To Touch and Be Touched

Nobel Laureate Ardem Patapoutian Delivers Annual Marshall Nirenberg Lecture

BY NIH CATALYST STAFF

Ardem Patapoutian was a teenager in the midst of re-escalating violence and hyperinflation in Lebanon, his native country, when his parents sent him and his brother off to live with an uncle in Los Angeles.

His family had known violence. His grandparents had fled Turkey during the unfolding genocide against the Armenian people in the early 20th century. His family was now scattered about the globe, mere fragments of the Armenian diaspora, numbering in the millions.

Arriving on his uncle’s doorstep with no money, few possessions, and limited English-speaking skills, Patapoutian couldn’t stay long. His uncle made it clear that he and his brother needed to quickly establish their independence. So Patapoutian took a job as a Domino’s Pizza delivery guy, saved up a little cash, and managed to enroll at the University of California, Los Angeles, where he received a degree in cell and developmental biology in 1990.

The rest, as the saying goes, is history. Patapoutian would go on to earn a doctoral degree in biology from the California Institute of Technology (Pasadena, California) in 1996 and embark upon a career, almost entirely at Scripps Research Institute in San Diego,

NIH Rare Disease Day 2023

Virtual No More, Rare Disease Day Comes Charging Back to the NIH

BY SATABDI NANDI (NIA), MICHAEL TABASKO (OD), AND NIH CATALYST STAFF

Rare Disease Day is a global event held on or near the last day of February to raise awareness among policymakers and the public about rare diseases and their impact on patients’ lives. Zebra stripes have come to symbolize the cause, a sassy retort to the old medical professor maxim, “if you hear hoofbeats, think horses, not zebras.”

Hundreds of researchers, medical industry representatives, patient advocates, and patients with a rare disease and their families dusted off their zebra-printed neckties, shirts, and shawls and packed the Natcher Conference Center for Rare Disease Day (RDD), the first in-person event after a pandemic-induced two-year hiatus.

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NIH has made substantial progress in the past several years toward recognition and correction of inequities in many different arenas. Although this progress can never be as rapid or as complete as would be optimal, it has been achieved in ways that are perhaps more likely to be conducive to durable culture change than if it were instantaneously imposed by an external force.

In light of this fact, I am thrilled to announce that, through careful observation, discussion, consensus building, and action, the NIH Intramural Research Program has begun a process that will correct long-standing inequities in stipends awarded to our summer student, postbaccalaureate, predoctoral, and postdoctoral scientist colleagues.

In the short time I have been at NIH, I have seen shifts in workforce and leadership demographics, salary equity, and trainee educational pedigree that let me know we are moving, however slowly, in the right direction. I have seen, too, and perhaps most impressively, major shifts in the comfort level of our workforce in making important observations and asking critical questions aloud and in public forums.

For many years, the magnitude of stipends awarded to the junior members of our scientific workforce has depended upon the institute or center (IC) in which they choose and are chosen to do their work. Sometimes, scientists doing the same mentored work in different ICs have been accorded markedly different stipend support.

Now, thanks to an effort spearheaded by Sharon Milgram, Director of the Office of Intramural Training and Education, and Darryl Zeldin, Scientific Director of the National Institute of Environmental Health Sciences, stipend ranges at every level will move toward equity across NIH ICs beginning this coming fiscal year and will be uniform across NIH by 2025. This plan has been approved by the NIH scientific and clinical directors, the Office of Intramural Research, and Lawrence Tabak, who is performing the duties of the NIH Director.

Diversity, equity, inclusion, and accessibility are words that have had broad and deep meaning since their linguistic inception. In some societies with populations that are minoritized and marginalized, those words might have somewhat different, more narrow implications. But what is humane, civil, good, and right should apply to us all and not be defined only in one or two spheres.

The Intramural Research Program should feel good that our leaders recognized and called out publicly that our junior scientists were not equitably supported across NIH and that this inequity and the resultant inadequacy of stipends for some held the potential to limit the diversity of scientists working across our institutes and centers. We should be proud that they acted on this recognition to accord equal pay for equal work regardless of venue or organizational unit affiliation.

This action will enable scientists of diverse economic, personal, and social circumstances to join us and focus on what they come to NIH to develop—their careers in, and contributions to, science. To be sure, we have a long way to go. But oh my, what an exciting road we are on.
Mind the Growth Mindset
Professional Development for Staff Clinicians
BY PARKER RUHL (NIAID AND NHLBI), WITH NIH STAFF CLINICIAN COUNCIL AND THE NIH CLINICAL FACULTY OF PHYSICIANS AND DENTISTS

My daughter was new to ice hockey this past season. Many of her teammates—mostly boys—had played for years. So, the coach worked with each player to set goals that fed into a cohesive strategy of play out on the ice. The coach instilled a growth mindset in every player, with a focus on a trajectory of learning and development. He simultaneously set the team’s sights on a common goal: to win each game with every player being a valued team member.

Team play transcends sports. Lawrence Tabak, performing the duties of the Director of NIH, underscored the team science nature of translational and clinical research when he noted that excellent clinical research requires excellent clinical care. Here in Building 10, home to the NIH Clinical Center, we proudly seek discoveries to advance human health. We navigate the halls from the laboratory to the clinic, intensive care unit, and operating room, and from the bench to the bedside and back again.

This “we” includes staff clinicians, first designated as “special experts,” playing an essential role in the clinical research enterprise since the inception of the NIH Clinical Center in 1953. We are 320 highly trained physicians and dentists spread across 18 institutes and centers (ICs). Like our clinical faculty counterparts in academic medical centers, staff clinicians continually adapt to revisions in clinical guidelines, improvements in human subject research protection, and new challenges in the practice of medicine, such as the COVID-19 pandemic. As career pathways in academic medicine continue to change dramatically, the NIH Intramural Research Program (IRP) must remain ahead of the curve to recruit and retain talented physicians and dentists with clinical expertise in rare diseases, surgical and procedural skills, and national reputations as clinical educators. Our patients, and their families, expect no less.

The IRP invests considerable resources to recruit staff clinicians, who join with a desire to grow, which the NIH has a responsibility to cultivate. Our mission on the Staff Clinician Council, a seven-member peer-elected body, is to support the professional development of our colleagues. We have data from a validated clinical faculty survey demonstrating that staff clinicians desire more mentorship and professional development at NIH. The path forward is clear.

This spring, our council welcomed our newest colleagues with our first in-person orientation for staff clinicians, sharing resources to navigate IRP careers. Nina Schor, Deputy Director for Intramural Research, noted that the staff clinician position is “challenging and intellectually rich because staff clinicians stand at the crossroads of performing research and clinical care of the patient. You will rely on one another at the NIH. Cast the net broadly as you teach one another.”

