

‘CUMULATIVELY COMMON’ Rare Diseases Are a Public Health Issue

BY ERIC BOCK

Rare diseases are a public health issue, said NCATS director Dr. Christopher Austin during NIH’s annual—and first virtual—observance of Rare Disease Day.

“Although they are individually rare, they are cumulatively common,” he said. People who have them make up about eight percent of the global population—that’s about the same proportion who have diabetes. “Everybody knows diabetes is a public health problem, but rare diseases are not appreciated as being a public health problem.”

SEE **RARE**, PAGE 8



Isabella and Julia Flysjo, age 4, are part of a first-in-human gene therapy trial at the Clinical Center for their rare disease.

Two Families Grapple with Rare Disease Diagnosis, Finding Treatments

BY DANA TALESNIK

It’s agonizing for parents to watch their children suffer and not know how to help them. When parents learn their child has a rare disease, consumed with grief and fear, they try to navigate the confusing medical lingo for diseases that have limited resources and few, if any, effective treatments.

Two families were among those who shared their rare disease journeys during NIH’s Rare Disease Day virtual event on Mar. 1. In both cases, their babies were born seemingly healthy. Then, around age 2, worrisome symptoms appeared that led these families to seek a medical evaluation.

SEE **TWO FAMILIES**, PAGE 6



Nature inspires two photographers to next level. See p. 12.

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NIMHD director Dr. Eliseo Pérez-Stable discusses CEAL at the Washington National Cathedral.

PHOTO: CHIA-CHI CHARLIE CHANG

A ‘LOVE YOUR NEIGHBOR OPPORTUNITY’ NIH’ers Join Faith Leaders at Vaccine Confidence Event

BY CARLA GARNETT

NIH director Dr. Francis Collins, NIAID director Dr. Anthony Fauci and NIMHD director Dr. Eliseo Pérez-Stable joined faith leaders, local health care providers and other public health officials Mar. 16 to promote immunization against Covid-19 and inspire

SEE **CATHEDRAL**, PAGE 4

THE SKINNY ON PEMPHIGUS

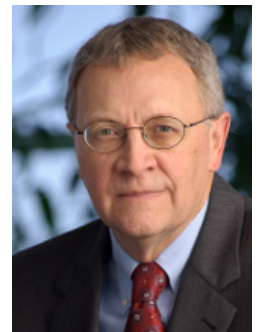
Yancey Traces Decades of Skin Biology Advances

BY RICH MCMANUS

The word pemphigus, from its sound alone, was never going to denote something lovely, like the words Cleopatra or Cassiopeia.

A group of rare, autoimmune intraepidermal blistering diseases that affect skin and mucous membranes, pemphigus is nevertheless a lens through which investigators have learned much about the biology of human skin.

In a recent Contemporary Clinical Medicine: Great Teachers talk, Dr. Kim Yancey



Dr. Kim Yancey

SEE **YANCEY**, PAGE 10

ODP Early-Stage Investigator Lectures Set

NIH's Office of Disease Prevention will host two Early-Stage Investigator Lectures.

On Wednesday, Apr. 28 at 11 a.m. ET, Dr. Morgan M. Philbin, assistant professor, sociomedical sciences, Columbia University Mailman School of Public Health, will present "The Social Side Effects of Biomedical HIV Technologies: Facilitating the Roll-Out of Long-Acting Injectable ART and PrEP."



Dr. Morgan M. Philbin

Philbin will discuss current research on long-acting injectable antiretroviral therapy (ART) and HIV pre-exposure prophylaxis (PrEP) with a focus on the multilevel barriers and facilitators to successful implementation. She will also highlight key points that must be addressed to scale up biomedical HIV technologies—in ways that maximize population health impact and reduce existing disparities—related to current formulations of PrEP and ART. Her research has been funded by several institutes, including the National Institute on Drug Abuse, the National Institute on Minority Health and Health Disparities, the National Institute of Allergy and Infectious Diseases and the National Institute of Mental Health.

On Wednesday, May 5 at 11 a.m. ET, Dr. Stephen



Dr. Stephen Juraschek

Juraschek, assistant professor of medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, will present "Dietary Patterns to Prevent Cardiovascular Disease."

Juraschek will describe novel evidence in support of healthy dietary patterns to prevent mechanisms of sub-clinical cardiovascular damage. He will also

discuss the status of healthy eating and opportunities to enhance adoption of healthy eating in the United States. His research has been funded by the National Heart, Lung, and Blood Institute, the National Institute on Aging and NIMHD.

Registration is required. Use this link: prevention.nih.gov/news-events/early-stage-investigator-lecture/2021-awardees. Lectures will be recorded and available on the ODP website approximately 1 week after each session.

New Alzheimer's Website Introduced

NIA recently announced [Alzheimers.gov](https://www.alzheimers.gov), a new educational resource and portal to federal information on Alzheimer's disease and related dementias for people with dementia, caregivers, health care providers, community and public health professionals and researchers. The website is designed to help people find Alzheimer's information from the government all in one place. Visit <https://alzheimers.gov>.

Introducing the new Alzheimers.gov!

Your destination for dementia information, resources, and research

Visit www.alzheimers.gov



ODP Early-Stage Investigator Lectures recognize early-career prevention scientists who have not yet competed successfully for a substantial NIH-supported project, but who have already made outstanding research contributions to their respective fields and are poised to become future leaders in prevention research.



Dr. Ryan Shaw

Shaw To Present NINR Director's Lecture

On Tuesday, Apr. 20, Dr. Ryan Shaw will present the second NINR Director's Lecture of 2021, from 1 to 2 p.m. (ET) via NIH Videocast. In his presentation, "Digital Health: Towards the Next Era of Healthcare Delivery and Chronic Disease Management," Shaw will discuss the role that digital health is playing in transforming health care delivery and in creating new opportunities for chronic disease management across the lifespan.

Shaw is an associate professor at the Duke University schools of nursing and medicine. He is the director of the Health Innovation Lab, an accelerator to test new technologies and care delivery processes in both real and simulated clinical environments. He also serves as the faculty lead of the Duke Mobile App Gateway—a digital health initiative of the Duke Clinical & Translational Science Institute.

