MEETING OUR MAKERS
NIH Inventors Introduced in New Series
BY AMBER SNYDER

In recognition of the National Week of Makers, celebrated annually in June, the NIH Record is kicking off a new series featuring the “makers” of NIH—intramural researchers who devise exciting new drugs, devices, applications, methods and other products.

In this first installment, we meet two scientists at the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) who are developing new contraceptive options.

First of its Kind
“I’m usually a glass half-empty type of person, but [with this product] I’m more like ¾ full,” NICHD’s Dr. Diana Blithe said recently.

What has her feeling so optimistic? NES/T, a revolutionary new contraceptive for men, is close to clearing a crucial clinical trial step. It is a transdermal gel that users apply daily to their back and shoulders to suppress sperm production.

Blithe is the program chief of NICHD’s Contraceptive Development Program (CDP). She and her team conduct translational and clinical research to develop novel methods.

COMMITTED TO DIVERSITY
Second DEIA Town Hall Provides Updates, Plans
BY ERIC BOCK

Kevin Williams envisions an NIH that’s welcoming to all, a workplace free of racism, discrimination and biases that exclude underrepresented groups from leadership opportunities.

“We want to create an environment that fosters psychological safety, so that everyone can share ideas and solutions,” said Williams, director of NIH’s Office of Equity, Diversity and Inclusion (EDI) during the 2nd Virtual Town Hall on Diversity, Equity, Inclusion and Accessibility (DEIA) held on May 18. “We need your help. We need your buy-in. We need your support as we work to get this done.”

In March 2023, NIH released its agency-wide strategic plan for DEIA. It

BLUE SKIES & JOYFUL RIDES
Employees Embrace Bike to Work Day

On a picture-perfect morning, NIH employees pedaled their way onto the Bethesda campus on May 19, joining the Washington area’s Bike to Work Day. More than 350 staff pre-registered for the event, many of whom chose to ride to Bldg. 1, one the more than 100 pitstops in the region.

NCI’s Dr. Lisa Finkelstein has participated in Bike to Work Day annually since she started working at NIH in 2005. Although

FABRIC OF COMMUNITY, SAVING LIVES
NIH Leaders Thank Campus Fire & Rescue
BY DANA TALESNIK

One of the first groups NIH leadership planned to thank for their exceptional service during the Covid-19 pandemic was the Division of Fire and Rescue Services (DFRS). The stars finally aligned on May 19 to make that stop on the “gratitude tour” a reality.

“You all literally put your lives on the
Celebration Features University of Michigan Provost McCauley, June 27

To celebrate its 75th anniversary, NIDCR is hosting a free symposium featuring speakers that include Acting NIH Director Dr. Lawrence Tabak and former NIH Director Dr. Francis Collins. Dr. Laurie McCauley, provost of the University of Michigan, will deliver the keynote lecture.

The event, on Tuesday, June 27 from 9 a.m. to noon in Lipsett Amphitheater, Bldg. 10, is open to the public and does not require registration.

The symposium will cover the institute’s vital contributions to the biomedical research enterprise, highlight the state of the science, include remarks from professional society partners and feature conversations among federal partners and NIDCR leadership about the critical role of collaboration for achieving the mission of oral health for all.

The event launches NIDCR’s yearlong slate of anniversary-related activities. For a full list, link to a live videocast of the event, or an archive of the videocast after the event has concluded, visit www.nidcr.nih.gov/about-us/75years.

Sign language interpreting and communication access real-time translation services are available upon request. Individuals needing these services and/or other reasonable accommodation should contact Nicole García-Quijano at nicole.garcia-qui@nih.gov or (301) 496-4260. Requests should be made at least five days in advance. To access Telecommunications Relay Services, call 711.

NHLBI’s Gibbons Wins Wenger Award

The 2023 Wenger Award for Excellence in Public Service was awarded to NHLBI Director Dr. Gary Gibbons at a reception in Washington in May.

Named after Dr. Nanette Kass Wenger, a pioneer in women’s cardiology, the award recognizes individuals and organizations for their extraordinary contributions to women’s heart health.

Gibbons has been a driving force behind improving women’s heart health and addressing heart health disparities in communities most affected by heart disease.

Throughout his tenure at NHLBI, he has led critical research on preventing and managing risk factors for heart disease throughout a woman’s lifespan, as well as on maternal health, pregnancy outcomes and heart disease. His leadership has been instrumental in advancing the understanding and treatment of heart disease, and his commitment to public service unwavering.

To learn more about the awards, see: https://tinyurl.com/s8b3zx3t.