With key guidance from Carl Hashimoto, Director of Faculty Development, Office of Intramural Research, we developed a pilot peer-mentoring program with 10 assistant research physician mentees, building bridges for mentee and mentor relationships across ICs. Our council, with the support of Schor and Janice Lee, Deputy Director for Intramural Clinical Research, is dedicated to ensuring equitable access to mentorship and support for a growth mindset among our colleagues in every IC, big or small. By embracing the need to reach every staff clinician, we can further the NIH IRP mission for equity, diversity, inclusion, and accessibility to ensure staff clinicians are not left unsupported in their careers. We are just getting started.

By the way, my daughter’s Rooftop Hockey League Grey Team won the championship this year because every team member improved their individual skills and came together on the ice. The IRP can do the same for staff clinicians, the NIH clinical faculty of physicians and dentists who are highly engaged at the bedside. To be successful, we must mind the growth mindset.

Parker Ruhl, M.D., M.H.S., is chair of the NIH Staff Clinician Council and Senior Advisor in the NIH Office of Intramural Research. In her spare time, she enjoys spending time with her family, being outdoors, and traveling.
investigating the biological receptors for temperature and touch.

His team identified a gene that encodes a protein that makes the cells sensitive to mechanical indentation, an ion-channel protein they named PIEZO1. They then identified a second gene encoding a closely related ion channel, which they named PIEZO2, essential for the detection of touch.

Patapoutian recounted his research journey at the annual Marshall W. Nirenberg Lecture on March 13 at the Lipsett Amphitheater. His work has earned him numerous accolades, including the prestigious Kavli Prize in 2020 and the Nobel Prize in Physiology or Medicine in 2021.

On the evening before his NIH Nirenberg Lecture, he was the guest of honor at the Armenian Embassy, an event organized in part by fellow Armenian Lana Yeganova, a Staff Scientist at the National Center for Biotechnology Information, National Library of Medicine.

“If you told me when I was growing up that I would win a Nobel Prize, I would have laughed at such an idea,” Patapoutian told the embassy gathering. He added that he has slowly grown to understand and accept, at first reluctantly, that he has become a role model, particularly for Armenian schoolchildren but also for many others living through hardships, in conflict zones, striving to reach their full potential.

A Tasteful NIH Connection

Among those in the near-capacity in-person audience for the Ardem Patapoutian lecture were Nicholas Ryba and Mark Hoon. Ryba leads the Taste & Smell Section in the National Institute of Dental and Craniofacial Research (NIDCR); Hoon, the NIDCR Molecular Genetics Section.

Both investigators in recent years have turned their research focus to understanding somatosensation and pain. But while Patapoutian was just starting his Nobel Prize-winning research on touch, Ryba and

Alexander Chesler, a Senior Investigator in the Sensory Cells and Circuits Section in the National Center for Complementary and Integrative Health, was the scientific host for Patapoutian’s NIH visit.

Chesler studies pain in the context of injury and inflammation, and he has been Patapoutian’s friend and collaborator for many years. In his lecture introduction, as only a friend could do, he set the tone for the day’s event.

“When Ardem won the Nobel Prize,” Chesler said, “I was part of this small group of people who got an impassioned message from his wife, Nancy Hong, that basically read: ‘Everyone, please, we have to keep his ego in check.’”

With Patapoutian laughing, Chesler did just that, concluding his introduction by stating that, despite Patapoutian’s accomplishments, “he will never be the most famous Armenian because that [position] is held by Kim Kardashian.”

To be expected, Patapoutian gave an informative lecture, at times humble and at times humorous. The lecture was titled “How Do You Feel?” Based on the reaction from the audience—the largest crowd the Lipsett Amphitheater had seen since before the pandemic—the answer was, we feel very fine, indeed.
Hoon and colleagues were well on their way to revealing somewhat of an analog to touch: the receptors on the tongue for taste. Over a period of about 20 years starting in the 1990s, the Ryba lab, in which Hoon was a postdoc, in collaboration with the laboratory of Charles Zuker, now an HHMI Investigator at Columbia University (New York), identified and characterized the receptors and cells mediating the five basic taste modalities—bitter, salty, savory (umami), sour, and sweet—as well as how taste is represented in the brain.

As with Patapoutian's discovery, their work has profound implications for eating and taste disorders. For example, they found that the sensation of taste is hardwired and that they could impart the sensation of sweetness or bitterness in mice by activating neural pathways in their brain, without the mice tasting any food.

An excellent overview of their research is presented in reviews in *Nature* (Nature 444:288–294, 2006) and *Cell* (Cell 139:234-244, 2009).

Watch the archive of Ardem Patapoutian’s lecture at https://videocast.nih.gov/watch=46072 (NIH only).

Yasmine Belkaid Appointed Institut Pasteur President

ADAPTED FROM INSTITUT PASTEUR NEWS RELEASE

The Institut Pasteur (Paris) has appointed Yasmine Belkaid as its next President. Belkaid is currently the scientific director of the NIH Center for Human Immunology, Inflammation, and Autoimmunity, as well as chief of the Laboratory of Host Immunity and Microbiome and chief of the Metaorganism Immunity Section in the National Institute of Allergy and Infectious Diseases (NIAID).

Belkaid will succeed British–French microbiologist Sir Stewart Thomas Cole, who has been in the position since January 2018 and whose term ends January 1, 2024. She will become the second female scientist to hold this position and the 17th President of the Institut Pasteur since it was founded by Louis Pasteur in 1887.

A French Algerian born in Algiers, Belkaid is an internationally renowned scientist who has focused her research on the relationship between microbes and the immune system. She began her scientific journey with training in infectious diseases at the Institut Pasteur, and her career has since encompassed a wide variety of fields including parasitology, microbiology, medical entomology, and virology, as well as tissue immunity, the microbiome, and human immunology.

Belkaid first came to NIH in 1996 for a postdoctoral fellowship in intracellular parasite biology at NIAID’s Laboratory of Parasitic Diseases. In 2002, she joined the Molecular Immunology Division at Cincinnati Children’s Hospital Medical Center (Cincinnati) before returning to NIAID in 2005 as head of the Mucosal Immunology Unit in the Laboratory of Parasitic Diseases.

The decision to appoint Belkaid as Institut Pasteur President follows a lengthy selection process that began in June 2021, conducted by a search committee chaired by Edith Heard, Director General of the European Molecular Biology Laboratory, Heidelberg, Germany.

“With her scientific, medical, and public health expertise, Yasmine Belkaid has the potential to lead innovative programs that will expand the Institut Pasteur’s international influence, capitalizing on its legacy, its interdisciplinary collaborations, and its capacity to train future generations of scientists, including more women,” said Yves Saint-Geours, Chairman of the Institut Pasteur’s Board of Governors. “This action is of particular importance in our highly competitive environment, which presents so many global and multiscale challenges to the Institut Pasteur today.”

