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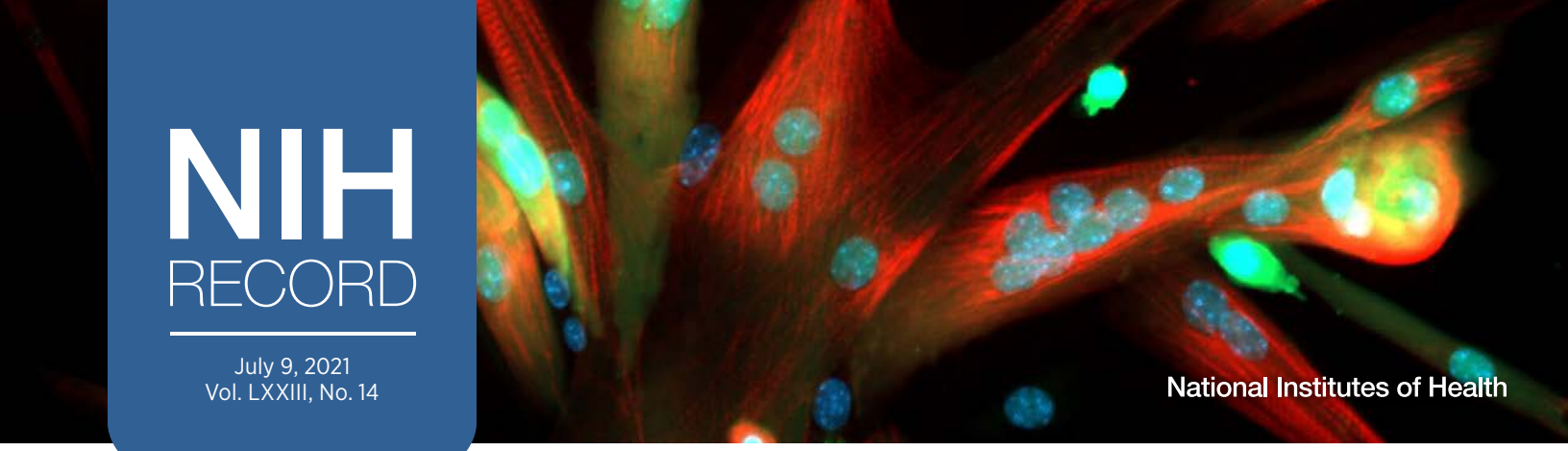


DRIVERS AND PASSENGERS

Chanock Explores Genetics of Cancer Susceptibility

BY DANA TALESNIK

Great teachers inspire as they impart wisdom. Such was the case during a recent lecture by NCI's Dr. Stephen Chanock, who managed to fit his professional journey, career advice, a history lesson and decades of research into a captivating hour.

"Trust your instincts and follow your interests, wherever they take you," advised Chanock, who called his professional path a tale of two long woods. He began his NCI career 30 years ago, though his connection to NIH started much earlier.

Chanock grew up on Longwood Drive near the Bethesda campus and fondly recalls visiting NIH with his father, who worked at NIAID. "Bldg. 7... was a standard Saturday morning playground for me as a young child," he said.

Dr. Stephen Chanock

Initially, Chanock didn't plan to study medicine. His interests first took him to study music in college. But then he wound up on Long Wood Ave., in Cambridge, Mass., studying medicine at Harvard.

His professional career would also take a turn. Chanock arrived at NIH in 1991 to study oncology and infectious diseases but his interests pivoted by 2000 as genomics research gained momentum. Mentors had told him to pursue the interesting questions, which for him turned out to be, not the section where he was a tenured investigator, but the Division of Cancer Epidemiology and Genetics, where he is currently the director.

Speaking at a virtual Clinical Center Grand Rounds Great Teachers talk, Chanock described some of the research his genetics lab has conducted into the biology, heritability and risks of cancer.

The Human Genome Project opened a whole new world of discovery. "The excitement of characterizing and sequencing nearly all 3.1 billion bases," said Chanock, "gives us the opportunity to over and over look both at the germline and the tumors to understand what kinds of changes we see—what changes are drivers and what changes

SEE **CHANOCK**, PAGE 6

NIH Director's 'Gratitude Tour' continues. Asymptomatic testing, screening teams applauded. See p. 12.

ALSO THIS ISSUE

POWER OF GENETICS

DNA Forensics Help Solve Wildlife Crimes, Conserve Species

BY ERIC BOCK

Genomics can help solve animal cruelty cases, prosecute wildlife crimes and conserve endangered species, said Dr. Rebecca Johnson, member of the Order of Australia and chief scientist at the Smithsonian National Museum of Natural History.

Dr. Rebecca Johnson

"DNA can really be a valuable tool for fighting wildlife crime when combined with museum collections," said Johnson during

SEE **DNA**, PAGE 4

MIT professor Dr. Hugh Herr
PHOTO: MATTHEW SEPTIMUS

'EMPOWER'

AMI Technique Gives New Life to Amputees

BY AMBER SNYDER

Hugh Herr was an accomplished young mountain climber when he suffered what should have been a career-ending accident. Both lower legs had to be amputated below the knee. Rather than end his climbing career, though, it inspired him to craft

SEE **EMPOWER**, PAGE 8

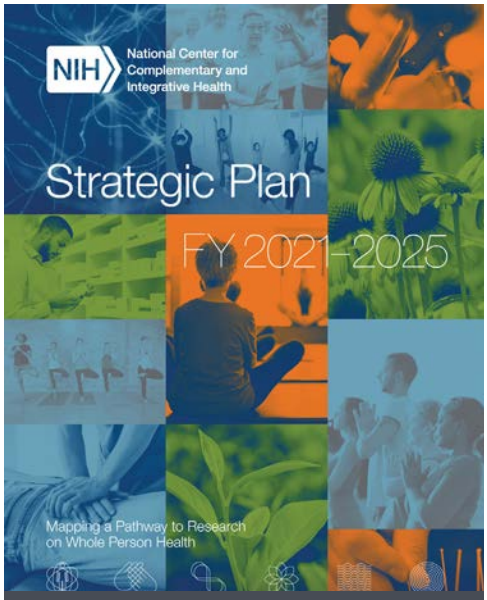
NCCIH Strategic Plan Focuses on 'Whole Person Health'

BY ELLEN O'DONNELL

In the current health care system, we tend to think about disease one organ system at a time. But a new strategic plan by NCCIH considers multiple factors that promote either health or disease, and focuses on restoring health, promoting resilience and preventing diseases across the lifespan.