Conference Set on Models for Building Equality, Equity in Research, July 19

The NIH Small Business Program Office and several institutes and centers are planning a government-wide conference on Collaborative Models for Building Equality and Equity in Research on Wednesday, July 19 at the Natcher Conference Center. The conference will focus on successes, best practices and new knowledge dissemination to strengthen and advance educational equality, excellence and economic opportunities in research at minority-serving institutions. Registration is limited and open now. For information, email Annette Owens-Scarboro: Scarbora@od.nih.gov.

BRIEFS

NIDCR at 75

NHLBI’s Gibbons Wins Wenger Award

Conference Set on Models for Building Equality, Equity in Research, July 19

Gibbons (c) with award namesake Dr. Nanette Wenger (third from l) and other honorees (from l) Dr. Stacey Rosen, Dr. Emelia Benjamin; Dr. Malissa Wood; Roxanne Watson, a heart transplant recipient; and Dr. Sharonne Hayes of the Mayo Clinic.

PHOTOS: JENNIFER SMUTEK PHOTOGRAPHY/WOMENHEART
NIH Takes Home 13 HHS Green Champion Awards

NIH received 13 Department of Health and Human Services Green Champion Awards for fiscal year 2022. The awards are given to employees who take on the challenge of reducing energy use, saving natural resources and minimizing the carbon footprint of the federal government. Winners will be celebrated at a virtual ceremony this fall.

Through the annual Green Champion Awards, HHS honors federal employees and Native American tribal members, small groups and projects or programs that demonstrate measurable results towards integrating sustainability and climate resiliency principles into the HHS mission and its daily operations. This year, the awards program announced a new category, Climate Resilience and Health Equity.

The Green Champions from NIH are:

Sustainable Acquisitions Category

Project/Program
The Laboratory of Cellular and Developmental Biology, National Institute of Diabetes and Digestive and Kidney Diseases, for reducing “the amount of single-use plastic generated, energy consumed and budget expenses by purchasing a CellDrop Automated Cell Counter from DeNovix to replace a traditional cell counter that used costly disposable slides.”

Change Agent Category

Individual
Timothy “Ty” Adkins of NIH’s Office of Research Facilities’ Division of Environmental Protection, for gathering “data from the entire waste management operations and building a Power BI (business intelligence) portfolio to convert all waste management data and reports into Power BI data analytics.”

Small Group
Willie Davis, Waquita Smith, Jessica Cullen, Margaret Straubinger and Edom Sefu of the NIH Division of Logistic Services’ Property Management Branch for creating “the Report of Survey Tracking System to automate all Report of Survey (HHS-342) forms, significantly reducing the amount of paper used for manually generated and processed Personal Property Forms.”

Electronic Stewardship Category

Small Group
The National Institute of Environmental Health Sciences’ Dr. Raja Jothi, Dr. Kevin Gerrish, Dr. David C. Fargo, Cheryl Thompson, Joseph D. Puccia, Justin P. Kosak, Stephanie L. Bishop, Kenneth T. Webb, Tina Berger and Steven R. McCaw for developing the “the Database of Laboratory Equipment for Sharing, an intranet-hosted searchable collection” that facilitates “timely sharing of equipment between laboratories.”

Energy and Fleet Management Category

Small Group
The NIH fleet management section’s Mark Minnick, James Lewis, John Cheatham, Terrance Coates, Michael Jones, Matthew Fortier and Michelle Milligan for meeting and exceeding electric hybrid vehicle acquisition “targets set by executive orders and the HHS Sustainability Implementation Plan.”

The National Institute of Environmental Health Sciences’ Kerri Hartung, Paul Johnson, Steve Novak; Bill Steinmetz, Alexander Sanchez, Kyle Askins, Bill Blair, Ben Hocutt, Lee

Water Use Efficiency and Management Category

Individual
Mark Miller of the NIH Division of Environmental Protection’s Environmental Compliance Branch for being a “leader in the strengthening of sustainable water use management best practices throughout NIH operations.”

Climate Resilience and Health Equity Category

Project/Program
The NIH Climate Change and Health Working Group for spearheading the “NIH Climate and Health Initiative.” The purpose of the initiative is to “assist in the nation’s capacity to better address the health impacts of climate change and extreme weather events, especially focused on the most vulnerable populations.”

A full list of winners and award summaries can be found at https://intragnet.hhs.gov/about-hhs/annual-initiatives/go-green/green-champions.

PHOTO: ERIC BOCK
Howell and Greg Leifer for completing “a Decarbonization Assessment, the first of its kind for NIH.”

PHOTO: TRIFF/SUBBTERSTOCK
The NIH Library Green Terrace serves as an outdoor garden oasis for NIH staff and visitors. The project previously won the HHS Green Champion Award for Sustainable Building Design.

PHOTO: DAVE McCAW
The NIH Freezer Challenge for going beyond the requirements of the NIH Freezer Policy “to further increase freezer and refrigerator reliability and reduce energy consumption.”