His research focuses on how data from mobile health and novel sensing technologies can be used for care delivery to improve health outcomes. He works to discover opportunities for integration of these technologies into software applications, including electronic health records, to leverage predictive analytics and forecast patient needs. With these data he engineers models of care

delivery that capitalize on the emerging digital health infrastructure of health systems and society.

The NINR Director's Lecture Series brings top scientists from across the nation who are advancing nursing science in significant ways to share their work and interests with a transdisciplinary audience at NIH and the broader biomedical research community. The event is free and open to the public. For more information and to register, visit <http://ow.ly/t2fa50E7laR>.

3-Day Virtual Postbac Poster Event Set

NIH Virtual Postbaccalaureate Poster Day 2021 will be held Tuesday, Apr. 27–Thursday, Apr. 29 via WebEx. There will be more than 120 poster sessions each with 5–7 poster presenters. Sessions will take place over 3 days and are organized into 4 timeslots. The event program book and presentation schedule are available on the event web page. Poster Day provides an opportunity for postbacs to share the research they have been conducting at NIH and develop scientific communication and networking skills. Investigators, staff scientists and scientific administrators can contribute by visiting posters and engaging authors in discussion. For details, visit https://www.training.nih.gov/virtual_postbac_poster_day.

NIHSA Seeks Students, Seasoned Sailors

The NIH Sailing Association (NIHSA) an R&W-supported club, offers an Introduction to Sailing course for NIH adult employees, contractors, fellows and patients. The spring course will be offered from May 4 to June 22. For details, visit www.nihsail.org. In-class sessions currently are held via Zoom. Instructor-led on-board sessions are conducted on Selby Bay and South River at the Selby Bay Marina in Edgewater, Md. Participants must provide their own transportation to and from the marina. For more information, email the basic training team at nihsa.basic.training1@gmail.com.

Experienced sailors, would you like to charter the NIHSA boats? Contact nihsa.contact@gmail.com about joining the club and doing a checkout sail. NIHSA is always looking for new members and experienced volunteers to help with in-class and on-board instruction.

CDC, NIH Collaborate to Bring Covid Self-Testing to Two Communities

Can frequent, self-administered Covid-19 testing help reduce community transmission? The CDC and NIH are teaming up on a community health initiative, “Say Yes! COVID Test,” to find out.

As many as 160,000 residents across Pitt County, N.C. and Chattanooga/Hamilton County, Tenn., will have access to free, rapid home-based antigen tests to use 3 times a week for 1 month.

“This testing initiative is the first of this scale to attempt to make free, rapid, self-administered tests available community-wide,” said NIH director

Dr. Francis Collins. “We hope to gain foundational data that can guide how communities can use self-administered tests to mitigate viral transmission during this and future pandemics.”

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“We hope to gain foundational data that can guide how communities can use self-administered tests to mitigate viral transmission during this and future pandemics.”

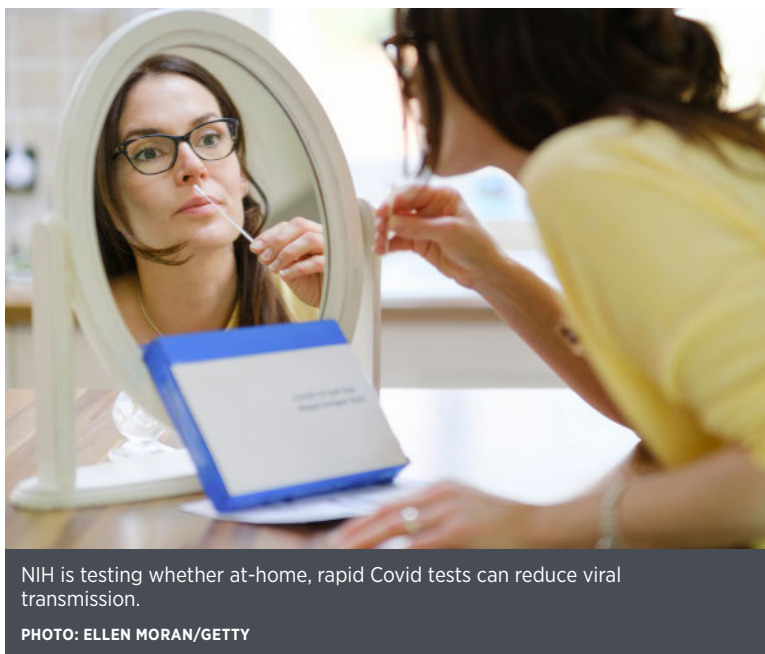
—NIH DIRECTOR DR. FRANCIS COLLINS

• • •

NIH is supplying those residents with the QuickVue test, developed by the company Quidel, which has received FDA emergency use authorization for at-home use with a prescription. The test, performed with a nasal swab, returns results within 10 minutes. The companion online

tool was developed by CareEvolution, with funding support from NIH.

This program will be facilitated by local health departments. A key component is ensuring that vulnerable and



NIH is testing whether at-home, rapid Covid tests can reduce viral transmission.

PHOTO: ELLEN MORAN/GETTY

underserved populations are aware and able to benefit from the opportunity. The communities were selected based on local infection rates, Covid tracking data, community relationships through NIH’s

Rapid Acceleration of Diagnostics Underserved Populations (RADx-Up) and local infrastructure to support the project.

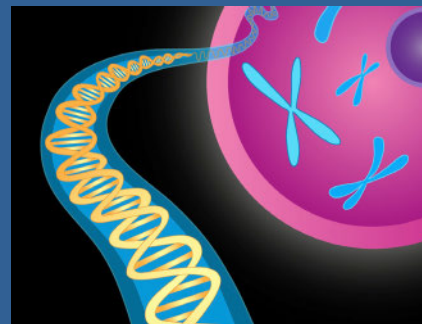
Researchers at NIH-supported University of North Carolina at Chapel Hill and Duke University

will work with the CDC and NIH to use publicly available Covid-19 case surveillance data on test positivity rates, Covid-related illness and hospitalizations and measurements of viral particles in sewage wastewater to evaluate viral transmission in the

community. At the same time, publicly available data will be reviewed from similar-sized communities that have not received widespread self-administered tests to evaluate the program’s impact.