NCCIH recently released its strategic plan for 2021-2025, *Mapping a Pathway to Research on Whole Person Health*. The plan builds on the center's current activities in research and information dissemination while advancing new strategies and ideas.

"Whole person health" refers to helping individuals improve and restore their health in multiple interconnected domains—biological, behavioral, social and environmental—rather than just treating disease. Research on whole person health includes expanding the understanding of the connections between these various aspects of health, including connections between organs and body systems.



NCCIH recently released its strategic plan for 2021-2025.

The framework of whole person health places health and disease on a spectrum. On this path, many factors, including one's biological makeup; some unhealthy behaviors, such as poor diet, sedentary lifestyle, chronic stress and poor sleep; as well as social aspects of life—the conditions in which people are born, grow, live, work and age—can lead to chronic diseases of more than one organ system. On the other hand, self-care, lifestyle and behavioral interventions may promote "salutogenesis" or the process by which an individual moves from a less healthy to a healthier state, involving the whole person.

"Currently, patient care focuses on diagnosing and treating individual diseases and not as much on protecting and restoring overall health. This is largely an unknown area," said NCCIH director Dr. Helene Langevin. "Integrative thinking and a study of networks at all levels have been well established in other scientific fields, such as ecology and systems biology, and now medicine is starting to catch up. This presents many exciting opportunities for NCCIH to advance basic and clinical research, patient care and public health, both on our own and through collaborations."

A whole person concept has existed for centuries in many traditional medical cultures, as reflected in practices such as meditation, yoga, acupuncture and herbal medicine.

"The concept of whole person health is so important now," Langevin added, "as we live in a time of convergent complex crises such as Covid-19, the opioid epidemic, the pain crisis, the obesity epidemic and climate change."

The objectives in NCCIH's plan are to advance fundamental science and methods development; advance research on the whole person and on the integration of complementary and conventional care; foster research on health promotion and restoration, resilience, disease prevention and symptom management; enhance the complementary and integrative health research workforce; and provide objective evidence-based information on complementary and integrative health interventions.

Ten priority research topics in the plan reflect public health needs, scientific promise, amenability of those topics to rigorous scientific inquiry, their potential to impact health care practices and their relationship to use and practice.

Read the plan at https://www.nccih.nih.gov/about/nccih-strategic-plan-2021-2025.

The University of Maryland Jazz Combo returns to the Clinical Center's atrium, featuring (from l) Danny Villanueva on congas, Gerry Kunkel on guitar, Joey Antico on drums, John Previti on upright bass and (not shown) Jon Ozment on piano.

PHOTOS: DANA TALESNIK

A Jazzy Afternoon at the Clinical Center

Lively jazz reverberated through the halls of the Clinical Research Center on June 10 when the University of Maryland Jazz Combo played a lunchtime concert in the atrium. It was their first return to campus since the pandemic began.

The crowd was smaller than usual as many NIH staffers have not yet returned to physical workspaces, but many more enjoyed the music that carries up through the halls and into patient rooms. Some patients walked or were wheeled over to check out all or part of the hour-long performance.

The quintet performed upbeat arrangements of classic tunes and lesser-known songs by well-known jazz greats. The repertoire included George Gershwin's *Summertime;* Thelonious Monk's *Nutty* and Antonio Carlos Jobim's *Once I Loved.* Bandleader and guitarist Gerry Kunkel also dedicated a song to the hardworking NIH staff: Duke Ellington's *Do Nothin' Till You Hear From Me.*—**Dana Talesnik**

Annual Food Drive Accepting Online Donations

NIH is participating in the Feds Feed Families virtual summer food drive now through Tuesday, Aug. 31. Federal agencies can help fight hunger in their communities. The campaign will again be run entirely online with three ways to contribute and track donations. The Office of Research Services is NIH's sponsoring organization. For more information, visit the website at https://www.ors.od.nih.gov/FedsFeedFamilies/Pages/default.aspx. Email questions about the campaign to FedsFeedFamiliesNIH@nih.gov.

HIGHLY UNLIKELY, BUT POSSIBLE

Pandori Discusses What We Know About Covid Re-Infections

BY AMBER SNYDER

Individuals who have recovered from SARS-CoV-2 may still be at risk for re-infection, said Dr. Mark Pandori, director of the Nevada State Public Health Laboratory (NSPHL) and associate professor of pathology at the University of Nevada, Reno School of Medicine. He spoke at a recent Covid-19 Insights Seminar hosted by NHLBI.

In his lecture, "Re-infection with SARS-CoV-2 and its Impact on Covid-19 and Public Health," Pandori discussed his efforts with NSPHL to identify re-infections and what these cases mean for the future of the pandemic.

His first experience with Covid-19 re-infection came in the beginning of the coronavirus crisis. A young man tested positive and was symptomatic for a month. He then had 2 consecutive negative tests and was symptom-free for 48 days before developing symptoms again and testing positive. The new round of Covid was more severe. The individual was hospitalized for low blood oxygen levels, but recovered quickly.

How could Pandori confirm that it was truly a re-infection? The patient lived with his mother, who also developed Covid at the same time as her son's second illness, which increased the likelihood that the man's infections were two distinct events. Pandori still needed a concrete method to validate his theory, so he decided to sequence the viral genomes from the man's positive tests.

"Covid mutates at a rate of about 2 base pairs per month," Pandori said, "so, if it had remained dormant in the individual for the 48 days between the 2 cases, then we would expect it to have mutated enough to change about 3 base pairs."

Base pairs are the subunits of genetic material: DNA in us, and RNA in viruses such as Covid-19. Mutations are often the result of changes in base pairs. Those changes may do nothing at all or may change a gene enough to alter its function. If a mutation creates a change that is helpful to the organism,

Dr. Mark Pandori

such as making a virus more infectious, that mutated strain will become more common in the population.

Pandori sequenced the genomes from the two different infections (cases A and B) and found that there was "considerable genetic distance" between them. There were 11 differences in base pairs between cases A and B—far more than the 2 or 3 that would be expected if this was the same illness that had lain dormant in the body between the 2 periods of symptomatic infection.

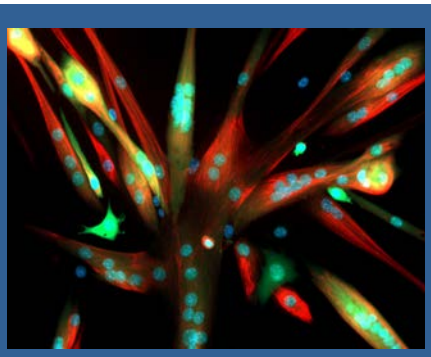
Other researchers throughout the world have been sequencing the genomes of Covid-19 infections and have constructed a map of all the different strains and their relatedness.