PHOTO: GOVIND BHAGAVATHEESHWARAN & DANIEL REICH/NINDS
Mansi Mehta of the NIH Office of Research Facilities’ Division of Environmental Protection (DEP) for spearheading “coordination efforts to establish a partnership between the NIH DEP and Montgomery County to implement a pre-consumer food scrap recycling pilot at several NIH cafeterias.”

PHOTO: TRAFF/STUBBTERSTOCK
Manuals of the NIH Office of Research Facilities’ Division of Environmental Protection for creating an outdoor garden oasis for NIH staff and visitors. The project previously won the HHS Green Champion Award for Sustainable Building Design.

PHOTO: GOVIND BHAGAVATHEESHWARAN & DANIEL REICH/NINDS
As part of the NIH Climate Change and Health Working Group for “assist in the nation’s capacity to better address the health impacts of climate change and extreme weather events, especially focused on the most vulnerable populations.”

PHOTO: SHUTTERSTOCK
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NIH National Institutes of Health
Turning Discovery into Health
Bike
CONTINUED FROM PAGE 1

her office is located at NCI-Shady Grove, she happily biked the four-mile distance from her home in Kensington to join her colleagues on the Bethesda campus.

NIAID’s Robin Eisch has biked to work regularly since 2007, traveling from her home in Silver Spring. With increased telework, she now enjoys biking along the seven-mile trail on the two days a week she commutes to campus.

NIMH’s Jerry McGuire chooses to bike to work on the two to three days each week that he comes to campus. In his four years at NIH, he can recall driving to campus only once, as biking has become his preferred mode of transportation.

Dr. Laura VanBlargan commutes to her on-campus NIAID lab every day, often relying on her bike. These days, she is biking for two; her baby is due in August.

Martina Lavrisha, a nurse at the Clinical Center, biked to work for the first time that day, embarking on a 20-mile journey from her home in Vienna, Va. She viewed it as training for the upcoming RAGBRAI, a challenging 500-mile bike ride across Iowa that she plans to undertake this summer.

Upon reaching Bldg. 1, cyclists took

Gathering for Bike Day are (from l) Sean Cullinane, Gerald Jordan, Joe Cox, Tammie Edwards, NIH Deputy Director for Management Dr. Alfred Johnson and two NIH police officers Kerin Cummings and Matt Mehilaff. At night, CC Nurse Martina Lavrisha (r) chats with Sarah Weltz, an NCI postbac fellow.
NIH’s Bike Club Honors Velez with the 2023 Henn Award
NIH’s Bike to Work Day celebrates cycling’s benefits to health and the environment. The event also celebrated NIH’er Frank Velez, who was honored with the 2023 Carl Henn Bicycling Advocacy Award.

Velez—who had led the clinical research informatics program in NIDDK’s office of the clinical director and recently switched gears to become the biomedical informatics projects manager in NHLBI’s Scientific Solutions Delivery Branch—has been committed to NIH’s Bicycle Commuter Club (NIHBCC) for years. He recently led the charge in getting freshly designed cycling jerseys and bibs for the club and streamlined the procurement process.

When activities shut down during the Covid-19 pandemic, Velez upheld club rapport and engaged by creating fun riding challenges members could access through a mobile phone app. He also helped bring back the NIH pitstop in front of Bldg. 1 to the National Capital Region’s Bike to Work Day event after its pandemic hiatus.

“I’ve worked hard to foster collaboration between the Washington Area Bicycling Association, the NIH Division of Amenities and Transportation Services and the NIH Bike Club,” said Velez. “We still have work to do, but I am pleased that our goals align.”

This award honors the memory and legacy of longtime NIH employee and cycling advocate Henn, a co-founder and president of NIHBCC and dedicated environmentalist who passed away unexpectedly in 2010.

Honoree Velez rides both for pleasure and competition, and he most enjoys casual rides with his family in the Montgomery County Agricultural Reserve in Maryland. He also enjoys tending to his small fleet of bicycles, including a Dutch-style bakfiets (“box bike”) and a few boutique race frames. Velez plans to continue to advocate for riders across NIH and the county. —Katie Clark

NIH researchers are looking for a diverse pool of participants diagnosed with cancer or a tumor and receiving standard or experimental treatment to join a new study that measures pain through facial expressions and vocal communications. Participants will need a smartphone or computer with a camera to complete a questionnaire and record selfie videos. Parental consent is required for minors. Compensation of up to $225 will be provided upon study completion. In addition, there is reimbursement for travel with mileage and accommodation up to but not exceeding $120/night. Contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #20-C-0130. Online: https://go.nih.gov/HTOAOtj.
line every single time you come to work,” said Colleen McGowan, director, Office of Research Services, introducing the hybrid event that began in the NIH fire station’s classroom.