“As the next Institut Pasteur President,” said Belkaid, “I aim to position the institute as a leading scientific research organization in life science and to strengthen its position in the surveillance, prevention, and identification of emerging pathogens at an international level.”
Women Scientists Advisors
30 Years of Advocating for Equality

BY JENNIFER HARKER

The NIH Catalyst shares both an anniversary and a vision with the Women Scientists Advisors (WSA). In our first issue (February 1993, pages 4-5), Hynda Kleinman, now a retired section chief of National Institute of Dental and Craniofacial Research (NIDCR), reported findings from the 26-member Task Force on the Status of NIH Intramural Women Scientists, which she led. The task force was formed in November 1991 by then-NIH Director Bernadine Healy to identify both real and perceived impediments to NIH women scientists.

The task force reported that although women in postdoctoral positions had risen to a level equivalent to the percentage of women nationwide who were completing doctoral programs in the life sciences, women at NIH in scientific career and leadership positions were far below acceptable levels. In fact, women represented only 18% of tenured scientists and 4% of lab chiefs.

The task force recommended increased communication, appointment of a career-development coordinator, a tenure-track plan, equal pay, improved visibility, and a flexible family leave plan. In response, the scientific directors (SDs) “unanimously endorsed the appointment of a Woman Scientist Advisor for each Institute, Center, and Division.” And thus, WSA was born.

Fast forward to the September–October 2001 issue of the Catalyst (pages 2–3) and a guest editorial by Joan Schwartz titled “Ten Years and Counting: Have NIH Women Scientists Advanced Since the Task Force Report?” Modest improvements had been made.

- Salary corrections in 1994
- The Margaret Pittman Lecture Series was developed to ensure women scientists also had the opportunity to present NIH-wide scientific lectures. Pittman was the first woman laboratory chief at NIH.
- Tenure-track women scientists increased to 25% in 2001
- Women SDs increased from 0 to 4
- The number of women lab and branch chiefs increased from 4% to 10% after a concerted effort in 1994–1995
- But tenured women scientists remained constant at 18%

Schwartz, then an assistant director in the Office of Intramural Research who had served on the Director’s task force, reported two impediments to progress: 1) gender schema and 2) accumulation of advantage. Gender schema refers to gender biases, conscious or otherwise; accumulation of advantage, Schwartz explained, was a phenomenon at NIH that “suggests a small bias that favors men on the tenure track with more space, larger budgets, and higher salaries.”

Fast forward once more, this time 20 years, and the accumulation of (dis)advantage for women scientists in senior scientific roles unfortunately has remained nearly constant.

“The fact that these issues existed 30 years ago, and that we still have such a long way to go, I think, says a lot,” said Mary Kearney, WSA Chair and Senior Scientist at National Cancer Institute’s Center for Cancer Research.

Kearney pointed out that over the past 30 years, significant movements occurred in the United States that brought attention to the issues faced by women in the workplace, such as the Anita Hill hearings in 1991, which may have been the impetus to forming the original task force. Since that time, progress has coincided with similar events.

“I think there can be backlash, too,” Kearney added. “When women and underrepresented groups try to make change, it is oftentimes two steps forward and one step back. So, progress has been slow. Still, we can ride on the coattails of nationwide movements and try to continue to make progress.”

Kelly Ten Hagen, Senior Investigator at the NIDCR and past WSA Chair,

<table>
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<tr>
<th>NIH POSITION</th>
<th>1993</th>
<th>2001</th>
<th>2022</th>
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<td>Scientific directors</td>
<td>0</td>
<td>4</td>
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<td>18%</td>
<td>27%</td>
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<td>42%</td>
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<tr>
<td>Research fellows</td>
<td>35.1%</td>
<td>40%</td>
<td>49%</td>
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*As of April 2023; **FY 2020 data is the latest reported for lab/branch chiefs.

Intramural scientists’ demographic information dating back to 2016 is available at https://oir.nih.gov.
expanding on what Kearney said, offered
the example of salary adjustments.

“For reasons that we don’t completely
understand there is this kind of creep that
occurs as salary disparities reappear,” said
Ten Hagen. “We see things that occurred
30 years ago, that were corrected, but now
30 years later, it is happening all over again.
We need to get to the bottom of that.”

Progress continues to be made by
WSA. Ten Hagen and WSA Executive
Committee Member Julie Segre, Senior
Investigator at the National Human
Genome Research Institute, both served on
the Advisory Committee to the Director
Working Group on Changing the Culture
to End Sexual Harassment; and Segre
and Ten Hagen were joint recipients of
the 2019 NIH EDI Award of the Year
in recognition for efforts to help design
and implement the NIH Anti-Harassment
and Personal Relationships Policies and
Workplace Climate and Harassment Survey.

“I think another thing that the WSA
can do, alongside other committees, is to
make recommendations for how women
and minorities can be supported in
leadership, be promoted into leadership,
and be retained in leadership positions,”
said Kearney. “Women and minorities leave
leadership positions more commonly than
white men because women and minorities
often face other challenges in addition
to the work. They might be dealing with
microaggressions, blatant racism, and
sexism. There are challenges there for which
we have to provide more support, including
administrative support.”

Ten Hagen agreed, adding that
research shows that women are penalized
for negotiating. “Negotiating can have
negative repercussions for women and other
underrepresented groups. But negotiating
is part of almost any position. If this is the
kind of general or societal bias that we face,
it puts us at a very distinct disadvantage.”

“Women have contributed to our
scientific knowledge and the biomedical
research enterprise, but we also have
been able to transform the landscape
and make significant progress to try to
level the playing field—with the caveat
being that the playing field is still not
level” Ten Hagen said, pointing out that
women should not be solely responsible
for trying to level the field.

The WSA aims to continue to be a
resource for the community—to ensure
equity and support for women scientists. The
WSA committee recommends NIH women
scientists at all career levels reach out to
their IC-based WSA representative if they
have concerns. They want to understand
the issues women are facing so that they
can advocate for change.

The WSA has made significant progress
over the past 30 years, but clearly there is
much left to be done.

To learn more about WSA, visit the
WSA website at https://sigs.nih.gov/
wsa or attend one of the upcoming WSA
30th Anniversary Seminar Series events.

Remember when?

Celia Hooper reflected on her
contributions to The NIH Catalyst during
her tenure as Scientific Editor (1993–2006).

“My managing editors and I liked to
reflect [on] some of the delightful, zanier
aspects of life at NIH,” Hooper wrote in
an email to the Catalyst. She shared some
of her memorable contributions.

• “Write Right. Ya Gotta.” (March–April
2000, page 4)
• “NIH’s Vanity Plate” (November–
December 1997, page 1 and page 5,
where you can read more about WSA’s
Schwartz’s vanity plates, too)
• A visit to the Rocky Mountain
Laboratory (September–October, 1998)
She “definitely recommends” we treat
readers to a Rocky Mountain revisit. We
definitely agree.

In our next issue, we will highlight
former cartoonist Alex Dent and share a
few scientific updates, too.

Want us to include your work or IC
with a then-and-now highlight? Stroll
through our archive repository at https://
irp.nih.gov/catalyst/archived-issues for
past coverage and then email us an update
to catalyst@nih.gov and let us know how
things have progressed over the years.