Case A looked like the strain that was circulating in Nevada at the time, while case B resembled the version of the virus that had initially emerged from Wuhan—the ancestral genotype. The odds of the virus from case A changing that drastically and reverting closer to the ancestral genotype were "vanishingly small," therefore making re-infection the most likely explanation.

Other instances of re-infection began to emerge around the same time as Pandori's first subject (in Nevada and around the world), and he was able to confirm several other cases through genomic sequencing.

Re-infection is still highly unlikely in most cases, Pandori said, but he is concerned that the virus will evolve the ability to mutate faster and possibly make vaccines less efficacious.

NIH'ers can view the entire lecture at https://videocast.nih.gov/watch=40179. R



ON THE COVER: *Multi-Nucleated Muscle Cells Grown in Culture. The cells have fused together to form myotubes that have many nuclei (stained blue). The cells are from mouse skeletal muscle stem cells treated with a harmless virus that caused them to glow green. The green color remained when the stem cells fused into myotubes. Some myotubes are stained red for a protein involved in muscle contraction (myosin heavy chain), a characteristic of mature muscle fibers. Researchers plan to use the same viral delivery system to genetically modify the cells and assess how impairing cell fusion alters myotube growth. The image was a 2017 winner in the BioArt competition of FASEB.*

IMAGE: KEVIN A. MURACH, UNIVERSITY OF KENTUCKY, WITH SUPPORT FROM NIAMS, NIA

The NIH Record

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National Institutes of Health
Turning Discovery Into Health

Johnson and a team of researchers successfully sequenced the koala genome, which has revealed information about diet and genetic diversity.

DNA

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the recent Louise M. Slaughter National DNA Day lecture.

The annual lecture honors the life and legacy of the late New York congresswoman, who was a strong advocate for genomics research. She was also responsible for passing the 2003 resolution in the U.S. House of Representatives that created National DNA Day. NHGRI established the Slaughter lecture in 2018.

In 2004, Johnson worked as a DNA laboratory manager at the Australian Museum, one of the world's oldest natural history museums, in Sydney, Australia. The museum contains millions of specimens from a vast number of countries around the globe and thousands of frozen genomic samples.

That same year, police asked for her help solving an allegation of animal cruelty. A man was accused of intentionally driving his car through a flock of cockatoos. After the incident, police found blood under the man's car, but they had no way of determining what animal the blood came from. The officers called Johnson.

"I thought, as a geneticist, I could certainly help with this identification," she said. "Working at the Australian Museum, I had plenty of access to cockatoos that I could use as reference samples." A detailed DNA analysis revealed the blood indeed was cockatoo.

Johnson has since analyzed many samples linked to wildlife crime, a fast-growing, multi-billion-dollar industry. Her background allows her to give authorities genetic data that provides evidence in court.

In one instance, her forensics lab developed a DNA test for the species identification of rhino horns. The greatest threat to these animals is poaching their horns for illegal trade. Rhinos are being killed faster than they can reproduce.

There are 5 species of rhinoceros—2 are endemic to Africa and 3 are native to Asia. Johnson said identifying where the horn originated is very important "if you're trying to prosecute a case based on where it might have come from or get intelligence as to what species is being targeted by poachers."

Her lab shared the testing method with several countries in southeast Asia because trade in rhino horns is higher in that part of the world. Several nations used the test before she could publish her results, a circumstance she described as both encouraging and depressing, because there's such a high demand for such testing.

Johnson's lab also developed a DNA test to track the source of echidnas in the illegal wildlife trade. Echidnas are egg-laying mammals native to Australia and a few countries in southeastern Asia.

Each year, more than 150 "captive-bred" echidnas are offered for sale to zoos and other collecting institutions. However, these animals are notoriously difficult to breed in captivity. Within the past 10 years, only 30 baby echidnas, or puggles, were born in Australian zoos.

"The equation didn't fit that 150 captive-bred animals were being sold," she said. "We thought this might be worth investigating. We worked with several zoos who really, really wanted to make sure they were sourcing their animal from ethical and legal sources."

In some instances, trafficking of a species declines once it's known there is a DNA test for that species. Johnson isn't sure if echidna trafficking has declined yet.

Australia has one of the worst extinction rates in the world. Since Europeans settled the country in 1788, more than 10 percent of Australian land mammals have gone extinct. One of the most famous examples is the thylacine, also known as the Tasmanian tiger, the last of which died on Sept. 7, 1936, in captivity.

"It's a reminder that you can't just sit by and watch. Intervention needs to happen well before you're looking at the last animal," Johnson warned.

As the climate gets hotter and urban development further encroaches on forested areas, many species are at risk for extinction, including red-tailed cockatoos and koalas.

Red-tailed cockatoos inhabit savannahs, deserts, temperate forests and woodlands across Australia. These large iconic cockatoos nest in hollows inside old trees. Unfortunately, these older trees are disappearing due to change in land use (land clearing) and climate change. This has decimated the bird species population in certain areas.

★★★

"[Exctinction is] a reminder that you can't just sit by and watch. Intervention needs to happen well before you're looking at the last animal."

-DR. REBECCA JOHNSON

★★★

Thanks to genomics, Johnson and her team have identified new cockatoo subspecies. This means her group can determine which subspecies are most at risk. In a southern area of Australia, for instance, one subspecies has fewer than 1,000 birds. This means conservationists can direct resources at conserving that population.

Another iconic Australian species, the koala, is under threat from habitat loss, climate change and disease. Over the next 15 years, several koala populations are projected to decline by up to 53 percent in some areas.

A few years ago, Johnson and a team of experts successfully sequenced the koala

Johnson's lab developed a test to identify where rhino horns originated.

genome, which has revealed important information about their diet and genetic diversity. The data was integrated into a plan to conserve the species.

A koala's diet consists primarily of leaves from toxic eucalyptus species. They are essentially "super-detoxing" organisms. Johnson explained, "They're one of the very few animals that has been able to specialize, to eat something that's not just unpalatable to most other species, but deadly in high enough quantity."

Understanding how koalas metabolize eucalyptus leaves has implications for veterinary care.

Some koala populations in Australia vary in genetic diversity. The population in the north is very diverse, while the population in the south is abundant, but inbred. "This is not a great practice to perpetuate," she said. "There's a lot of discussion about how this might be handled going forward."

Now at the Smithsonian, Johnson is working hard to develop the museum's genomics department. "We have an extremely active genomics community and are specializing our environment that maximizes our ability to extract valuable information from museum collections, so we can be good contributors and collaborators to the knowledge of biodiversity," she concluded.