These last few years, DFRS not only maintained their regular operations, but they also put in extensive overtime throughout the pandemic.

“Covid impacted everything that everyone did,” said NIH Acting Principal Deputy Director Dr. Tara Schwetz. “I know you all performed specialty transports to the Clinical Center’s Special Clinical Studies Unit, which was critical to the work [doctors and staff] were doing with Covid-positive patients.”

In addition, DFRS became incident commanders who managed operations for the car-line site that tested symptomatic employees. “We at NIH became a model and example of what could be done” to limit the spread of Covid-19 and keep staff healthy, said Schwetz.

“I don’t think people realize how much you are a fabric of the Montgomery County community,” said McGowan, noting the services provided by DFRS extend well beyond the NIH campus where the firehouse is located.

In 2022, DFRS responded to nearly 2,500 emergency incidents on the Bethesda campus and throughout the county and has already responded to more than 700 incidents so far this year.

“You risk your lives every day to save lives and we thank you for that,” said NIH Deputy Director for Management Dr. Alfred Johnson. He mentioned his daughter is a volunteer firefighter and paramedic.

“When she’s on call, I don’t sleep so well so I can imagine [the challenges you and your families face] on a regular basis.”

They respond at a moment’s notice to emergency calls—building fires, explosions, accidents. Recently, an NIH firefighter saved a person trapped underneath a Metro train. Some of them have been injured in the line of duty.

“This is the only group of people I know of that, as part of their [job] description, are running into buildings as other people are running out,” said Bill Cullen, NIH associate director for security and emergency response. He highlighted the extraordinary dedication of DFRS, which celebrates its 70th anniversary this year. At least 10 firefighters are always on call, sleeping in bunk rooms at the station; most are working 72 hours per week.

“I know what it takes to go down a smoke-filled hallway…That’s tough work,” said DFRS Acting Director Mat Chibbaro. “I know it’s a significant risk decision to bring your crew into an unstable portion of a building after the other half just blew up.”

DFRS firefighters all undergo specific training in hazmat, given the potential exposure to chemicals, contagions and radiation at NIH, as well as emergency medical services.

Chibbaro said there’s also a soft skills element to their jobs, “whether it’s getting slimed at the Children’s Inn or changing a tire for the elderly.”

Beyond gratitude, the event provided...
CC 70th Anniversary Events Continue

Former NIH Director Dr. Francis Collins will give a special Grand Rounds Lecture to mark the Clinical Center’s 70th anniversary on Wednesday, June 28 at 1 p.m. in Lipsett Amphitheater, Bldg. 10. There will be limited seating and the lecture will be available online at https://videocast.nih.gov/. Collins, a senior investigator at the National Human Genome Research Institute and special advisor to President Biden, will discuss the CC’s past and its future prospects.

Next month, the CC will feature “Science Related” artwork with a scientific focus or created by people with scientific and medical backgrounds.

The exhibit, on display beginning July 8 throughout the building’s first floor—will feature artists with disparate mediums: wood art and illustrations from Candice Tavares, a clinical pharmacy specialist in palliative care at Medstar Washington Hospital Center; large format botanic photographs from Amy Lamb, a former NIH postdoctoral fellow; abstract paintings inspired by science and medicine from Michele Banks, who studied at George Washington University and Harvard University; paintings of historic microscopes from the Golub Collection of Antique Microscopes at University of California-Berkeley by Sue Fierston; and art from printmaking photographer Barbara Southworth, who combines her twin passions of art and science.

2023 Hybrid Graduate & Professional School Fair

The 2023 NIH Hybrid Graduate & Professional School Fair will be held in-person on Wednesday, July 19 at the Natcher Conference Center and virtually July 24 through Aug 11. The fair provides an opportunity for NIH summer interns (especially those in college) and postbacs, as well as other college students in the D.C. area, to prepare for the next step in their careers by exploring educational programs leading to the Ph.D., M.D., D.D.S., M.D./Ph.D. and other graduate and professional degrees.

More than 250 colleges and universities from across the U.S. send representatives of their graduate schools, medical and dental schools, schools of public health, and other biomedically relevant programs in hopes of recruiting NIH trainees.

The fair will consist of hybrid workshops on getting to graduate and/or professional school and exhibitor sessions that provide opportunities to learn more about participating educational programs. Exhibitor sessions will be offered both in-person (July 19) and online (July 24-Aug 11). A list of participating institutions and registration information can be found at https://www.training.nih.gov/gp_fair.
articulates NIH’s commitment to embracing, strengthening and integrating DEIA across all agency activities, including the intramural and extramural communities.