Participants will also have the option to participate in a survey designed to determine whether frequent self-administered testing has made a difference in behavior, knowledge on preventing spread of the virus and thoughts about Covid vaccination.

“If self-testing is shown to effectively reduce viral spread in the selected communities,” said Dr. Elizabeth DiNenno, CDC associate deputy director for surveillance, epidemiology and laboratory sciences, “the hope is that it will lead to wider distribution and acceptance of frequent home testing across the country.” **R**



ON THE COVER: Illustration of chromosomes and DNA double helix.

IMAGE: NIMH

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Turning Discovery Into Health



Cathedral

CONTINUED FROM PAGE 1

confidence in the coronavirus vaccines. Held at the Washington National Cathedral, the event brought together representatives of 25 religious organizations—socially distanced and masked—to show a unified front in the pandemic fight.

“I’m honored to be in this sacred space with these leaders of multiple faiths,” said Collins. “Let us all recognize that the last year has been one of struggle and lament for all of us. And yet, we now have reasons for hope. As a believer and as a scientist, I can see the opportunity to use the tools of science to be part of God’s plan for healing. These vaccines have been in many ways, for many people, an answer to prayer. They are safe and effective beyond what we had a right to expect. And yet, they will not help people by sitting on the shelf. They need to be delivered into the arms of those who need them.”

In his turn at the lectern, Fauci, who also serves as chief medical advisor to President Joe Biden, presented facts about Covid



Above, after the remarks ended, several faith leaders were vaccinated on camera as examples for their worship communities. At right, Dr. Joseph L. Wright (l), senior vice president and chief medical officer of Capital Region Health within the University of Maryland Medical System, talks to Pérez-Stable (c) and Collins.



Above, NIH director Dr. Francis Collins speaks from the lectern at the Washington National Cathedral. At top left, NIAID director Dr. Anthony Fauci describes how Covid-19 vaccines work.

PHOTOS: CHIA-CHI CHARLIE CHANG

vaccines, how they were developed and the way they work in the body. He also answered several frequently asked questions about vaccination, and struck down several myths and misperceptions about the vaccines.

Pérez-Stable talked about NIH’s CEAL (Community Engagement Alliance Against Covid-19 Disparities), which works closely with populations hit hardest by Covid-19, including African Americans, Hispanics/Latinos and American Indians/Alaska Natives.

“I thought it was fitting for us to be here today, working to support and encourage all of our communities, all of our communities of color, to do what we can do to be safe, and

help end this pandemic that has devastated so many families in this country and around the globe,” he said. “This pandemic has illustrated inequities in our society that we knew about for decades, but really have been put in contrast in a rapid way.”

Also seated on stage was Melissa Rogers, executive director of the White House Office of Faith-based and Neighborhood Partnerships, who briefly addressed the assembly.

“This is one great example of a partnership between government and faith-based organizations,” she said. “As President Biden has recognized, faith-based organizations can play key roles in helping Americans get vaccinated... Indeed, partnerships with diverse faith communities can be a powerful affirmation of our pluralism, and our unity across our differences in background and belief.”

Clergy representing multiple Christian denominations (Presbyterian, Episcopal, Methodist, African Methodist Episcopal,





Dr. Comfort Panda, a nurse practitioner with the Montgomery County department of health and human services, chats with Collins.


Baptist and non-denominational) as well as Judaism and Islam attended the event, which was organized by the Washington National Cathedral's canon missionary and minister for equity and inclusion, The Rev. Canon Leonard Hamlin, Sr.

“Over the past year,” he said, “words such as community, spirit, compassion, justice and a host of other words have been elevated in our vocabulary. The words are significant, but they have power only when they are connected to our actions. This evening, we have gathered in this space recognizing the challenge of this moment. But we come together embracing the opportunities that are in front of us.”

In addition to multiple faith communities and NIH, a number of regional health departments and jurisdictions sent representatives, including the District of Columbia, Montgomery and Prince George's counties in Maryland, Virginia's Arlington County and City of Alexandria, as well as Howard University Hospital and University of Maryland Capital Region Health.

After the remarks ended, more than two dozen faith leaders lined up to be vaccinated—most, publicly on camera—as examples for their worship communities.

“Houses of worship are houses of hope,” Collins said. “The National Cathedral represents that. Today, all of you are putting hope into action—hope for an end to the terrible suffering and loss of life from Covid-19, hope for an end to the economic devastation it has caused, hope that the vaccine can protect not only you, but also if we do this together, your family, your friends, your community, your nation, your whole world. This is a love-your-neighbor opportunity to spread that hope.”

View the entire event online at www.youtube.com/watch?v=8unIKvq_LAU. 

New NIH History Lecture Series Begins

PAST INFORMS THE FUTURE

The Office of NIH History and Stetten Museum recently announced its new biomedical history lecture series, with 3 exciting talks over the next 3 months. What lessons can be learned through examination of past failures and successes? Tune into these thought-provoking lectures.

Former NIDDK director Dr. Allen Spiegel kicks off the series with a talk titled “A Brief History of Eugenics in America: Implications for Medicine in the 21st Century” on Thursday, Apr. 22 from noon to 1 p.m. ET at <https://video-cast.nih.gov/watch=41818>.

Spiegel is a professor of medicine and molecular pharmacology and former dean of the Albert Einstein College of Medicine in New York. For his talk, he will review the eugenics movement in early 20th century America,

which was based on a limited understanding of human heredity and culminated in a nationwide program of forced sterilization of those deemed unfit to reproduce. He then will discuss the thorny questions raised by striking advances in biomedicine in the 21st century, such as in vitro fertilization, preimplantation genetic diagnosis, non-invasive prenatal fetal screening, genome editing and reproductive cloning.



Dr. Robert Lefkowitz

The next speaker in the series will be Dr. Robert Lefkowitz, the James B. Duke professor of medicine and professor of biochemistry and chemistry at Duke University Medical Center and co-winner of the 2012 Nobel Prize for Chemistry. Lefkowitz will discuss his career as an “accidental scientist” and the transformational training he received from 1968 to 1969 in the NIH Associates Training Program, performed to fulfill his Vietnam War draft obligation. His talk will be at noon on Thursday, May 27.