'INTEGRATING SEX, GENDER IN RESEARCH'

5th Pinn Symposium Features Dean, Fauci

By Eric Sarlin

ORWH, in partnership with the Foundation for the NIH, virtually hosted the 5th annual Vivian W. Pinn Symposium, in honor of the office's first full-time director. This year's event, "Integrating Sex and Gender into Biomedical Research as a Path for Better Science and Innovation," focused on illustrating the scientific, societal and economic opportunities of integrating sex and gender into biomedical research.

The annual Vivian W. Pinn Symposium honors ORWH's first full-time director.

After remarks by current ORWH director Dr. Janine Clayton, FNIH president and executive director Dr. Maria Friere and NIH director Dr. Francis Collins, U.S. Rep. Madeleine Dean of Pennsylvania's 4th District delivered the symposium's keynote address. She discussed efforts to ensure inclusion of women in federally funded scientific studies, the benefit of recruiting and retaining women and people of color in health care and the progress that has been made in integrating sex as a biological variable throughout biomedical research.

Dean described sex differences in Covid-19 symptoms and outcomes as well as the adverse economic and mental health effects facing women throughout the pandemic.

The 2-day symposium featured several thoughtful panel and breakout session discussions: how academic institutions and federal agencies can lead sex and gender integration, how reporting and communication can advance such integration, how businesses can find economic opportunities in sex- and gender-based research as well as other topics.

Congresswoman Madeleine Dean (D-PA) speaks virtually at the recent symposium.

Day 1 of the symposium concluded with a "fireside chat" with Pinn and NIAID director Dr. Anthony Fauci. He spoke about how Covid-19 has increased attention to sex and gender differences in medicine.

Pinn discussed her career at ORWH, mentorship, the challenges of being a women of color in medicine, the role of men in women's health research, women in government leadership and ORWH's research supplements to promote re-entry into biomedical and behavioral research careers.

Pinn closed the 2-day symposium by reviewing ORWH's past, current and future missions and goals.

ORWH developed a "virtual environment" for the symposium that includes exhibits, agendas, videos and other materials related to the integration of sex and gender into biomedical research. The environment will remain available until spring 2022.

Video recordings of the symposium are available at https://videocast.nih.gov/watch=41820 and https://videocast.nih.gov/watch=41819.

Day 1 featured a "fireside chat" with Pinn (top, l), ORWH's Jamie White and NIAID director Dr. Anthony Fauci.

Chanock

CONTINUED FROM PAGE 1

may be passengers—due to the cancer phenotype being expressed."

Medical observations of cancer running in families began more than a century ago, before anyone had ever described a gene. Then came a game-changer, in 1969, when research by two NCI scientists—Drs. Fred Li and Joseph Fraumeni—launched the era of cancer genetics.

"This really changed the landscape, the capacity to see that different types of cancer could arise in families with supposedly the same genetic makeup," said Chanock.

He has devoted his career to the genetic underpinnings of cancer, from identifying mutations to understanding genetic-environmental interactions that make some people more susceptible to cancer. Most attributable risks, he said, come from environmental factors such as smoking, obesity and exposure to toxic chemicals and radiation.

"These activities, these environmental/lifestyle choices—or sometimes they're not choices, but exposures—interact with the host genome," he said. "That relationship is really the central question I see that the next 20 years of cancer research has to investigate thoroughly to understand the fundamentals that would better enable us to come up with both precision preventive models and also therapies."

Environmental stimuli lead to mutations in the cells. Cancer develops progressively over time, as different driver mutations take over, explained Chanock.

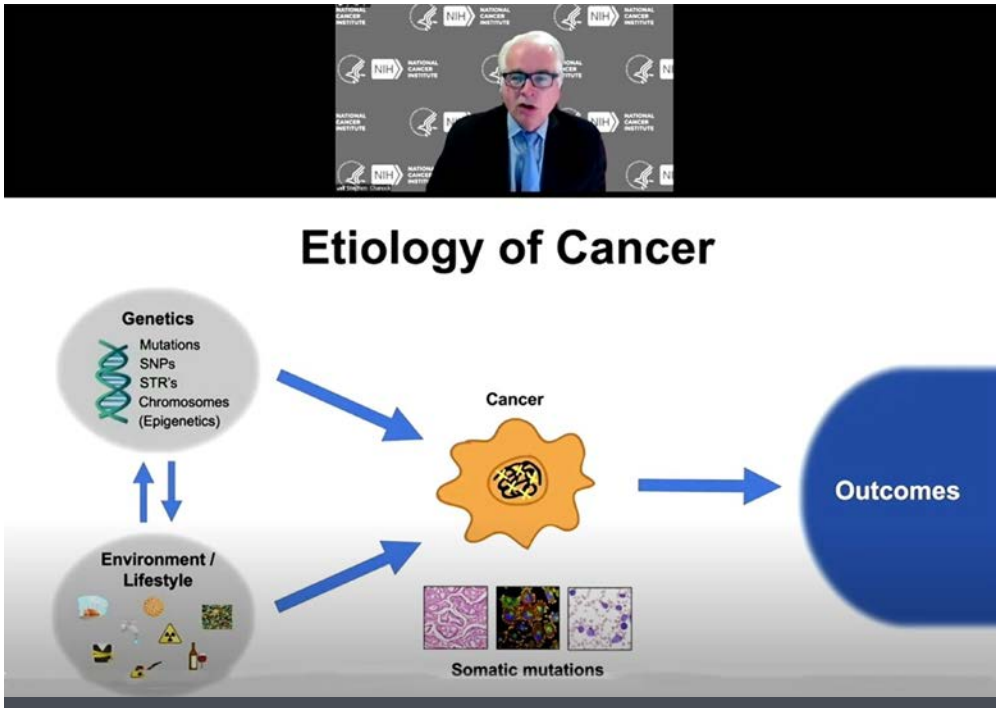
"Somewhere between the exposures of lifestyle and baseline genetics, our genetic germline is indeed falling apart," he said. His lab continues to isolate variations in large population and family studies, trying to understand not only the interaction between exposures and mutations, but also what happens in between.

One large, longterm study exploring the interaction between genetics and environmental exposures is looking at the effects of radiation exposure from the 1986 Chernobyl nuclear accident in Ukraine. One recent finding, said Chanock, is that in people younger than 18 at the time of exposure who developed cancers over the next 20 years, nearly 95 percent of the mutations involved a specific pathway, MAPK. A separate family study is looking at whether direct radiation exposure in the cleanup workers could affect successive generations. Thankfully, the data do not support a strong transgenerational effect. This has important implications for those exposed after the Chernobyl accident but also those exposed after the 2011 Fukushima nuclear accident in Japan.