The plan has three objectives:

• Grow and sustain DEIA through structural and cultural change
• Implement organizational practices to center and prioritize DEIA in the workforce
• Advance DEIA through research

These objectives promote transparency, communication and engagement; foster sustainable change; and harness data, said NIH Acting Principal Deputy Director Dr. Tara Schwetz. “NIH efforts on DEIA did not start and will not end with the release of the strategic plan.”

Last year, NIH leadership conducted one-hour listening sessions organized by EDI with seven special emphasis populations. During the sessions, members of each population shared their experiences and offered recommendations for change.

Each population emphasized the need to unify DEIA activities across NIH, create a greater sense of belonging and inclusivity, standardize cultural-competency training and focus on targeted outreach and recruitment for all underserved populations.

Summaries of the sessions can be viewed at: go.nih.gov/04iEho0.

The NIH steering committee DEIA working group is responsible for implementing the plan and synchronizing all activities developed by institutes and centers, said Dr. Marie Bernard, NIH’s chief officer for scientific workforce diversity. The working group works closely with the UNITE Initiative.

Since launching in 2021, UNITE has made progress identifying and addressing structural racism. The initiative required each IC to develop Racial and Ethnic Equity Plans. The plans will identify, and provide a framework to dismantle, any racial and ethnic disparities that may exist. Planned strategies are broad and will be of benefit to the overall workforce.

“Each IC has leaned into this process of making sure that they looked at things with a racial and ethnic equity lens,” Bernard said.

Other accomplishments include revising the selection process for NIH Director’s Awards and launching the NIH Common Fund’s Faculty Institutional Recruitment for Sustainable Transformation program. Funding opportunities are now available for science education, researchers who are involved in DEIA initiatives and institutions that have received limited amounts of NIH grants historically.

The Office of Human Resources (OHR) supports NIH’s commitment to DEIA, said Julie Berko, director of human resources and chief people officer. In 2021, the office launched NIH’s new employer branding to recruit a diverse pool of candidates.

“The new look and messaging are specifically designed to incorporate the real faces and places of NIH—not stock photos,” she said.

OHR has taken steps to reduce implicit bias during the NIH management intern selection process. They have worked with EDI to develop new senior executive DEIA applicant requirements. Candidates must now provide examples that illustrate their commitment to DEIA.

In future, Berko said OHR is ready to provide tools to help inform hiring, pay and recognition decisions being made by IC leadership, managers and supervisors.

“The strength of our agency derives in large part from our diversity,” concluded Acting NIH Director Dr. Lawrence Tabak. “We need to do more to foster a culture in which all feel welcomed at NIH and within the research communities we support.”

The event was coordinated by NIH’s Office of Communications and Public Liaison.

To watch the full town hall, visit: https://videocast.nih.gov/watch=49589.

MILESTONES

NIH-Wide Strategic Plan for Diversity, Equity, Inclusion, and Accessibility

NIH-Wide Strategic Plan for Diversity, Equity, Inclusion, and Accessibility

Dr. Monica Webb Hooper

NIH-Wide Strategic Plan for Diversity, Equity, Inclusion, and Accessibility

Lauded for Advancing Science of Health Disparities

Dr. Monica Webb Hooper, deputy director of the National Institute on Minority Health and Health Disparities (NIMHD), recently received two accolades for her leadership and influence across biomedical and behavioral research.

In April, she was recognized as one of the Most Influential People of African Descent (MIPAD) Class of 2023 Global Top 100 List for Healthcare and Wellness in support of the United Nations’ International Decade for People of African Descent 2015-2024.

The MIPAD honor identifies high achievers of African descent in public and private sectors who have distinguished themselves in advancing people of African descent worldwide. The MIPAD Class of 2023 will be recognized at a formal ceremony on Oct. 1 at the Millennium Hilton in New York City.

Webb Hooper has also been acknowledged by Academic Influence (AI) as one of 25 Influential Black Psychologists and among 50 Influential Black Anthropologists from the past 30 years.

AI is a data science organization that ranks the top schools, disciplinary programs and academic thought leaders based on statistical analyses of scholarly journals and keyword searches. Their data show Webb Hooper is one of America’s most cited and searched Black scholars.

In 2020, shortly after joining NIMHD, Webb Hooper was established as a leading federal authority on Covid-19 disparities when she authored an article, “Covid-19 and Racial/Ethnic Disparities,” highlighting the disproportionate burden of the coronavirus on people from racial and ethnic minority groups.

The article was published in the Journal of the American Medical Association and cited more than 2,300 times.
NIH’s ComboMATCH Will Test New Drug Combinations Guided by Tumor Biology

NCI has launched a large precision medicine cancer initiative to test the effectiveness of treating adults and children with new drug combinations that target specific tumor alterations.