Then, next up is Dr. Sarah Leavitt, a historian previously with the National Building Museum, where she curated an exhibit called “Architecture of an Asylum: St Elizabeths, 1855–2017.”

Leavitt will provide a history of St. Elizabeths, the first federally operated psychiatric hospital in the United States, established in 1855 as the Government Hospital for the Insane. Her talk will be at noon on Thursday, June 24.



Dr. Allen Spiegel



Dr. Sarah Leavitt



Hampus Flysjo, 5, settles in for a 6-month stay at the Children’s Inn. His parents, Jessica and Niclas, discuss their journey.

Two Families

CONTINUED FROM PAGE 1

In March 2020, a family arrived at NIH, having flown from Sweden just days before the Covid-19 pandemic closed the U.S.

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“For the first time since the diagnosis, we found a spark of hope.”

—JESSICA FLYSJO

★ ★ ★

border to flights from Europe. The couple’s three young children were set to begin a groundbreaking clinical trial.

Niclas and Jessica Flysjo recounted

how their 5-year-old son Hampus began having trouble with balance and speech at age 2. After 18 months of tests, a neurologist informed them Hampus had a rare, fatal genetic disorder called GM1 gangliosidosis. Soon after, they took their then-2-year-old twin daughters, Isabella and Julia, to get tested and learned they also had this

recessive, neurodegenerative disease. Devastated, the couple connected with foundations and heard about gene therapy research. “For the first time since the diagnosis, we found a spark of hope, and we began to research everything there is to know about first-in-human gene therapy,” said Jessica.



Savannah Salazar (l), now 27, was a healthy baby. At 2, she began having seizures and would later be diagnosed with Lennox-Gastaut syndrome. Her mom, Dr. Tracy Dixon-Salazar (r), heads the LGS Foundation and advocates for health literacy in the rare disease community.



The Flysjo family flew in from Sweden last April, just before the border closed during the Covid pandemic. Hampus, Isabella and Julia are part of a rare disease clinical trial at NIH.

Months later, they learned of a small, first-in-human gene therapy trial at NIH, headed by Dr. Cynthia Tift, NHGRI deputy clinical director. It would be an open-label study, meaning there were no placebos; every child would get the experimental treatment. The 3 Flysjo youngsters would be among 8 children accepted into the study. “It took months to complete all the necessary tests and waiting for each result was nerve-racking,” Jessica said. “Our journey could end at any point for any of our children.”

The thought of receiving an immunosuppressing treatment in the middle of a pandemic was frightening, said Niclas, but postponing treatment could mean Hampus’s disease progression might disqualify him from the trial.

The gene therapy was administered in April 2020. Within weeks, the children headed to recuperate at the Children’s Inn, where they stayed for the next 6 months. It’s still too early to know whether the treatment is working, but the Flysjos are grateful for the opportunity of a treatment that may save their children’s lives.

Throughout the RDD event, patients or families of patients, advocates and clinicians offered their perspectives. One presenter, Dr. Tracy Dixon-Salazar, is all three: a concerned parent whose daughter has a rare disease, patient advocate and researcher. Wondering if she needed a Ph.D. to understand her daughter Savannah’s rare disease led her to pursue a neuroscience doctorate.

Savannah’s daily seizures began at age 2. Three years later, she was diagnosed with Lennox-Gastaut syndrome (LGS). From ages 2 to 18, Savannah would have more



“It strikes me as [counterintuitive]—the mammoth costs associated with this, the confusion for the patient,” said Dixon-Salazar.

“A number of times, I learned something from the medical record or from a scientific talk I otherwise wouldn’t have been at,” she said, advocating for improved health

than 40,000 seizures and tried and failed 26 different treatments.

“With every doctor we saw across our journey, we would hear different things about LGS, so there’s not even an institutional knowledge about it,” said Dixon-Salazar, who is executive director of the LGS Foundation.

One doctor told her it didn’t matter whether LGS was the correct diagnosis because, if need be, they could try all the dozens of seizure medications out there.

literacy for all rare diseases. “We use a lot of these big words that don’t really mean anything to patients. Trying to get to the bottom of what [the terms] mean can be really challenging.”

Dixon-Salazar recommends more plain language—and common institutional language—for rare diseases as well as more community engagement, funding and global coordination.

For anyone living with a rare disease,



The Flysjö family is scheduled to return to the Clinical Center this month for a follow-up appointment.

better health literacy can help promote access to appropriate medical care, improve patient quality of life and lay the groundwork for successful clinical trials and better treatments. **R**

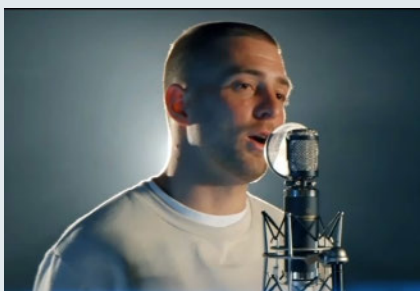
NCATS CHALLENGE WINNER

Poet with FA Finds Hope in Music, Faith

Jacob Thompson played baseball growing up and had dreams of going pro. But those dreams were dashed during high school. Once an athletic kid, his muscles were beginning to atrophy.

Thompson started turning to other outlets, ones where he might help and inspire others. He began coaching and volunteering and became active in youth ministry. He also found creative outlets in music and poetry.

After college, Thompson got married, began working with a record label and continued mentoring and coaching kids. Everything was going well, until he began feeling unwell: nausea, fatigue, dizzy, spells of vertigo. And his balance was getting worse. This began a journey of physical therapy,



MRIs and other tests. Then came the diagnosis: Friedrich’s Ataxia.

Thompson learned he was born with FA, which was slowly eroding his physical abilities. Doctors told him in the coming years, he’ll end up in a wheelchair. There’s still no effective treatment for this rare disease.

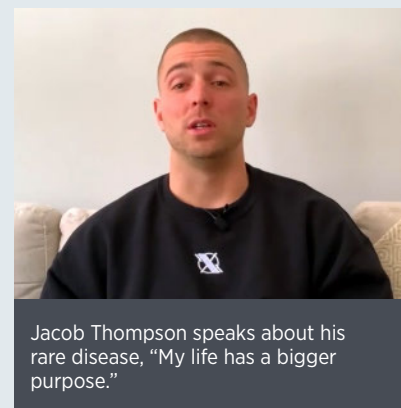
“This was hard news to hear at age 24, when it seemed I had my whole life ahead of me,” said Thompson, during NIH’s Rare Disease Day virtual event. “Anybody in that place, just know you’re not alone. Never give up hope.”