Chanock has served as medical director at Camp Fantastic, a recreational camp for pediatric cancer patients, for 25 years.

Looking at large populations through genome-wide association studies (GWAS) helps investigators stratify cancer risk. To date, investigators can validate and fully understand only 5-10 percent of all GWAS signals. They do know there are more than 1,200 separate regions across the genome associated with 1 or more, and up to 30, cancers, said Chanock. But it takes years to understand and ascribe functions to each one of these specific GWAS loci.

"What's also striking is that only a handful of these 1,200 [regions] have a strong signal that's associated with outcome," he said. "So what we're looking at is this complex temporal model of cancer. What kinds of perturbations set the stage for cancer to develop in an individual may be very different than what's responsible for either protecting or not protecting an individual as they undergo therapy and try to control cancer that's growing out of control."



Chanock discusses the complex interplay of lifestyle choices, environmental exposures and genetics in propagating cancer.

Above (from l): Former Children's Inn CEO Kathy Russell joins Chanock, Diane Baker and her husband NIH director Dr. Francis Collins at a 2013 Camp Fantastic event.

PHOTO: ERNIE BRANSON

Further complicating the landscape, many variants each contribute a small effect to a large fraction of cancers. And each cancer has a different genetic architecture. About 85 percent of variants are specific to a certain cancer. With only 15 percent of variants shared between cancers, different strategies are needed to target different cancers.

Advances in cancer research rely on pooling dozens of large, distinct GWAS studies from around the world. "[These studies allow us] to work forwards and backwards to keep getting bits and pieces or handles on what we see as the complex paradigm of development of cancer," Chanock said. "The value of data-sharing couldn't be overstated, because it's really team science at its best."

GWAS helps investigators assign polygenic risk scores with the goal of using the data for clinical care. Looking within a population, Chanock and colleagues examine all the SNPs ("snips"—or, single nucleotide polymorphisms—which are variations at a single point in DNA) associated with risk for a particular cancer that has high heritability. "That helps us to have a risk score with a predictive ability," he said.

In a study of more than 100,000 people, for example, investigators found higher genetic risk profiles for prostate cancer in men of African-American ancestry. By assigning risk scores to populations of different descents, researchers can better understand unique biologic features that could lead to better therapies and better opportunities to stratify groups of individuals at high risk for more intensive screening.

For breast cancer, the deleterious mutations in the BRCA 1 and 2 genes explain less than a fifth of cases in the U.S., said Chanock. GWAS data has helped piece together another 40 percent of breast cancer-causing genes, but a third of cases remain unexplained. Large, multi-ancestral GWAS are helping researchers understand subtypes and discover variants to improve treatment, prevention and survival.

• • •

"That relationship [between environmental exposures and the host genome] is really the central question I see that the next 20 years of cancer research has to investigate thoroughly."

DR. STEPHEN CHANOCK

• • •

"Don't be afraid to look at old problems with new approaches," advised Chanock, who reiterated the importance of team science. "Context matters. Numbers matter even more. Your colleagues matter most."

NLM's Altschul Named Scientist Emeritus

NLM recently announced the appointment of Dr. Stephen Altschul as a scientist emeritus at NIH. He is the first NLM intramural investigator to receive the honor.

Dr. Stephen Altschul

In this role, Altschul will continue to collaborate with scientists inside and outside NIH, complete existing and join new research projects and write and review scientific journal articles.

Altschul retired as a senior investigator in the Computational Biology Branch at the National Center for Biotechnology Information in September 2020. Over the course of 35 years at NLM, he managed a robust bioinformatics research portfolio.

OD Launches Well-Being Campaign

A happy, healthy workforce is a productive one. With that in mind, the Office of the Director Resilience through Well-Being campaign has launched to help support staff in these changing times. The campaign was inspired by the pandemic, which magnified stress and disrupted lives, and now leaves many people feeling apprehensive in the face of constant change. Building on NIH leadership's commitment to fostering work-life balance, the campaign features tools, events and shareable resources designed to empower staff to embrace well-being with increased awareness.

Resources available in the new shared hub include:

• Interactive platforms to share information and discuss well-being topics

• A supervisor's toolkit to foster a healthier, more resilient and supportive culture among their teams

To learn more, visit the OD intranet site at https://employees.nih.gov/pages/od-well-being-campaign/index.aspx. Also see: employees.nih.gov/pages/coronavirus/wellness-resources-aspx.

OD will share resources with other interested institutes, centers and offices. Connect with campaign staff at nihchangemanagement@od.nih.gov.

EMPOWER

CONTINUED FROM PAGE 1

specialized prostheses that allowed him to climb even better than before. His interest in prostheses led him to a career in bionic limb design. Herr is currently a professor at MIT, directing the biomechatronics research group and co-directing the MIT Center for Extreme Bionics.

Herr describes bionics as "this glorious interplay between biology and engineering design" and utilizes this interplay in the research that has produced his current legs (and the legs that have given new life to many other amputees): "EmPower."

In his recent Wednesday Afternoon Lecture Series presentation, "On the Design of Bionic Limbs: The Science of Tissue-Synthetic Interface," Herr spoke about a new surgical technique developed by his lab that allows for direct communication between the nervous system and bionic prostheses like EmPower.

Up until very recently, amputation surgeries were what Herr referred to as "Civil War-era amputations." The limb was removed with little thought as to how it would interact with a prosthetic device. Herr saw a way to improve this system, namely, by linking a bionic–computer-powered–limb to the wearer's nervous system. He calls it "neuro-embodied design," or, a way to "co-design the biological body with [a] synthetic construct to maximize bi-directional communication between the device and the human nervous system." In other words: a computer-powered bionic limb can both send and receive electrical signals to and from the wearer's nervous system.

• • •

"Human beings aren't broken. They aren't weak. They aren't disabled. The technology is weak and disabled and broken."

-DR. HUGH HERR

• • •

The Civil War surgeries that Herr described remove limbs with little regard for the musculature at the end of the appendage. In 2015, he and his colleagues devised a new surgery: agonist-antagonist myoneural interface (AMI).

Muscles typically work in groups of two to move an appendage: the antagonist is stretched as the agonist contracts. Typically, the agonist muscle contracts when it receives an electrical signal from the central nervous system (CNS). The connections between many agonist-antagonist groups are often severed in the old amputation method, but AMI reconnects these pairs (native) and/or builds new ones (regenerative).

Herr saw a way to improve interaction between the body and prosthetic devices by linking a bionic–computer-powered–limb to the wearer's nervous system.