Known as the Combination Therapy Platform Trial with Molecular Analysis for Therapy Choice (ComboMATCH), the initiative is the largest of its kind to test combinations of cancer drugs guided by tumor biology. The endeavor aims to identify promising treatments that can advance to larger, more definitive clinical trials outside of ComboMATCH.

ComboMATCH comprises numerous phase 2 treatment trials that will each evaluate a drug combination—usually either two targeted drugs or a targeted drug plus a chemotherapy drug. Some trials will include patients with specific changes in their cancer cells, no matter where the cancer arose in the body, whereas others will enroll patients with specific cancer types.

“The majority of treatments that patients get nowadays are not genomically determined,” said Dr. James Doroshow, director of NCI’s Division of Cancer Treatment and Diagnosis. “With ComboMATCH, we’re trying to show that genomic abnormalities can be used to determine the most effective treatment combinations for patients.”

ComboMATCH is a cross-group collaboration among NCI and all five U.S. clinical trial groups within NCI’s National Clinical Trials Network. ComboMATCH is a successor to NCI-MATCH, NCI’s groundbreaking precision medicine clinical trial.

In NCI-MATCH, people were assigned to treatment based on genetic changes in their tumor rather than their type of cancer. For the most part, NCI-MATCH evaluated single drugs targeting the mutation thought to be driving the growth of a patient’s tumor. However, many patients quickly developed resistance to these single drugs.

Human Pangenome Boosts Accuracy, Reflects Diversity

Genetic differences between people can cause or alter the severity of various diseases and influence the effectiveness of treatments. Scientists identify such genetic variants by comparing an individual’s genome sequence to a standard, which is known as a reference genome.

A reference genome is created by assembling parts of the genomes of many different people into a single sequence. The original reference genome was developed by the Human Genome Project two decades ago. It has been continually updated as genome sequencing has become more accurate and more data became available. But a single reference genome can’t represent the genetic diversity of the human species. In particular, larger genetic variations, known as structural variations, are difficult to identify using a single reference genome.

An NIH-funded consortium has developed a reference “pangenome” that represents more human genetic diversity. The pangenome resembles a transit map, with different lines representing each component genome. The lines overlap where the sequences match and branch out where the sequences diverge. A first draft of the pangenome was published in Nature. Four companion papers were published as well.

To estimate the completeness of the genomes, the researchers compared them with the first complete human genome sequence released in 2022. On average, the genomes covered more than 99% of the expected sequence. More than 99% of each genome was accurately assembled.

The pangenome captured nearly all human genomic variants that have been identified using the existing reference genome, called GRCh38. But it also went beyond the existing reference in several ways. The researchers found more than 1,100 cases of gene duplication in the pangenome that were missing from GRCh38. The pangenome also contains more than 100 million more base pairs—the “letters” of DNA—than GRCh38.

Structural variations can be especially hard to detect using a single reference genome. These involve the deletion, duplication or rearrangement of long DNA stretches. Most of the new base pairs found in the pangenome were in regions that were previously unresolved due to structural variation. The researchers identified previously unknown structural variations at several locations where many such variations are possible. In all, the average number of structural variations identified more than doubled.

The authors note that the published pangenome is only a first draft. The consortium ultimately hopes to produce a more detailed pangenome that incorporates genomes from 350 people. Having a diverse reference may help ensure that future genomic research can benefit people of all backgrounds.—adapted from NIH Research Matters

NIH Scientists Find Treatment for Rare Genetic Skin Disorder

Researchers at NIH and their colleagues have identified genomic variants that cause a rare and severe inflammatory skin disorder, known as disabling pansclerotic morphea, and have found a potential treatment.

Scientists discovered that people with the disorder have an overactive version of a protein called STAT4, which regulates inflammation and wound healing. The work also identified a drug that targets an important feedback loop controlled by the STAT4 protein and significantly improves symptoms in these patients. The results were published in the New England Journal of Medicine.

The study was led by NHGRI researchers in collaboration with researchers from the University of California, San Diego and the University of Pittsburgh. Researchers from NIAMS and NIAID also participated in the study.

Only a handful of patients have been diagnosed with disabling pansclerotic morphea, a disorder first described in the medical literature around 100 years ago. The disorder causes severe skin lesions and poor wound healing, leading to deep scarring of all layers of the skin and muscles. The muscles eventually harden and break down while the joints stiffen, leading to reduced mobility. Because the disorder is so rare, its genetic cause had not been identified until now.
of contraception for women and men. The NES/T study is a collaboration with the Population Council and the developers of Nestorone.

Her product is the first of its kind: A male hormonal contraceptive absorbed through the skin to block sperm production while still maintaining functional levels of testosterone elsewhere in the body.