When he first learned about his rare disease, Thompson said he felt hopeless, ruminating about all the things he’d never do in life. But he found comfort in his faith and continued to pray. He also dove back into his music and poetry, realizing the messages of perseverance in his lyrics were not just for others, but also for himself.

“Rare disease came and knocked me off track; but I won’t be defeated. Instead, I fight back,” he utters during a hip-hop video called *Keep on Fighting*, an entry that earned him first place in the NCATS 2020 Rare Diseases are Not Rare Challenge. The nationwide annual competition aims to raise awareness about rare diseases and highlight the need for research and new treatments.

Today, Thompson runs a high school mentoring program and coaches football and basketball. He continues recording music. And, he and his wife are busy raising their young son.

“My life has a bigger purpose that FA can’t take away,” said Thompson. “I made a commitment that no matter what happens, I’m gonna keep fighting.” —Dana Talesnik



Jacob Thompson speaks about his rare disease, “My life has a bigger purpose.”

Rare

CONTINUED FROM PAGE 1

Researchers now know the molecular basis of almost 7,000 rare diseases, or conditions that each affect fewer than 200,000 people in the United States. Austin said while that's something to be celebrated, especially when it comes to finding a diagnosis, the sad fact is treatments haven't followed at the same pace as disease gene discovery.

Unfortunately, fewer than 500 rare diseases have an FDA-approved treatment. At the current rate, it will be over 2,000 years before there is a treatment for every rare disease.

"The current development of new treatments takes far too long and fails far too often and is therefore far too expensive," Austin said. "Translational science is the key to improving this record."

Austin called for "disruptive change." At NCATS, researchers are now trying to identify similarities across diseases in order to develop treatments for multiple disorders at one time, develop models that better predict a person's reaction to treatment and design clinical trials for smaller populations.

Rare Disease Day 2021 featured updates from researchers, stories from patients and their families and panel discussions.

"We've got a long way to go to fill in that big gap between our diagnostic and therapeutic abilities," agreed NIH director Dr. Francis Collins.

Many of the FDA-approved treatments for rare diseases only address symptoms. While these treatments are encouraging, they aren't cures. Collins promised, "We're not going to rest until we find those."

Collins' own lab at NIH studies progeria, a rare and fatal pediatric disease, characterized by dramatic, rapid aging, beginning in childhood. In November 2020, the FDA approved a treatment for progeria. While the drug does extend the life of patients, "it's not the end of the story," Collins explained. His lab is now working on other ways to attack the disease using RNA-based approaches and DNA editing technologies.

NIH supports several networks to better understand rare diseases, including NCI's My Pediatric and Adult Rare Tumor Network and the NCATS Rare Disease Clinical Research Network. Clinical Center



NCATS director Dr. Chris Austin (l) participates in a brief Q&A session with NIH director Dr. Francis Collins during a virtual version of NIH's annual observance of Rare Disease Day.

scientists, too, have several studies on rare diseases underway.

Some of today's therapeutic interventions "we didn't even dream about in 2011," noted Collins. The gene editing system CRISPR is one of them.

"This is an opportunity to figure out how we could take this approach—which has the potential of searching out every possible place in the genome where there's a misspelling in a tissue and delivering a gene editing apparatus to try and fix that," Collins said. "That sounds like it would be straightforward, but it's not. The ability to do that safely and effectively requires you to have the appropriate delivery systems in place."

To speed up gene editing technologies, the NIH Common Fund's Somatic Cell Genome Editing program is working to improve approaches to help reduce the burden of diseases caused by genetic changes. Additionally, the NCATS-led Platform Vector Gene Therapy (PaVe-GT) seeks to make it easier to start clinical trials by using the same gene delivery system and manufacturing methods for multiple rare disease gene therapies.

NIH is also working with industry to launch the Bespoke Gene Therapy Consortium, which is dedicated to making gene therapy a reality for people with genetic diseases affecting populations too small to be viable from a commercial perspective.

"We're in a pretty good place here to be able to see a real change in the approach and the ability to scale to lots of disorders," Collins said.

The Covid-19 pandemic has shown it's possible to develop new technologies, such as vaccines and diagnostic testing, faster than ever.

"We've done things that most people wouldn't have guessed could have happened in just a year," he said. "We can apply some of those lessons as we go forward."

Despite pandemic-related restrictions, patients and researchers must continue to work together in new and innovative ways.

"We can do things together that are phenomenal and breathtaking," Collins concluded. "We have been, we are, and we aim to continue to be not just the National Institutes of Health, but the National Institutes of Hope." **R**

VOLUNTEERS

People with Crohn's Disease Sought

NIAID is seeking people with Crohn's disease. Researchers are investigating whether Vorinostat is safe for people with Crohn's. Participants will receive maintenance therapy with Stelara after successful treatment with Vorinostat. Study-related tests, medication and procedures are provided at no cost. Call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Online <https://go.usa.gov/xsRg8>. Refer to NIH study 17-I-0101.

Sickle Cell Study Needs Participants

NHLBI invites people ages 18 and older with sickle cell anemia including HbSS, HbS-β0 thalassemia to participate in a study evaluating the best non-invasive predictor of renal function. Results of this research may help ensure the most accurate assessment of kidney function. Compensation provided. For more information about study 19-H-0100, call 1-866-444-2214 (800-877-8339 TTY/ASCII) or visit <https://go.usa.gov/xmFYg>.

Kohanski To Lead NIA Division

The National Institute on Aging recently appointed Dr. Ronald Kohanski as director of the Division of Aging Biology (DAB).

Kohanski will provide strategic vision, expertise and oversight for DAB's scientific portfolio, including all grants and cooperative agreement research activities, as well as administrative, budget and staffing management. He also will serve in an advisory role to the NIA director, deputy director and executive officer.