Artificial muscle electrodes are placed on each AMI pair and communicate with computers within the bionic limb. When the agonist muscle contracts due to electrical activation (from the CNS or prosthetic computer), that contraction stretches the antagonist muscle, and these dynamics are communicated to the CNS, giving the person a sense of muscle length, speed and force. This sense is known as proprioception, or awareness of the position and movement of the body. It's absent or much diminished in patients who did not undergo the AMI procedure.

Conversely, amputees who received AMI feel the motion of their bionic limbs, and can also move them in natural, reflexive ways.

Herr is also conducting trials to improve prosthetic technology further. The studies involve implanting magnetic beads into AMI muscle pairs to allow the bionic limb's computers to better track muscle contractions, and linking cutaneous (skin) nerves to the limb to replicate the sensation of touch.

He ended his lecture with a video of an AMI recipient returning to the site of his accident, where he completed his climb with his bionic limb.

"Human beings aren't broken; they aren't weak; they aren't disabled," Herr concluded. "The technology is weak and disabled and broken. [We should] always strive for better and better rehabilitation and assistive technology interventions, with the long-term goal of dramatically mitigating or even eliminating disability."

Employee Asymptomatic Testing Clinic Changes Hours

The Employee Asymptomatic Testing Clinic on the 5th floor of the CRC has changed its days of operation. Now, employee asymptomatic testing is available only on Tuesday and Friday. The change was made on July 6.

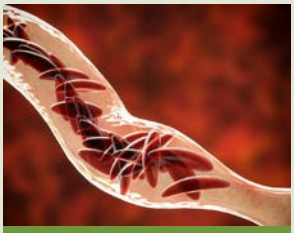
Testing for SARS-CoV-2 involves a traditional nasopharyngeal swab, which looks like a 6-inch Q-tip. The swab is inserted through the nose to the back of the throat, rotated several times and left in place for 10-15 seconds. The hospital also offers Covid-19 saliva tests.

To sign up for asymptomatic testing, NIH'ers can visit https://clinweb.cc.nih.gov/cct.

Can Base Editing Fix the Sickle Cell Disease Gene?

Researchers recently treated sickle cell disease in mice by directly editing the defective gene that causes the disease. Several NIH institutes supported the research, which appeared online in *Nature*.

"The approach offers promise as the basis of a potential one-time treatment, or perhaps even a one-time cure, for sickle cell disease," said senior author Dr. David Liu of the Broad Institute.



In sickle cell disease, red blood cells take a crescent, or sickle, shape that can block blood vessels.

IMAGE: DR. MICROBE/ISTOCK/GETTY

In SCD, a T replaces an A at a key location in the *HBB* gene, causing hemoglobin molecules to stick together and form sickle-shaped red blood cells. This can lead to blood cell rupture, anemia, recurring pain, immunodeficiency, organ damage and early death.

New SCD treatments currently under development edit the genes of the patient's own bone marrow cells to produce normal-functioning hemoglobin. Because these treatments involve introducing new DNA and cleaving existing DNA strands, they carry risks of side effects.

In the new study, researchers used base editing to convert the problematic T to a C instead. This produces a naturally occurring, non-pathogenic hemoglobin variant called Hb-Makassar. Unlike other gene-editing techniques, base editing changes a single letter of the genome without cutting any DNA.

The researchers edited blood-forming stem cells from human SCD patients. Up to 80 percent of cells had the sickle-cell hemoglobin gene converted to the Makassar variant. For testing, the team transplanted the edited human cells into a mouse model of SCD. After 16 weeks, 68 percent of the donor-derived stem cells had *HBB* genes edited to Hb-Makassar. Red blood cells derived from these stem cells had significantly reduced sickling.

The team next edited stem cells taken from a mouse SCD model and transplanted them into another set of mice. After 16 weeks, the Makassar variant made up almost 80 percent of the hemoglobin in the recipient mice. Control mice that received unedited cells had characteristic SCD symptoms. Mice given the edited stem cells had greatly improved symptoms without side effects.

The team is now working to develop the concept further, with the eventual goal of reaching patients.—**Brian Doctrow**, *NIH Research Matters*

Study Offers New Evidence of Early Covid Infections in U.S.

A new antibody testing study examining samples originally collected through NIH's All of Us Research Program found evidence of SARS-CoV-2 infections in five states earlier than had been reported initially. These findings were published in the journal *Clinical Infectious Diseases.*

The results expand on findings from a CDC study that suggested SARS-CoV-2, the virus that causes Covid-19, was present in the U.S. as far back as December 2019.

In the All of Us study, researchers analyzed more than 24,000 stored blood samples contributed by program participants across the country between Jan. 2 and Mar. 18, 2020. Researchers detected antibodies against SARS-CoV-2 in 9 participants' samples. These participants were from outside the major urban hotspots of Seattle and New York City, believed to be key points of entry of the virus in the U.S.

An All of Us team member handles participant samples.

The positive samples came as early as Jan. 7 from participants in Illinois, Massachusetts, Mississippi, Pennsylvania and Wisconsin. The study authors noted they did not know whether they became infected during travel or while in their own communities. Most positive samples were collected before the first reported cases in those states, demonstrating the importance of expanding testing as quickly as possible in an epidemic setting.

All of Us worked with Quest Diagnostics to test samples on the Abbott Architect SARS-CoV-2 IgG ELISA and the EUROIMMUN SARS-CoV-2 ELISA (IgG) platforms. The results include only samples that tested positive on both platforms.

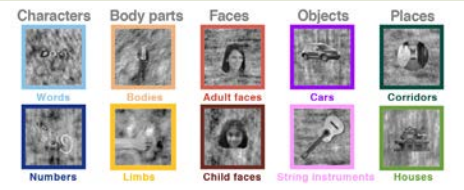
Researchers looked in participant samples for a type of antibodies [proteins in the blood that can demonstrate prior infection] called IgG, which do not appear until about 2 weeks after a person has been infected, indicating that participants with these antibodies were exposed to the virus at least several weeks before their sample was taken. In this study, the first positive samples came from participants in Illinois and Massachusetts on Jan. 7 and 8, 2020, respectively, suggesting the virus was present in those states in late December.

NEI Study Shows Children Recycle Brain Regions When Acquiring New Skills

Scientists studied the brain activity of school-age children and found the brain can repurpose parts when learning to recognize faces and to read. Brain regions that activated upon seeing limbs subsequently activated upon seeing faces or words when the children grew older.

The research by Stanford University scientists reveals new insights about vision development in the brain and could help inform prevention and treatment strategies for learning disorders. The NEI-funded study is published in *Nature Human Behaviour*.