NES/T accomplishes this through a combination of two hormones. Progestin (the “NES” comes from Nestorone, the brand name of the progestin in the product) acts on the brain to block pituitary hormones that control natural testosterone production in the testes. The “T” stands for replacement testosterone.

Under normal circumstances, the testes maintain high testosterone levels (about 100 times higher than blood levels) to support sperm production. By blocking testosterone production locally, sperm production falls to low or nonexistent levels. However, the male body needs to maintain some level of testosterone for normal functioning—which is where the replacement testosterone comes in. It “replace[s] the blood testosterone at the normal physiologic level” while keeping the testes level low enough that it can’t restart sperm production, Blithe explained. Sperm counts recover to normal levels after participants cease using the gel.

So, why gel instead of a pill?

“Pill forms of testosterone are not absorbed well,” Blithe explained. In trials, participants needed to take multiple doses a day to achieve the same effects as the transdermal gel.

In the current study, daily application of the gel reduced participants’ sperm counts to less than 1 million per milliliter, which is low enough to be considered contraceptive.

Studies of hormonal control of sperm production have been around for more than 60 years, but with little success until recently. “We knew we could do it, but the delivery was the issue,” Blithe recalled.

Two components inspired the gel. Replacement testosterone gel has been around since about 2002; Blithe got the idea to combine it with Nestorone in 2004, when CDP and the Population Council were working on a different product that contained Nesterone.

NES/T now is in phase 2B of clinical trials that evaluates the efficacy of the method to prevent pregnancy in couples.

“The effectiveness is much higher than we expected,” Blithe said.

Current study participants hail from sites around the world. Couples use the gel as their only form of contraceptive for one year (with additional time to monitor sperm decline and rebound before and after the year of gel-only contraceptive usage).

The next step, Blithe said, is to take the data to the Food and Drug Administration (FDA) and find out what additional data they would need to approve the product.

The significance of this product is not lost on Blithe. In surveys over the past 20 years, about 50% of men surveyed have expressed the desire for a reversible form of contraceptive. Now that it is a reality, men who have used the gel are overwhelmingly impressed with the drug’s effectiveness and safety.

“It’s very reassuring that we have so many men who would like to continue to use it,” Blithe said.

One aspect she didn’t realize at first was the benefit to the female partner in being able to stop whatever contraceptive she was using.

“The anxiety of having to go back on a [contraceptive] method that isn’t perfect for her is palpable,” Blithe noted. “It’s a women’s health issue as well as something for men.”

Removing Hurdles

Dr. Min Lee said he “never came across things [he] thought would make it as a product” until two certain products evolved in NICHD’s Contraceptive Development Program (CDP): NES/T and an injectable contraceptive for women that Lee co-invented.

A Ph.D. and chemist with CDP, Lee has a long career in drug discovery and development, so that statement carries weight. He came to the extramural program in NICHD from
it has enough progestin and can stop making negative feedback loop…by telling the brain pregnancy. progesterone) that works to prevent hypertension that can co-occur with obesity. often not recommended for obese women contraceptives that contain estrogen are women who are obese. density—and also may be less effective in side effects for some women—weight gain, trained medical professional, but SQ injections don’t have the same limitations. Lee’s product is poised to have a big impact. Many women face obstacles coming to a doctor’s office every few months to stay up to date on their contraceptive regimen. Also, about one-third of women who are of reproductive age are obese. Unplanned pregnancies in the U.S. make up about 45 percent of pregnancies each year, Lee noted, and he hopes LB will fill the niche for a safer, more convenient alternative to current injectable contraceptives. “This will be a good option for women because it gives them more freedom,” Lee said. “It will remove a lot of hurdles.”

Sample bottle of the LB contraceptive injection

the private sector 13 years ago and joined CDP in 2017.
Since then, he has been working on his invention: levonorgestrel butanoate (LB). Levonorgestrel butanoate is an injectable prodrug (an inactive drug that is metabolized into its active form) that breaks down in the body to provide levonorgestrel, the active drug. It is a progestin-only contraceptive being developed as an alternative to Depo-Provera, the only other injectable birth control for women.

**“This will be a good option for women because it gives them more freedom.”**

- DR. MIN LEE

Depo-Provera has several unwanted side effects for some women—weight gain, mood swings, decreased bone mineral density—and also may be less effective in women who are obese.

Additionally, other forms of hormonal contraceptives that contain estrogen are often not recommended for obese women because of conditions like diabetes and hypertension that can co-occur with obesity.

Levonorgestrel is a strong progestin (a synthetic version of the human hormone progesterone) that works to prevent pregnancy.