Join the conversation on Twitter with
hashtag #NIHCatalyst30.
Christopher McBain Named New NICHD Scientific Director
Accomplished Scientist and Leader to Head Diverse Research Portfolio

BY DIANNE LEE, NIMH

Christopher McBain, Ph.D.

In January, The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) announced the selection of Christopher McBain as its new Scientific Director (SD). McBain had been serving as Acting SD since June 2021.

In the announcement, NICHD Director Diana W. Bianchi lauded McBain’s reputation as an internationally renowned research scientist and an accomplished leader. “He has contributed to our understanding of synaptic transmission, developed and led highly competitive and innovative programs, fostered numerous interdisciplinary collaborations, trained many scientists, and implemented novel scientific infrastructure,” Bianchi said.

McBain will oversee an annual budget of $200 million and more than 1,000 scientific and contract personnel who conduct clinical and basic science research. “That’s where NICHD’s Division of Intramural Research (DIR) shines,” said McBain. “We have a broad portfolio of science that captures genetics, biophysics, cell biology, neuroscience, model organisms, women’s reproductive health, and contraception. We have investigators cross the divide and think about things on the basic research level and translate them back to the clinic. That’s NICHD’s real strength.”

McBain’s first order of business as SD has been to create a new leadership position within NICHD’s DIR—the Associate Scientific Director for Diversity, Equity, Inclusion, and Accessibility. Filling that important role is Senior Investigator Stephen Gilman along with Senior Investigator Anirban Banerjee serving as Deputy Director. Together, they will incorporate best practices for recruiting diverse teams. “It’s been a shot in the arm for the way we think about workplace diversity issues,” said McBain, adding that the institute was founded in 1962 and has historically been predominantly male. “But if you look at our tenure-track candidates, it’s split evenly 50:50 between male and female and [includes] an incredibly diverse pool of investigators.”

Since 2000, McBain has been Senior Investigator in the Section on Cellular and Synaptic Neurophysiology and has published more than 100 peer-reviewed journal papers. His research focuses on understanding excitatory and inhibitory synaptic transmission between specific neuronal cell subtypes during hippocampal and cortical formation. Using electrophysiological and other genetic approaches, his team’s work contributed to our understanding of the basic physiological properties of hippocampal inhibitory interneurons.

Deficits in inhibitory interneurons are linked to epilepsy, schizophrenia, and Alzheimer’s disease.

McBain’s research contributions have been acknowledged both within and outside of NIH. His many accolades include the prestigious NIH Director’s Award in 2021 and three NICHD Director’s Awards. He was named a Fellow of the American Association for the Advancement of Science in 2023.

McBain has been at NICHD since 1993, when he started as an investigator in the Laboratory of Cellular and Molecular Neurobiology. At the time, he was the first to practice as a slice physiologist in the intramural program, where he studied hippocampal circuitry in brain slices. In 2001, he became Chief of the newly formed Laboratory of Cellular and Synaptic Neurobiology and then served as Chief of the Program in Developmental Neurobiology in 2011.

In his 30 years at NIH, McBain has mentored over 60 trainees including postdoctoral fellows, graduate students, postbaccalaureates, and numerous undergraduate and high school students. He has received several NIH and NICHD mentoring awards including the Mentor Award for NIH Undergraduate Scholarship Program.

Today, more than ever, McBain believes that mentoring the next generation of young scientists is vital to successful science. “It’s an incredibly challenging time for postdocs right now. The candidate pool entering these positions is getting smaller and smaller,” he said. “We need a revolution in what we expect our postdocs to do and what we expect them to earn.”

Christopher McBain Named New NICHD Scientific Director
Accomplished Scientist and Leader to Head Diverse Research Portfolio

BY DIANNE LEE, NIMH

Christopher McBain, Ph.D.
NEI: National Eye Institute researchers identified rare genetic variants that could point to one of the general mechanisms driving age-related macular degeneration, a common cause of vision loss in older adults. Shown: Complement factor 8 proteins in the membrane attack complex. Genetic variants produce malformed C8A and C8B proteins that alter MAC stability, which may drive a chronic inflammatory response in the retina.

NEI: ULTRA-RARE GENE VARIANTS LINKED TO AGE-RELATED MACULAR DEGENERATION

Age-related macular degeneration (AMD), a common cause of vision loss in older adults, has several contributing factors, including advanced age, environment, lifestyle, and genetic predisposition. Although there are treatments to slow the progression of some forms of AMD, there is no cure for the condition. An NEI study identified ultra-rare genetic variants that indicate a potential cause of AMD, which could lead to new treatments or preventive therapies.

Researchers examined genetic variants in unrelated families that had multiple members diagnosed with advanced AMD. Individuals with AMD from four such families had mutations in one of two complement factor 8 (C8) proteins: C8-alpha or C8-beta. In addition, investigators reviewed Age-Related Eye Disease Study (AREDS/AREDS2) AMD cohort data, which showed significantly higher prevalence of the C8 variants in that study’s AMD participants compared with the general population.

C8 proteins are part of the terminal stage of the immune system’s complement cascade, a series of inflammatory responses that fight pathogens. The terminal stage of complement pathway forms a ring-like structure called the membrane attack complex (MAC), which helps regulate inflammatory processes in tissues like the retina.

The C8-alpha and C8-beta variants affect the ability of the C8 proteins to interact, potentially altering MAC formation and stability. The authors believe that changes in MAC stability contribute to chronic inflammation in the retina, driving AMD progression.

The new findings strengthen understanding of genetic factors linked to AMD pathogenesis and indicate MAC could be a therapeutic target to slow or prevent disease. (NIH authors: L. Zelinger, J. Advani, L. Campello, M.A. English, C. Weber, Y.V. Sergeev, R. Fariss, E.Y. Chew, and A. Swaroop, iScience, 2023; DOI:10.1016/j.isci.2023.106417)

[BY KIMBERLY MORGAN]

NCATS: SCIENTISTS REVEAL A POTENTIAL NEW APPROACH TO TREATING LIVER CANCER

Oftentimes in science, the answers you uncover are not the ones you were expecting. Such was the case for NCATS researchers and their colleagues at Massachusetts General Hospital (Boston, Massachusetts) studying cholangiocarcinoma, a cancer arising from liver bile ducts associated with a mutation in the IDH1 gene. After screening thousands of compounds to find a potential therapeutic targeting cells with mutant IDH1, they identified a promising compound called YC-1.

To their surprise, although YC-1 was effective at killing liver cancer cells both in culture and mice models, it had nothing to do with IDH1.

Instead, it depended on the sulfotransferase SULT1A1, an enzyme expressed in most liver cells. The investigators discovered that SULT1A1 chemically alters YC-1 through a process known as sulfonation, which converted the molecule into an anticancer drug.

Armed with this new knowledge, the researchers then examined an NCI database of cancer therapeutics to find compounds similar to YC-1 that also required sulfonation to activate their cytotoxic activity. Each compound they found had unique target-binding properties that could target different proteins within a cell—a finding that opens the window into an entirely new class of potential cancer drugs. The scientists published their findings in Nature Cancer after an eight-year collaboration.