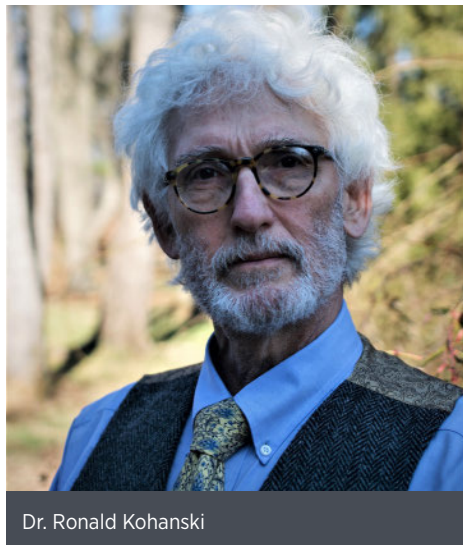
"NIA is pleased that Ron will continue to bring his stalwart and deep commitment to advancing aging biology as director of our aging biology division," said NIA director Dr. Richard Hodes. "His deep understanding of the field combined with his long history of creativity, collegiality and collaboration will help our institute build on its tradition of innovation and exploration moving forward."

Kohanski started with DAB as a program officer in 2005 and became the division's deputy director in 2007. He has been serving as acting director since the departure of Dr. Felipe Sierra last year.

Kohanski is a co-founder and the current leader of the trans-NIH Geroscience Interest Group, which has grown since its founding a decade ago to include program staff from most NIH institutes and centers. Geroscience is an emerging scientific field built on the hypothesis that slowing the rate of aging can delay the onset and reduce the severity of chronic disease and dysfunction that occur late in adult life.

Kohanski has long connected NIH and global researchers across multiple disciplines within the biology of aging, covering basic, applied and translational research through DAB's diverse scientific portfolios. The division has roots linking back 30 years to NIA's Longevity Assurance Genes funding opportunities, with a strong emphasis on

how genetic, environmental, dietary and pharmaceutical factors impact the rate at which we age, and the overall lifespan and health of older adults.



Dr. Ronald Kohanski


Kohanski earned his Ph.D. in biochemistry with Robert L. Henrikson at the University of Chicago in 1981. After a postdoctoral fellowship with M. Daniel Lane at Johns Hopkins University School of Medicine, he held a faculty position at the Mount Sinai School of Medicine before returning as a JHU faculty member. His fields of research

included enzymology and developmental biology of the insulin receptor.

He has authored or co-authored 48

peer-reviewed scientific articles, contributed to 6 books or book chapters and has written published reviews of literature pertinent to areas in his scientific field. Kohanski has received numerous NIH merit awards over his career for outstanding contributions that have advanced the NIA and broader NIH missions.

Kohanski said his future priorities for DAB include continuing to support expansion of research in the basic biology of aging in human populations, with special attention to health equity research, while fostering more academic and industry collaborations.

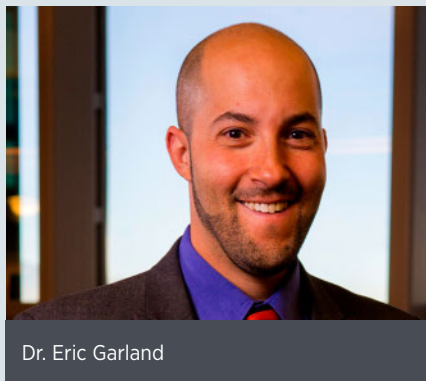
"Our core mission is to support research on the fundamental mechanisms leading to dysfunction and increased risk of disease in older adults," he said. "I am humbled by the opportunity to lead such talented colleagues as we seek new understanding of the hallmarks of aging and how they are integrated at the cellular and physiological levels." 

Garland To Lecture on Innovative Strategy for Reducing Pain, Addiction

INTEGRATIVE MEDICINE SERIES

This spring, NCCIH will host two virtual lectures on a theme of "Novel Approaches at the Intersection of Mental Health and Pain" as part of its Integrative Medicine Research Lecture Series. The events are rescheduled from spring 2020 and reflect several of the center's research priorities.

On Tuesday, May 4 at noon ET, Dr. Eric Garland will present on "Mindfulness-Oriented Recovery Enhancement (MORE): Restructuring Reward Processing in Addiction, Stress and Pain." Garland is professor and associate dean for research at the University of Utah College of Social Work and director of the Center on Mindfulness and Integrative Health Intervention Development.



Dr. Eric Garland

Some of our most pressing "diseases of despair," such as addiction and chronic pain, disrupt the brain's capacity to experience healthy pleasure and extract meaning from naturally rewarding events and experiences. For example, prolonged opioid use in the context of chronic pain and distress can blunt positive emotions and compel opioid misuse as a way to hold on to a shrinking sense of well-being.

Garland will describe the development and testing of an integrative, nondrug treatment strategy, MORE. This approach unites traditional mindfulness meditation practices with techniques from cognitive behavioral therapy and principles of positive psychology. Rooted in affective neuroscience, MORE is designed to reduce addictive behavior and improve physical and emotional pain by restructuring reward processes in the brain.

The lecture will be streamed at <https://videocast.nih.gov/watch=41741>. Find details about the series at <https://www.nccih.nih.gov/news/events/imlectures>.

The second virtual lecture, "Cooperative Pain Education and Self-Management (COPES): A Technology-Assisted Intervention for Pain," will be on Tuesday, June 8 at noon ET, by Dr. Alicia Heapy, Yale School of Medicine and VA Connecticut Healthcare System.

Yancey

CONTINUED FROM PAGE 1

Yancey, professor and chair of the department of dermatology at the University of Texas Southwestern Medical Center in Dallas, traced decades of research that deepened understanding of skin biology that began since he first entered the field of dermatology in 1978. His eventual membership in NCI's Dermatology Branch, headed by Dr. Steve Katz, helped launch not only Yancey's career, but also the careers of a generation of notable skin biologists.

Pemphigus affects the epidermis, the oral mucosa, throat, the esophagus and other stratified squamous epithelia.

"It is a disease mediated by autoantibodies that bind to epithelial cells and cause loss of cell-cell adhesion, or acantholysis," said Yancey, speaking by videocast from Texas. "It may be fatal, even today."

The disease comes in two major forms—pemphigus vulgaris, the most common form, which affects about 95 people per million annually worldwide, and pemphigus foliaceus, a more superficial version, which affects about 10 people per million each year, globally.

