one of his patients to the group.

Next up was a conference room briefing with NIH director Dr. Francis Collins and several IC



NIH director Dr. Francis Collins (c) greets Williams and Bardis before various science briefings and tours begin.

PHOTOS: CHIA-CHI CHARLIE CHANG

directors—Dr. Anthony Fauci of NIAID, Dr. Gary Gibbons of NHLBI, Dr. Richard Hodes of NIA, Dr. Stephen Katz of NIAMS and Dr. Roderic Pettigrew of NIBIB.

As a final stop, the group went to the NIH Cogeneration Plant, where they were met by Office of Research Facilities Director Dan Wheeland, Dr. Farhad Memarzadeh, director of

ORF's Division of Technical Resources, and Joe Nieves, chief of the division's Utilities Generation Branch, for a tour of the facility.

NIH owns and operates a plant that uses natural gas as a fuel and produces electricity and steam for the Bethesda campus.

"NIH cogeneration produces about 40 percent of the required steam and electricity simultaneously," Memarzadeh pointed out. "It is one of the lowest emission cogeneration plants in the world. Cogeneration saves NIH an estimated \$7 million a year in steam and electricity costs.

"NIH Central Utility Plant, CUP, is one of the largest utility plants in the world," Memarzadeh continued. "Annual electricity consumption for the chiller plant is equivalent to 100,000 Maryland homes. Annual natural gas consumption for the heating plant is equivalent to 26 million gallons of gasoline. Over 20 million data points a day are collected and analyzed using 300,000 advanced calculations from about 4,500 continuously running analyses."



At left, Bardis hears Joe Nieves, chief of the Utilities Generation Branch, ORF Division of Technical Resources, describing the data-capture system and NIH's ability to use the data for complex calculations. At right, ORF's Dr. Farhad Memarzadeh points out cost-savings data and energy-efficient measures implemented in the CUP. He also described the process of procuring natural gas in the open market and how this has saved millions of dollars for NIH.