The authors note that because different sulfotransferases are expressed in other regions of the body, target compounds could be cherry picked depending on the type and location of the malignancy, giving doctors yet another precise tool in the war on cancer. (NIH authors: M.I. Davis, K. Kong, T.D. Lee, J.H. Shrimp, W. Zhao, S.E. Kearney, S. Patnaik, M.B. Boxer, M. Shen, and M.D. Hall, Nat Cancer 4:365-381, 2023)

[BY JONATHAN CHU, NIAID]
NHGRI: NIH researchers have developed and released an innovative software tool to assemble truly complete genome sequences from a variety of species.

NHGRI: NIH SOFTWARE ASSEMBLES COMPLETE GENOME SEQUENCES ON DEMAND

An innovative new software tool is now able to assemble truly complete genome sequences from a variety of species commonly used in research. Named Verkko, which means “network” in Finnish, the tool was developed by NHGRI scientists and their colleagues, and grew out of assembling the first gapless human genome sequence last year as part of the Telemere-to-Telemere consortium (T2T).

The software compares and assembles different types of genomic puzzle pieces generated by different DNA sequencing technologies, creating an accurate picture of the genome sequence. And although the T2T project took several years to complete, Verkko can finish the task of assembling complete genome sequences in just a few days.

“Now with Verkko, we can essentially push a button and automatically get a complete genome sequence,” said Associate Investigator Sergey Koren, who led the project. The researchers tested Verkko with human and nonhuman genome-sequencing data, and note that the new software will make assembling complete genome sequences as affordable and routine as possible.

Generating gapless genome sequences from various plants, animals, and other organisms will aid in comparative genomics, the study of the differences and similarities among the genomes of diverse species. And with Verkko, scientists can better assess human genomic diversity, such as regions of highly repetitive DNA, across the human population. (NIH authors: M. Rautiainen, S. Nurk, R.P. Walenz, A. Rhie, A.M. Phillippy, and S. Koren, Nat Biotechnol 2023; DOI:10.1038/s41587-023-01662-6)

[NHGRI: NIH researchers have developed and released an innovative software tool to assemble truly complete genome sequences from a variety of species.

NIH: DNA SEQUENCING DURING TREATMENT PREDICTS SURVIVAL FROM ACUTE MYELOID LEUKEMIA

Acute myeloid leukemia (AML) is a deadly blood cancer and the most common type of acute leukemia in adults. In a recent study, NHLBI scientists demonstrated that testing for the persistence of AML genetic variants after initial treatment predicted survival rates and might be used as a tool to improve long-term outcomes for patients with AML.

The research team used next-generation DNA sequencing to screen the blood of 1,075 adults in remission from AML. All the patients were scheduled to complete treatment by receiving a bone-marrow transplant, which often improves survival outcomes.

At initial diagnosis, 822 of those study participants had mutations in at least one of two genes, FLT3 and NPM1, both commonly associated with AML. After apparently successful initial treatment, the investigators found that 142 of those adults still had residual traces of these mutations despite being classified clinically as in remission.

After then receiving a bone-marrow transplant, almost 70% of patients with the lingering mutations relapsed and just 39% survived after three years. In comparison, only 21% of adults without this evidence of trace leukemia relapsed after three years and 63% survived.

The researchers also found that adults with persistent mutations, but who received higher doses of chemotherapy and/or radiotherapy as part of their transplant, were more likely to remain cancer-free after three years than those receiving lower doses.

Those adults who didn’t receive stronger treatment as part of their transplant appeared to do better when lower-dose therapy included the chemotherapy drug melphalan. (NIH authors: L.W. Dillon, G. Gui, N. Ravindra, Z.C. Wong, G. Andrew, D. Mukherjee, and C.S. Hourigan, JAMA 329:745-755, 2023)

[NHLBI: DNA sequencers during treatment predicts survival from acute myeloid leukemia]

NIA: TEAM FINDS NOVEL FUNCTION FOR PROTEIN ESSENTIAL TO SARS-CoV-2 LIFE CYCLE

NIA scientists determined a protein that is crucial to the life cycle of SARS-CoV-2, the virus that causes COVID-19, has a new role. They found that Nsp13 helicase, a protein mainly responsible for unwinding DNA or RNA, displaces proteins from RNA, a remodeling function not previously attributed to coronavirus helicases. Helicases are involved in many biochemical processes in the cell and are found in all living organisms and viruses.

NIA Senior Investigator Robert Brosh led the team that made the discovery using molecular and biochemical techniques. Since age is one of the greatest risk factors for the severity of COVID-19 symptoms, he suggests therapeutics that target Nsp13 could represent an important avenue of translational research that could potentially help older adults recover from COVID-19.

Nsp13’s ability to remove proteins tightly bound to RNA allows the proofreading mechanism of SARS-CoV-2 to correct errors made by the virus’ replication machinery, the system the virus uses to make copies of itself. These mistakes occur when the wrong nucleotides—the basic building blocks of genetic material—are inserted into viral RNA.

If left unrepaired, they are incorporated as mutations in future rounds of replication. The authors suggest antiviral drugs that impair Nsp13’s RNA remodeling activity may offer a promising approach to induce...
Biochemical studies provide new insight into Nsp13's role in proofreading of errors that occur during coronavirus replication. Shown: Nsp13 displaces proteins from RNA, a remodeling function not previously attributed to coronavirus helicases.

The authors of this study showed that mutations in the SMCHD1 gene resulted in an overproduction of DUX4, killing the precursors of the human nose known as nasal placode cells. The same protein has also been shown to cause muscle cell death in FSHD2.

Using a patient-derived cell line from the two diseases, the authors discovered that expression of DUX4 increased when a cell line was converted to placode cells.

Variable degrees of cell death were observed, leading the authors to believe there could be an environmental component that triggered the disease, such as a virus. Indeed, the investigators then demonstrated that cells infected with herpes simplex virus expressed DUX4 in arhinia and FSHD2 cell lines.

These findings suggest that the toxic protein may be activated by an environmental modifier, such as a virus, in developing fetuses with genetic risk factors. (NIH authors: K. Inoue, H. Bostan, M.R. Browne, O.F. Bevis, C.D. Bortner, N.P. Martin, S. Chen, A.B. Burkholder, J. Li, and N.D. Shaw, Sci Adv 9: eabq7744, 2023; DOI: 10.1126/sciadv.abq7744)


[BY ROBIN ARNETTE, NIA]

NIEHS: TOXIC PROTEIN THAT CAUSES A RARE MUSCULAR DYSTROPHY ALSO KILLS THE PRECURSORS OF THE HUMAN NOSE

NIEHS researchers and their collaborators have found that the transcription factor DUX4 is toxic to the precursor cells of the human nose, and such toxicity may result in arhinia (absence of a nose). Previously, DUX4 has been implicated in a rare type of muscular dystrophy called facioscapulohumeral muscular dystrophy-2 (FSHD2), which causes progressive muscle weakness.