In LB, the levonorgestrel “acts as a negative feedback loop…by telling the brain it has enough progesterin and can stop making its own progesterone,” Lee explained. Through series of signaling cascades, the lack of natural progesterone inhibits ovulation.

The road to the current LB began in the 1980s, when NICHD, the World Health Organization (WHO) and other collaborators were working together to develop an injectable contraceptive using levonorgestrel butanoate. That project fell through and NICHD picked it up again in the early 2000s. They tweaked the formulation to make it more stable and last longer. The butanoate prodrug portion of LB was the key to improving the drug’s lifespan.

Lee and co-inventors then discovered something else surprising—LB was also effective for longer duration when it was injected subcutaneously (SQ) rather than as an intramuscular (IM) shot.

“We did not expect to see this,” Lee recalled. “We knew this was a significant breakthrough when we saw the SQ data.” IM shots lasted about two months. Conversely, the SQ injections last between three and five months. In the current phase of clinical trials (2A), the CDP clinical team dropped the IM version of the drug entirely and are now focusing their efforts on the SQ version.

In addition, the SQ delivery route is exciting because women can self-administer the drug. An IM shot must be given by a trained medical professional, but SQ injections don’t have the same limitations.

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Have a question about some aspect of working at NIH? You can post anonymous queries at https://nihrecord.nih.gov/feedback and we’ll try to provide answers.

Feedback: I am grateful that NIH mail services are back in full, but we had 45 pieces of mail in our box this week—all of them individually wrapped in plastic and with a piece of paper denoting the delivery address. Each one. Individually. That is 45 pieces of plastic in the waste stream and 45 pieces of paper to dispose of. That seems like an enormous waste of time and resources. Is there any indication as to when this practice will stop and mail will be delivered “as is”?

Response from the Division of Mail Management Services (DMMS), Office of Research Services (ORS): DMMS does not individually wrap pieces of mail. However, they do wrap the entire day’s mail delivery in one plastic bag after receiving complaints about wet and damaged mail handled and delivered during inclement weather. Also, plastic bags and paper mail slips are recyclable, and we encourage staff to participate in NIH recycling efforts. If you had 45 pieces of mail in your mailbox, it means you hadn’t checked your mail in a minimum of 45 workdays, so our mail staff also recommend you check your mail more often in case there are important and time-sensitive communiques waiting for you.

Feedback: Will the [concession] stand reopen in Bldg. 31?

Response from ORS’s Division of Amenities and Transportation Services (DATS): DATS has been in conversation with leaders of the Maryland Business Enterprise Program for the Blind about reopening the Bldg. 31 concession stand, as well as other NIH locations. We have been closely monitoring the food service traffic in the cafeterias to get a sense of food and beverage demand to gauge the consistency of building populations.

This state program has multiple small business owners who operate the various stores. Their responsibility is to ensure there is enough anticipated demand for service to be profitable. Each location is being evaluated independently. Once there is consensus that there is enough sustained traffic expected to be financially viable, we will see them reopen. Check DATS’s food page (https://go.nih.gov/K385TpE) for updates and operational status.
SMOKE SIGNALS POOR AIR QUALITY
NIH Worksites in D.C. Region Feel Effects of Wildfires in Canada

NIH’ers in mid-Atlantic areas on June 7-8 likely noticed the hazy, smoky conditions that blanketed much of the eastern U.S., tingeing the sun an eerie red and making the outside air hazardous to breathe. The smoke was swept southward from more than 100 active wildfires in Quebec, Canada.

Employees on the Bethesda campus reported the palpable scent of smoke and hazy skies. The air quality index (AQI) peaked there around 220, which falls into the Code Purple “very unhealthy” category, according to the Metropolitan Washington Council of Governments. It was the first time ever that the D.C. region recorded a purple code for fine particle pollution. At this level, health risks are elevated for the general public and people should avoid spending time outdoors.

The AQI measures the amount of pollution in the air. It is rated on a scale of 0-500, with levels below 100 deemed safe for the general public. The main component of wildfire smoke is fine particulate matter (PM2.5), tiny particles measuring less than 2.5 micrometers in diameter. These particles are so small that they can be inhaled deep into the lungs and can even pass into the bloodstream.

To monitor the AQI in your area, visit AirNow.gov.—Amber Snyder

Above, the haze seeped into the platform area of the Medical Center Metro Station. PHOTO: ERIN BUTLER

At left, wildfire smoke blanketed NIH’s main campus, as seen from the top floor of MLP-9. PHOTO: ERIC BOCK

Above, at 8:30 a.m. on June 8, the Clinical Research Center is in a fog in this photo taken from the Safra Lodge parking lot. PHOTO: DEVON VALERA At right, an early morning view of the sun shown with a smoky haze in Frederick, Md. PHOTO: AMBER SNYDER