Grill-Spector's team used functional MRI to study areas in the ventral temporal cortex (VTC) that are stimulated by the recognition of images. About 30 children, ages 5 to 12 at their first MRI, participated in the study. While in the MRI scanner, the children viewed images from different categories, including words, body parts, faces, objects and places. The researchers mapped areas of VTC that exhibited stimulation and measured how they changed in intensity and volume on the children's subsequent MRI tests over the next 1 to 5 years.



IMAGES: KALANIT GRILL-SPECTOR AND MARISA NORDT

Results showed that VTC regions corresponding to face and word recognition increased with age. Compared to the 5- to 9-year-olds, teenagers had twice the volume of the word-selective region in VTC. Notably, as word-selective VTC volume doubled, limb-selective volume in the same region halved. Investigators noted the decrease in limb-selectivity is directly linked to the increase in word- and face-selectivity, providing the first evidence for cortical recycling during childhood development.

Study authors suggest that cortical recycling in VTC likely reflects adjustments to changing visual demands during childhood. For example, infants tend to look at faces. As they grow into toddlers and learn language, they are exploring objects and deciphering gestures. Word recognition becomes increasingly important as children learn to read.

Shingler Retires After More Than 35 Years of Federal Service

BY CARLA GARNETT

Felicia Shingler's NIH career has come full circle. She began in 1981 hand-carrying documents to Bldg. 1 and last year (about 35 years later), just before lockdown, she found herself hand-carrying items to Bldg. 1. Back in the 80s, she was a summer aide getting her first taste of federal government work. This June, she retired as manager of the NIH Director's Awards Program in the Office of Management, Office of the Director.

Felicia Shingler

"From the beginning, NIH has always represented excellence and a high purpose for me," Shingler said. "I've always tried to meet or exceed that level in every position I've had here. I could've continued forever as the NIH Director's Awards program manager, because this is really a dream job. Managing this program is not like work. I love what I do."

Longtime NIH'ers past and present could have predicted Shingler's success.

"I knew from the moment I hired her as my secretary that she would leave me in a short time—but it was worth it," said Dr. Carole Heilman, retired former director of NIAID's Division of Microbiology and Infectious Diseases and one of Shingler's early supervisors. "Felicia had the drive, the work ethic and the smarts to make it worth my while to help her leave the job she would shortly be overqualified to do."

Over the course of her career, Shingler served in several NIH components and roles. In addition to NIAID and OD, she worked at the Division of Research Grants, the precursor to the Center for Scientific Review.

As a writer-editor, she worked for more than 25 years as the NIH activity codes' manager. She also served as lead for the eRA documentation and training team and worked briefly on the *NIH Guide*.

Ever interested in equity issues, Shingler was selected by then-NIH director Dr. Bernadine Healy to serve on a 17-member Task Force on Fairness in Employment Practices that was instrumental in establishing the reprisal and retaliation section in the *NIH Policy Manual*.

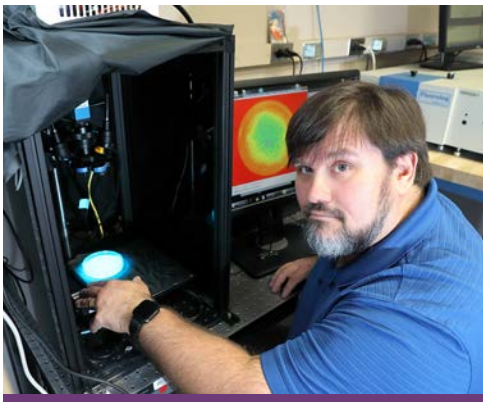
In 1991, Shingler was elected as chair of a newly established Young Adult Resources and Development (YARD) group within NIH's chapter of the Blacks In Government (BIG) organization. That fall, the BIG YARD chair invited former NIH researcher and D.C. council member Dr. Charlene Drew Jarvis to NIH as guest speaker at a special forum in Lipsett Amphitheater.

Shingler's responsibilities and commitment to BIG service grew as her career progressed. In time, she was elected as NIH chapter president, chaired the organization's national communications and public relations component, served as national secretary and sat on BIG's board of directors. In 2014, BIG named Shingler to its Distinguished Service Hall of Fame, the organization's highest honor.

In 35-plus years at NIH, Shingler has at times met with agency luminaries, including NIH director Dr. Francis Collins and NIAID director Dr. Anthony Fauci—interactions that have new meaning in the age of Covid-19 and NIH's higher profile.

"They were both so down to Earth and willing to talk to anyone—no matter where people worked in the organization—that I was honored to have an opportunity to interact with them," Shingler recalled. "To have Dr. Collins recognize me and say, 'Felicia, you're doing a fabulous job. Thank you so much for putting this together'...was a definite highlight of my career at NIH."

Last fall, with the majority of NIH'ers working remotely, Shingler singlehandedly packaged and mailed more than 660 award items to NIH Director's Award recipients, because the in-person ceremony could not be held due to the pandemic. Distributing the awards is a job that usually requires a dozen volunteers, but Shingler handled it personally. She hopes that her dedication and work ethic will be how colleagues remember her federal service.



Dr. George Patterson

NIBIB Investigator Patterson Is Mourned

Dr. George Patterson, a tenured senior investigator in the NIBIB intramural section on biophotonics, passed away on June 20 after a battle with cancer. He was 50.

A groundbreaking and world-renowned researcher in the development of photoactivatable fluorescent probe imaging, he was a respected global leader in the photoactivatable microscopy field and was widely considered unrivaled in the development of new methods using photoswitching and photoconversion of proteins.

Patterson joined NIH in 1999 as a postdoctoral fellow in the laboratory of Dr. Jennifer Lippincott-Schwartz in the National Institute of Child Health and Human Development. Four years later, he accepted a staff scientist position in Lippincott-Schwartz's laboratory, collaborating with Drs. Eric Betzig and Harald Hess on their new PALM fluorescence imaging technique.

Patterson's discoveries with photoactivatable genetically encoded proteins made fundamentally enabling contributions to the work that led to Betzig's 2014 Nobel Prize in Chemistry.

Since starting his own lab at NIBIB in 2009, Patterson continued to innovate in the development of novel fluorescent proteins and their application to biological discovery. He was honored by the Royal Microscopical Society as 2021's first recipient of the society's Scientific Achievement Award. He received an NIH Director's Award in 2016.

Patterson was an internationally respected pioneer in the development of probes and techniques for diffraction-limited

and sub-diffraction limited fluorescence imaging, with more than 13,000 citations on the Web of Science, including 1,000 citations per year for the past 6 years.