Dysregulated Lyn kinase boosts the concentration of neutrophils—white blood cells of the immune system—and can lead to tissue-damaging inflammation.

Next, the researchers performed experiments to better understand how Lyn kinase interacts with neutrophils and alters inflammatory signals. Further drug screening assessments found that TNF inhibitors effectively reduced systemic inflammation, and that the kinase inhibitor dasatinib resolved liver fibrosis.


[BY DARWING PADILLA ROLON, NIAID]
ScHARe Platform Promotes Minority Participation in Science

BY PETER MANZA, NIAAA

Obesity, cancer, opioid addiction, and long COVID: these are just a few examples of intractable public health crises fueled by disparities in living conditions and access to care. Making matters worse, artificial intelligence tools created to improve health outcomes often introduce biases—such as how cancer-screening tools not optimized for darker skin can misdiagnose—exasperating inequities.

Enter the Science Collaborative for Health Disparities and Artificial Intelligence Bias Reduction (ScHARe). ScHARe is a joint National Institute on Minority Health and Health Disparities (NIMHD) and National Institute of Nursing Research initiative designed to advance the science of health disparities and to improve health care delivery by revealing and minimizing biases.

ScHARe is a cloud platform that provides centralized access to population science datasets, including social determinants of health. It connects people underrepresented in data science, such as women and populations experiencing health disparities, to use big data and cloud computing tools to conduct research in health disparities, health care delivery, and health outcomes. Moreover, the resource aids in developing strategies to mitigate bias in artificial intelligence.

“We know the importance of all the social determinants of health [such as education, poverty, and familial support], but we don’t know which ones and in which combinations for different stages of various diseases and disorders have the greatest impact on a person’s health outcomes,” said Deborah Duran, ScHARe co-founder (with NIMHD Biostatistician Luca Calzoni) and Senior Advisor to the Director for data science at NIMHD. Duran hopes that a better understanding of the mechanisms of how our health is influenced by where we work, live, and play in relation to our biology will help inform tailored interventions at the right time across life span and disease progression.

Many population-science and applied scientists lack the technical knowledge, resources, and collaborative environment to best use complex databases and cloud computing resources. To overcome those problems, ScHARe provides a comprehensive infrastructure that includes hands-on think-a-thons, which are virtual training sessions with dedicated collaboration time bringing together researchers of diverse backgrounds and varying skill levels. Duran envisions sessions where early-career researchers teach data-science skills and where more senior investigators instruct on research techniques as well as health disparities and health care delivery content.

According to NIMHD Research Fellow Kelly Jones, ScHARe aims to not only improve research on health inequities, but also resolve disparities in who conducts the research itself. For example, some historically Black colleges and universities (HBCUs) might not have the resources to compete with other schools.

“We want to support the questions and the science that come out of those places as well,” said Jones.

The program also offers unparalleled opportunity to wrangle data more efficiently. “I’ve always wanted to look at the impact of redlining on health care utilization and access,” said NIMHD Staff Scientist Paula Strassle, referring to the discriminatory practice of denying services, such as financial services or health care, to people who live in certain minority neighborhoods. Even with strong computing resources, analyzing data for that sort of project would traditionally take weeks. “Before, that was an insurmountable barrier,” Strassle added. “But now, [using ScHARe], I can run analyses in a couple of hours.”

How will researchers make the most of the nearly 300 datasets stored at ScHARe? Interoperability built into the platform will allow researchers to access, link together, and then analyze a wealth of datasets that share common elements, providing insights into health disparities and health outcomes that only big data can reveal.

“We’re going to better study and solve issues within the most marginalized populations,” said Strassle. She hopes the massive amount of harmonized data...
will shed light on health outcomes for populations that have been historically difficult to study, such as transgender people and American Indian and Alaska Natives, who are often left out of research because of their small numbers.

Now, scientists can combine similarly conducted studies on those underrepresented populations.

ScHARe also helps mitigate bias in health care applications that use artificial intelligence. Widespread health disparities have emerged because those applications often train algorithms on populations lacking diversity or missing data.

For instance, even the most advanced skin cancer detection algorithms do not perform equally across skin tones. As a result, people with darker skin tones routinely receive diagnoses much later than those with light skin tones, leading to poorer outcomes.

ScHARe creates a virtual space for users to convene to evaluate algorithmic biases and develop mitigation strategies, ushering in an era of more equitable artificial intelligence.

Though the platform is in its infancy, demand has been high. There were over 300 registrants for the first ScHARe think-a-thon in February, when more than 150 users at secure workspaces accessed the new cloud-based datasets and computational tools.

The long-term goal of ScHARe is to not only reduce health disparities but also change the way we think about how environment and biology shapes well-being and public health. For Jones, this means increasing awareness of how social determinants of health tangibly affect our everyday lives. “Maybe one day, neighborhood and environmental context will be considered just as important as your diet or health insurance.”

Peter Manza, a research fellow at the National Institute on Alcohol Abuse and Alcoholism, is studying how chronic drug use changes brain function and how the brain recovers after people enter treatment for substance-use disorders. In his spare time, he enjoys cooking, hiking, strumming the guitar, and playing beach volleyball.

To register for ScHARe or learn more, visit https://www.nimhd.nih.gov/resources/schare/platform-components.html.

TIPS for using ScHARe

- To register, use a Gmail account or another email account associated with a Google identity.
- Users can access, plot, and save data from datasets on ScHARe through the Google Cloud Public Datasets Program.
- Email schare@mail.nih.gov for help.
Since 2011, the NIH Clinical Center (CC) and the National Center for Advancing Translational Sciences (NCATS) have hosted RDD to call attention to the fact that upwards of 10 percent of the United States population has a rare disease, and the study of such conditions—ranging from accelerated aging to painful inflammation—can benefit us all.

Links to the Feb. 28 archived NIH VideoCast are at https://ncats.nih.gov/events/rdd/past-events. The Catalyst reports on a few event sessions, below.

One platform, many treatments
Most rare diseases are genetic and caused by a defect in a single gene. One treatment called adeno-associated virus (AAV) gene therapy has already shown promise in treating some of those conditions. The technology uses a modified version of a virus to deliver a working copy of a defective gene into the cells affected by a given disease. But developing an AAV gene therapy treatment for many other monogenic disorders faces stiff headwinds. The process is far from standardized. And often, private industry is reluctant to invest time and money into a therapeutic that might treat only a single condition with very few patients.

The ongoing NCATS-led Platform Vector Gene Therapy (PaVe-GT) program hopes to change that. In the day’s first session, Scientific Project Manager Richa Madan Lomash at the NCATS Therapeutic Development Branch (TDB) spoke about the collaborative project, which is testing a single streamlined manufacturing and clinical testing procedure using AAV to develop separate treatments for four distinct rare diseases.

“Our goal is to develop common processes throughout the preclinical development for the four diseases, covering manufacturing, safety, regulatory, and clinical activities and operations,” Lomash said.