"In early pemphigus vulgaris, the disease is almost exclusively mucosal, mostly oral," said Yancey. Lesions can appear inside the mouth and on the tongue. Skin lesions develop later, often on the upper part of the body—the scalp, face, neck and upper trunk.

"The loss of this much epithelium can compromise the barrier of skin, leading to infections," Yancey noted.

Skin fragility is another feature, along with pain that can be severe. "I've had patients tell me it's like the worst sunburn they ever had," said Yancey.

Histologically, pemphigus vulgaris is quite distinctive, he noted. In pemphigus vulgaris, blisters form in epithelia just above the basal cell layer; in pemphigus foliaceus, blisters form superficially in the granular cell layer of the epidermis. Immunopathology studies show in situ deposits of autoantibodies on the surface of epithelial cells and circulating autoantibodies that react with the surface of normal stratified squamous epithelia.

In pemphigus foliaceus, patients develop "puff pastry" scale crusts that accumulate across the surface of lesions. "The disease can be widespread and severe," noted Yancey,



Members of NCI's Dermatology Branch, circa 1995, include (from l) Drs. Steve Katz, Mark Udey, Maria Turner, John Stanley, Jon Vogel and Yancey.

"and skin pain and secondary infection can occur," even though blisters are more superficial than those in pemphigus vulgaris.

"It has always amazed me that an injury to stratified squamous epithelium that is so superficial, in a tissue that only has the thickness of several sheets of notebook paper, can elicit a disease that is so severe and potentially life-threatening," Yancey said.

Over the past 60 years, investigators have learned an extraordinary amount about pemphigus pathophysiology, he recounted. It wasn't until the late 1940s and early 1950s that pemphigus was distinguished from pemphigoid, a group of subepidermal autoimmune blistering diseases. The 1960s brought advances through light and immunofluorescence microscopy. In the mid-1980s, animal models were developed and pemphigus autoantigens (i.e., what patient autoantibodies were targeting in skin and mucosa) were first identified.

"This taught us not only about pemphigus, but epithelial biology as well," Yancey said.

Treatment changed, too. Corticosteroids were an early therapy. But high doses of prednisone over time "often proved as detrimental to patients as the disease itself," said Yancey. By the 1980s, it was recognized that steroid therapy put some patients at risk of death.

A paper in the *New England Journal of Medicine* in 1982, involving studies of mice, turned the field's attention to autoantibodies in pemphigus, Yancey said. "This set the stage for a number of questions about those autoantibodies. What did they bind? Did all autoantibodies bind the same autoantigen? What role do these autoantigens play in skin? How do patients' autoantibodies cause blisters?"

Studies of radiolabeled keratinocytes yielded useful information on autoantigens in both forms of pemphigus, and the role these molecules play in cell-cell adhesion were gradually identified. Using enzyme immunoassays, researchers developed a distinct autoantibody profile in patients with pemphigus.

But why does it develop in the first place?

That question has led investigators overseas to Brazil, where endemic forms of pemphigus foliaceus occur.

In Brazil, the endemic form is known as fogo selvagem, which is Portuguese for "wildfire."

"These patients feel like their skin is on fire," Yancey noted. In Brazil, the distribution of fogo selvagem often overlaps with leishmaniasis. Interestingly, the insect vector responsible for leishmaniasis has salivary antigens that elicit antibodies that cross-react with the pemphigus foliaceus autoantigen—a possible example of an environmental exposure that leads to loss of tolerance to skin (i.e., autoimmunity), he observed.

Over the past 20 years, treatment with the monoclonal antibody rituximab (accompanied by low doses of short-term systemic corticosteroids) has emerged as "frontline" therapy in pemphigus.


"This has transformed our approach to these patients," Yancey said. "[Pemphigus] potential to cause death within 1 year has remarkably changed... We have much more to offer patients with this disease. Early treatment may well prove to change the natural history of [pemphigus]."

Yancey said that CAR T-cell therapy has also shown promise in animal models of pemphigus and that other new therapies are emerging.

"The sky is the limit for pemphigus therapeutics," he concluded.

During a brief Q&A session, he underscored the importance of early intervention in what he called one of the most deadly dermatologic diseases.

"If the immune response can be interrupted before high-affinity, pathogenic autoantibodies and long-lived plasma cells emerge within a patient," he said, "it is thought that the hardened, treatment-resistant form of pemphigus may be averted."

The full lecture is archived at <https://videocast.nih.gov/watch=40133>. 

Engineered Immune Cells Prevent Cancer Spread

Scientists have genetically engineered immune cells, called myeloid cells, to precisely deliver an anticancer signal to organs where cancer may spread. In a study of mice, treatment with the engineered cells shrank tumors and prevented the cancer from spreading to other parts of the body. The study, led by NCI scientists, was recently published in *Cell*.

“This is a novel approach to immunotherapy that appears to have promise as a potential treatment for metastatic cancer,” said the study’s leader, Dr. Rosandra Kaplan of NCI’s Center for Cancer Research.

Before cancer spreads, it sends out signals that get distant sites ready for its arrival. These “primed and ready” sites, discovered by Kaplan in 2005, are called premetastatic niches.

In the new study, the NCI team looked at the lungs of mice after tumors formed in the leg muscle but before cancer reached the lungs.

Normally, when myeloid cells detect a threat, they make interleukin 12 (IL-12), a signal that alerts and activates other immune cells. But myeloid cells in the lung premetastatic niche instead sent out signals that told cancer-fighting immune cells to stand down, the researchers found.

The NCI team wondered if they could manipulate the myeloid cells to deliver a different message that would spur the immune system into action. So, they used genetic engineering to add an extra gene for IL-12 to myeloid cells—nicknamed GEMys—from lab mice.

The GEMys produced IL-12 in the primary tumor and in metastatic sites. As hoped, GEMys recruited and activated cancer-killing immune cells in the premetastatic niche and lowered the signals that suppress the immune system.

“We were excited to see that the GEMys ‘changed the conversation’ in the premetastatic niche. They were now telling other immune cells to get ready to fight the cancer,” Kaplan said.