"We are grateful for his groundbreaking scientific contributions and the opportunities many of us have had to work with and learn from George over his distinguished 22-year NIH career," said NIBIB director Dr. Bruce Tromberg. "George created a warm and inclusive laboratory environment with an emphasis on interdisciplinary collaboration, and mentoring."

Patterson provided valuable service to the NIH and greater biomedical communities, most recently as a proposal reviewer for the Chan-Zuckerberg Initiative; as a member of the Earl Stadtman investigator search committee (biomedical imaging/biophysics/physics); and on NIBIB's anti-harassment working group.

He will also be remembered as an outstanding mentor with a commitment to recruiting diverse staff to his laboratory.

"Patterson's passing is a great loss for his many colleagues and friends in NIBIB, around the NIH and around the world," concluded a coworker.

He is survived by his wife Susanne Neumann, and children Isabella (11) and Max (9).

RML Campus Mourns Loss of Photographer Kercher

BY KEN PEKOC

Bryan Kercher, who was responsible for practically every NIH photo over the last decade showing the serene Montana setting at NIAID's Rocky Mountain Laboratories, died in a climbing accident on May 8. He was 55.

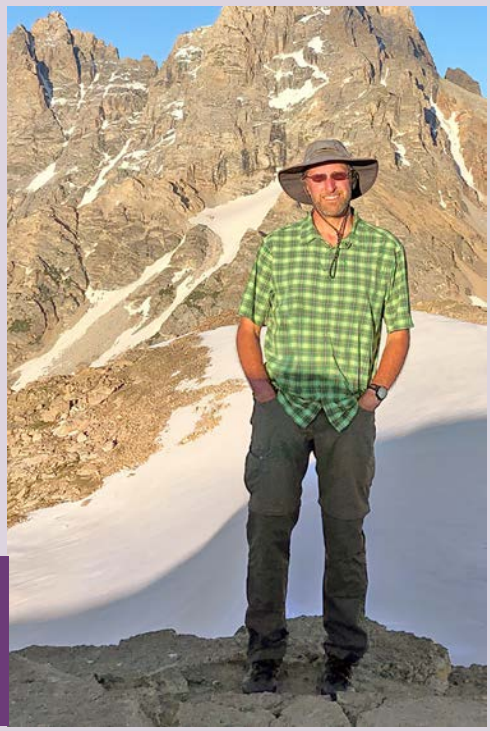
The accident took place on Sugarloaf Peak, about 30 miles south of the RML campus in Hamilton, where Kercher had worked for nearly two decades. He began as an RML security guard in the early 2000s before NIH's Office of Research Facilities hired him in 2008 as an engineering technician, the position he held at the time of his death.

Along with having key roles in most every facility project at RML, Kercher also was heavily involved with Club RML, part of the NIH Recreation and Welfare Association. He was a mainstay in several community groups and activities, from Boy Scouts of America to the Rocky Mountaineers. His knowledge of, and stories from, local trails and peaks—Glacier National Park in particular—regularly inspired friends and coworkers.

Whether at work or play, Kercher often carried multiple cameras so he could be sure to share his experiences: Progress on an RML construction project; a moose wandering next to the RML campus; the glistening spray from Sweathouse Falls; breathtaking views from an ascent of Alaska's Denali.

An exemplary worker, Kercher always led by his humble and quiet demeanor, willing to do whatever was needed, with a smile, and often behind the scenes.

"Bryan played an absolutely critical role on our facilities management team," said his supervisor at RML, Eric Hanssen, during a campus memorial gathering. "With all he was involved in and responsible for, he is truly irreplaceable. Not only have we lost an incredibly talented coworker and colleague, we have lost a friend who we interacted with almost every day."



Bryan Kercher in 2020 stands atop Table Mountain in the Teton Mountains of Wyoming. Below, one of the last photos he took of the RML campus, May 6, via a drone

Capt. Ann Marie Matlock (l) chats with NIH director Dr. Francis Collins about construction of the screening booths and how much of an improvement they were over the carts and plexiglass that were used at the beginning of the pandemic. Shown in the background is registered nurse Aisha Bundu-Wurie; at right is Anitra Fitzgerald-Monroe, senior clinical research registered nurse. In photo at right, Collins talks with staff in the 5th floor atrium.

Director Hails Asymptomatic Testing, Screening Staff

NIH director Dr. Francis Collins visited on June 7 with staff who conduct Covid-19 asymptomatic testing and screening at the Clinical Center. CC CEO Dr. James Gilman accompanied Collins on a tour of operations that began at Bldg. 10's north entrance, where the director thanked screeners and guards. The tour next stopped on the 5th floor where Collins met with various groups, then continued to the South Lobby where he applauded staffers there. Capt. Ann Marie Matlock, chief of the medical surgical specialties service at the Clinical Center who took the lead on asymptomatic testing, was also on hand for the tour. In the last few months, Collins has been on a "Gratitude Tour," lauding NIH operations and employees who performed unusual and extraordinary services throughout the pandemic.

Screening Facts

• Screening began March 2020 in the north, south and P1 lobbies

• Additional morning screening for staff began in October at the P3 garage entrance and in June 2021 at the Blood Bank entrance

• Total persons screened (as of June 3, 2021): 1,462,994

• Most screened persons in one day (Apr. 21, 2021): 5,920

• Most screened persons in a 6-hour block (6 a.m.-noon): 2,251 in the South Lobby

Testing Facts

• NIH Bethesda Patient Care began testing on May 21, 2020

• Campus began testing on Aug. 11, 2020

• Total tests (5th fl. as of June 3, 2021): 111,713 tests run with specimens from 12,517 staff

• Highest 3 days for testing (5th fl.): 1,307 tests (Dec. 22), 1,148 tests (Nov. 23) and 1,110 tests (Nov. 24)

• Highest 3-day test total for Clinical Center: 2,379 (Dec. 20-22)

• Tests per person: 309 people tested between 40-49 times, 44 people more than 50 times, 8 people more than 60 times, 3 people more than 70 times, and 2 people more than 80 times

• Saliva testing began Sept. 13; 25 percent of first-time testers choose the saliva test

• Number of platforms for testing: 6

• Number of validations of SARS-CoV-2 PCR: 14 (due to supplies and equipment shortages, combined with platforms with different turnaround times). Typically, only 1 validation for a single viral target

• Highest month for Patient Portal support calls: 1,274 calls in and 1,078 out (November)

Collins (shown at right in these photos) toured several testing and screening operations in several locations around the Clinical Research Center. In every area, he met with staff and chatted about their roles in the effort that began in March 2020 and experienced a number of busy periods as the pandemic evolved.

PHOTOS: CHIA-CHI CHARLIE CHANG