Once those hurdles are cleared, the AAV platform could serve as a scaffold to develop other rare disease gene therapies. PaVe-GT is focusing on two neuromuscular junction disorders and two metabolic diseases. All four inherited conditions are under study by investigators at NHGRI, the National Institute of Neurological Disorders and Stroke, and the CC.

Lessons learned from PaVe-GT could smooth over the path for others. From proof-of-concept studies to interactions with the FDA that clear the way to develop and test an investigational new drug, the program’s templates and applications are being made publicly available on the PaVe-GT website. And the TDB team recently published a paper (Hum Gene Ther 34:5-6, 2023) that describes how the first treatment candidate received two valuable FDA designations—the Orphan Drug and the Rare Pediatric Disease—which provide financial incentives for the development of rare disease treatments. “It’s very important for us to share the lessons learned in our platform-development journey to help future gene-therapy projects,” said Lomash. The development of the other three gene therapy products is also in progress.

Meeting the needs of adolescents and young adults
Session two concentrated on the needs of adolescents and young adults (AYA). These rare disease patients can fall through the cracks: too old for pediatric care, with its toy-filled waiting rooms and tiny tables etched in crayon scribble; yet too young for adult care, with the scary independence thrust upon them at age 18.

These patients are maturing physically and emotionally, yearning to fit in, be expressive, and prepare for adulthood, explained Alison Silberman, the CEO of Stupid Cancer, Inc., who participated in a panel discussion.

In that same panel discussion, Lori Wiener, Senior Associate Scientist in the National Cancer Institute Pediatric Oncology Branch, relayed her research on psychosocial therapeutic tools and interventions to help AYA navigate an uncertain future. She led an NIH team in the creation of an advance-care planning tool for AYA facing end of life (EoL), called Voicing My Choices. The booklet, first published in 2012, helps AYAs relay to family and friends how they wish to be honored and remembered.

Research by Wiener and her colleagues has found that the tool significantly decreased anxiety about EoL discussions in those who completed several pages of the document. Their clinical study continues today in a new phase of comparative research at NIH and at three university medical centers to assess patient preferences between the original and revised versions of Voicing My Choices.

Wiener’s work is helping patients
take control of their lives. The same can be said for Abbey Hauser, an AYA rare disease advocate. Through the course of the day, Hauser, who has Ehlers-Danlos syndrome, a rare genetic connective tissue disorder, staffed an information booth for the EveryLife Foundation, which advocates for science-driven legislation that advances the equitable development of lifesaving diagnoses, treatments, and cures. In session two, Hauser presented a talk titled “Becoming the Captain.”

Hauser, who grew up on the water in Minnesota, the land of 10,000 lakes, used the captain analogy to describe the challenging process of needing to take charge of the ship that was her life when she became a legal adult. When she started on her “rare disease voyage” at age 6 she was “not the captain of this ship.” Indeed, there were times when she did not know who was steering.

For Hauser, rare disease is like a ship with a varied crew—physicians, nurses, pharmacists, family—each with different yet important roles to keep the ship afloat. Her caring parents might have been at the helm, but a multitude of specialists and constant change of course left her seasick.

Hauser needed surgery just six days after her 18th birthday, when she was barely a legal adult and suddenly pushed out of pediatrics. She felt small in a big, new world. She wasn’t prepared to be the captain.

She managed, of course: Here she was lecturing at the NIH. But her advice to the audience was that parents need to educate their children well about their disease to prepare them for that transition to captain at age 18.

Where there is research, there is hope

“It is your personal decision what you’re going to do to move forward…but think about what you can do to help others,” said National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Staff Clinician Marcela Ferrada. In 2015, she was diagnosed with relapsing polychondritis (RP), a rare disorder characterized by recurrent bouts of painful swelling and inflammation of cartilage and other tissues throughout the body. Now recognized as an expert and world leader in RP research, Ferrada spoke in the day’s third session to share her personal challenges and triumphs.

Growing up in a family of doctors and nurses, Ferrada always wanted to be a doctor. She completed a dual fellowship in critical care medicine at the NIH CC and in infectious diseases at Johns Hopkins Hospital (Baltimore, Maryland). However, when she was diagnosed with RP, she completely changed her career trajectory.

She remembers asking her doctor James Katz, then-Director of the NIAMS Rheumatology Fellowship and Training Branch, “Can you fix it?” but little was known about the disease at the time. Ferrada began reading articles and documenting her own experience. “During that time, being hopeful was very hard and what got me going was thinking about setting up an RP study [to help others],” said Ferrada. She decided to stay at NIH to do an additional fellowship in rheumatology, to be able to see patients and do research in RP.

During her rheumatology fellowship she was able to create a prospective cohort of patients with RP, under the guidance and support of many members of NIAMS, particularly Peter Grayson, currently Chief of the Vasculitis Translational Research Program.

That study has since identified three unique clinical presentations of RP (Arthritis Rheumatol 72:1396-1402, 2020), and enrolled patients are being followed over several years to closely monitor the disease’s progression. Ferrada’s group found that most people are diagnosed in middle age. By identifying the disorder’s main clinical symptoms along with those that are largely unknown, more individuals with RP might be diagnosed earlier.

To find hope during the difficult times, Ferrada has often considered the advice of her NIH colleagues and mentors, such as Anthony Suffredini, Deputy Chief of the CC’s Critical Care Medicine Department, who told her “to have very good mentors, to have a very good environment, to be persistent, and to believe in what you are doing.”

Remarkable progress; more work to be done

NCATS Director Joni Rutter estimates that there are more than 7,000 rare diseases, but fewer than 600 have an FDA-approved treatment. Yet on display this year was palpable optimism amid reports of advances in both treatments and services.

One other thing that isn’t rare is the staggering success of NCATS in bringing FDA-approved drugs for rare diseases to the market—44 such drugs and counting, all in just a brisk decade of research since the center was established in December 2011. Today, RDD has grown into a significant scientific event with over 570 attendees, nearly 2,000 live viewers, 33 scientific posters, and 44 exhibit booths.

“Rare Disease Day at NIH has it all—the moving patient stories, promising research advances, advocacy to spur more action—and this year’s event was no exception,” Rutter told The Catalyst. “The day ended with a special announcement about the first FDA-approved treatment for Friedreich ataxia, marking an incredible moment for the rare diseases community and reminding us what’s possible.”

Things get really rare next year, as RDD is celebrated on February 29.

Satabdi Nandi, a Postdoctoral Fellow in the National Institute on Aging Laboratory of Molecular Biology and Immunology, is investigating the generation of antibody diversity in mouse B cells. Outside of work, she enjoys visiting museums to learn about the past, diverse cultures, and the motivation behind artists’ creations.
COVID-19 Timeline at NIH (March–April 2023)

March 1: FBI Director Christopher Wray states his agency’s stance that the COVID-19 pandemic may have resulted from an accidental laboratory leak in China.