As a result, mice treated with GEMys had less metastatic cancer in the lungs, smaller tumors in the muscle, and they lived substantially longer than mice treated with nonengineered myeloid cells. The researchers found similar results in mice with pancreatic tumors that spread to the liver.

The NCI team also found encouraging results when combining GEMy treatment with chemotherapy, surgery or T-cell transfer therapy. When the researchers reintroduced cancer cells into mice that had been cured by the combination treatment, tumors didn’t form. This suggests the combination treatment leaves a long-lasting “immune memory” of the cancer.

As a final step, the researchers created GEMys from human cells grown in the lab, which produced IL-12 and activated cancer-killing immune cells. Next, the team plans to test the safety of human GEMys in a clinical trial of adults with cancer.

NIH To Enhance Tribal Engagement Efforts

NIH will expand and strengthen commitments to respectfully engage American Indian and Alaska Native (AI/AN) people and support their inclusion in the All of Us Research Program, a landmark health research effort that aims to find more precise ways to prevent and treat disease.

In response to tribal leader input gathered from an extensive consultation process, All of Us will initiate specialized education efforts for researchers, take steps to ensure the perspectives and needs of AI/AN communities are integrated into the program and support ongoing engagement activities with Tribal Nations to pave the way for expanded collaborations.

All of Us, which seeks to build a 1-million participant cohort nationwide, aims to engage communities that have been left out of past research.

“We have a real opportunity to help address underrepresentation in research and uncover factors that contribute to health disparities,” said All of Us chief operations officer Dr. Stephanie Devaney.

There are 574 federally recognized tribes within the U.S., each with their own governments and laws. All of Us leaders reaffirmed baseline commitments to Tribal Nations, including rules to never recruit on tribal lands or disclose participants’ tribal affiliations without a tribe’s consent. Further, the program committed to continue holding back the data and samples of self-identified AI/AN participants to allow for tribal consultations and the option to withdraw before any AI/AN information is ever shared for research.



PHOTO: FANGXIANUO/GETTY

“We’re committed to a robust consent process and encouraging all members of tribal communities to speak with tribal leaders,” said Michael Hahn, All of Us tribal engagement lead. “We hope this consultation is a signal to tribal leaders that we’re listening.”

African Americans Who Smoke May Be at Higher Risk for Heart Disease

African Americans who smoke appear to have more than twice the risk of developing coronary heart disease compared to non-smokers. The new study—the first up-close look at the relationship between smoking and coronary heart disease in this population—also examined the risk for plaque buildup in the arteries, a predictor of heart attacks and heart failure.

The findings, published in the *Journal of the American Heart Association*, draw on data from nearly 4,500 participants in the Jackson Heart Study, the largest cohort study investigating cardiovascular disease exclusively in African Americans. That study, as well as the new research, is supported by NHLBI and NIMHD.



African Americans who smoke are more vulnerable to heart disease.

PHOTO: DME PHOTOGRAPHY / GETTY

Coronary heart disease affects more than 20 million adults in the U.S. and causes 1 in 7 deaths, according to the CDC. Compared to whites, African Americans are more likely to die from coronary heart disease.

Despite a marked decline in smoking among African-American adults in recent years, almost 15 percent reported current cigarette smoking in 2019. Yet the link between

cigarette smoking and coronary heart disease has been understudied in this population.

African Americans have disproportionately higher rates of hypertension, diabetes and obesity—known risk factors that partly explain the greater death toll from coronary heart disease in this community,

“But smoking is also a well-documented risk factor, which, combined with the others, suggest that African-American smokers represent a particularly vulnerable population for this disease,” said lead study author Dr. Adebamike Oshunbade, a postdoctoral fellow at the University of Mississippi Medical Center.

The investigators used coronary artery calcification (CAC) scores, measured by CT scans, to assess the degree of calcified plaque buildup in participants’ coronary arteries. The study followed 4,432 participants without a history of coronary heart disease at the time (2000-2004) through 2016. The researchers found that current smokers had an increased likelihood of a higher CAC score and double the risk of coronary heart disease.

“Smoking is a modifiable risk factor for cardiovascular disease,” said Dr. David Goff, director of NHLBI’s Division of Cardiovascular Sciences. “Fully addressing tobacco-related disparities requires addressing conditions where people live, work and play.”



Clockwise from above: great egret, Great Falls, painted bunting

PHOTOS: MICHAEL BENDER



Nature's Glory

When the *NIH Record* asked readers to share images of nature, two photographers took the assignment to new levels. Here are just a few of the pictures we received.

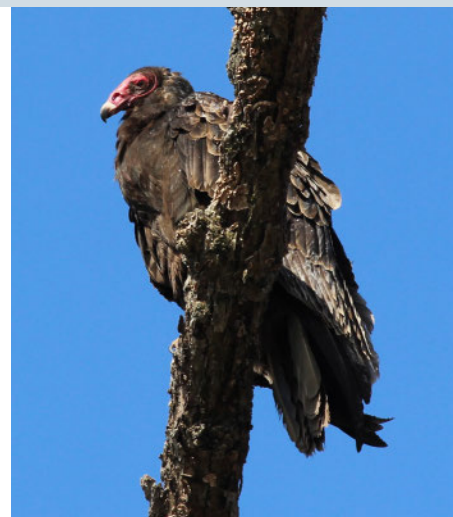
Dr. Michael Bender, program director in the NIGMS Division of Genetics and Molecular, Cellular and Developmental Biology, sent a "fall migration" series he took near Riley's Lock and the Great Falls Visitor Center on the C&O Canal. Over the last year, he also shared several images from McKee Beshers Wildlife Management Area in Montgomery County. He takes pictures in Rock Creek Park, at Hains Point and at Lyndon Baines Johnson Memorial Grove on the Potomac, located on Columbia Island.

Deborah Henken, program officer at NICHD, sent us images from the Ottauquechee River in Hartford County, Vt., Great Seneca Highway and Seneca Creek State Park in Gaithersburg, Md., and most recently, a series heralding the first signs of spring.



From left, Seneca Creek State Park, helleborus and yellow crocus

PHOTOS: DEBORAH HENKEN



Above, turkey vulture; below, yellow-rumped warbler

PHOTOS: MICHAEL BENDER



Mushrooms at Seneca Creek State Park

PHOTO: DEBORAH HENKEN