March 1: A study by NIA scientists found that a protein crucial to the life cycle of SARS-CoV-2 has a new role in the virus’ replication and genetic proofreading process. (J Biol Chem 2023; DOI:10.1016/j.jbc.2023.03.005)

March 3: The CDC updates its COVID-19 community levels: Rocky Mountain Laboratories in Hamilton, Montana, moves from medium to high community level; Phoenix, Arizona, moves from medium to low; Framingham, Massachusetts, moves from low to medium; all other NIH locations remain at their current levels.

March 8: A House Select Subcommittee begins hearings investigating the origins of the coronavirus pandemic.

March 6: The Building 12B cafeteria and Building 50 coffee bar resume service at NIH’s Bethesda, Maryland, campus.

March 10: The CDC announces that it will no longer require travelers from China to present a negative COVID-19 test before boarding their flights to the United States. [https://www.cdc.gov/quarantine/china-proof-negative-test.html]

March 11: Former NIAID Director Anthony Fauci speaks to CNN to discuss the minority view that the COVID-19 virus occurred as a result of work in a Chinese lab.

March 14: The NIH Clinical Center announces that the plexiglass shields in the north and south lobbies have been removed and that the round circles in the elevators (also known as Twister decals) may also be removed soon.


March 17: The CDC updates its COVID-19 community levels: Rocky Mountain Laboratories in Hamilton, Montana, moves from medium to high community level; all other NIH locations remain the same.

March 20: A NIAID-supported study finds that prior SARS-CoV-2 infection weakens immune-cell response to vaccination and suggests the need to boost CD8+ T cell response after infection. (Immunity 2023; DOI:10.1016/j.immuni.2023.03.005).

March 24: The CDC updates its COVID-19 community levels: Rocky Mountain Laboratories in Hamilton, Montana, moves from high to medium community level; all other NIH locations remain at their current levels.

March 29: A study by NIDA and other collaborators found that the expanded availability of opioid use disorder-related telehealth services and medications during the COVID-19 pandemic was associated with a lowered likelihood of fatal drug overdose among Medicare beneficiaries (JAMA Psychiatry 2023; DOI:10.1001/jamapsychiatry.2023.0310).

March 31: The CDC updates its COVID-19 community levels: Rocky Mountain Laboratories in Hamilton, Montana, moves from medium to low community level; all other NIH locations remain the same.

April 10: The Clinical Center updates its COVID guidance. Asymptomatic patients undergoing any procedures, including high-risk aerosol-generating procedures, are no longer required to undergo SARS-CoV-2 pre-procedure testing. All patients will continue to be screened for symptoms and recent exposure to SARS-CoV-2 using the emerging infection screening tool before any procedures.

April 10: President Joseph Biden signs a bipartisan congressional resolution to end the COVID-19 national emergency, bringing it to a close after three years and weeks before it was set to expire alongside a separate public health emergency. On January 31, 2020, then-Health and Human Services Secretary Alex Azar first declared a public health emergency and then-President Donald Trump declared the COVID-19 pandemic a national emergency that March.

April 10: The Biden administration launches Project Next Gen, a $5 billion-plus program to accelerate development of new coronavirus vaccines and treatments to better protect against a still-mutating virus and to protect against other coronaviruses that might be a future threat.

April 18: The FDA releases updated guidance to simplify the use of COVID-19 vaccines.

April 24: The NIH Clinical Center returns to in-person quarterly Town Halls in the Lipsett Amphitheater. Three sessions will be held at 7:30 a.m., 1 p.m., and 5:30 p.m. The 1 p.m. session will be videocast for those unable to attend in person and archived for later viewing. •
News From and About the Scientific Interest Groups

REBRANDED SIG: Digital Health Scientific Interest Group

The mHealth SIG has been re-envisioned as the Digital Health Scientific Interest Group. If you are in the digital health space and wondering how to launch a mobile app, which wearable device to use in your study, or how to analyze data from a digital health study, this is a SIG for you!

Digital technologies are present in everyday life. From mobile and information technologies to telemonitoring and telehealth, digital technologies are now core to national and international strategic plans promoting health and wellbeing. Digital health is an ever-evolving field focused on the use of digital technologies to improve health and medical care.

The Digital Health Scientific Interest Group is a forum for sharing ideas and resources to advance digital health research at NIH. Specifically, the SIG aims to:

- Connect intramural researchers conducting or interested in conducting digital health research
- Provide opportunities to present and receive feedback on research, to network with intramural and extramural researchers, and to promote collaborative research
- Share resources around digital health including conferences, journals’ special issues, and academic centers, organizations, and commercial companies in the digital health space, to name a few

Membership is open to federal employees and select extramural experts in digital health. SIG members will meet quarterly to present their research, and meeting frequency can increase as membership expands. Beyond regular meetings, the SIG will hold an annual brainstorming workshop at which presenters can get detailed feedback on study design and implementation in digital health. We will also aim to submit proposals for special issues with prominent journals and conference panels to highlight digital health work done at NIH.

For more information, go to https://oir.nih.gov/sigs/digital-health-scientific-interest-group or contact Co-Chairs Sherine El-Toukhy, (National Institute on Minority Health and Health Disparities) at sherine.el-toukhy@nih.gov and Tiffany M. Powell-Wiley, (National Heart, Lung, and Blood Institute) at tiffany.powell-wiley@nih.gov.

To join the Digital Health Scientific Interest Group LISTSERV email list and receive notices of meetings, go to https://list.nih.gov/cgi-bin/wa.exe?SUBED1=DigitalHealth-L.

SAVE THE DATE: NIH Research Festival
Sept. 18–20

The Office of Intramural Research is pleased to announce the return of the NIH Research Festival in-person for the first time since 2019.

Highlights include talks in Lipsett Amphitheater; poster presentations on the FAES Terrace; vendor exhibitions...Maybe food trucks. Maybe music. Maybe YOU!

Watch for a call for posters.

The Research Festival Steering Committee will post information at: researchfestival.nih.gov
Star-Nosed Moles, Electric Eels, and Other Tales of Evolution’s Mysteries Solved
Kenneth Catania Presents the First Porter Book Club Lecture

BY ELISA GUMA, NIMH

“Nature was my first classroom,” said Kenneth Catania to an engaged group of about fifty people gathered for the inaugural Porter Book Club event. Catania is the Stevenson Professor in the Department of Biological Sciences at Vanderbilt University (Nashville, Tennessee), and presented his book *Great Adaptations: Star-Nosed Moles, Electric Eels, and Other Tales of Evolution’s Mysteries Solved*, to NIH staff on March 10. He shared a personal account of the unexpected and fascinating discoveries made during a career spent investigating nature’s most mysterious animals.

Catania’s journey to becoming a biologist and neuroscientist started as a young boy growing up in Columbia, Maryland, where he collected interesting critters inhabiting the surrounding forests, lakes, and streams. And it was there, in that natural classroom, where he first encountered the elusive star-nosed mole. The unfortunate creature was dead, perhaps forced out of its habitat due to nearby developments, but it made a lasting impression on young Catania.

Years later, that encounter would help him land his first research internship. As an undergraduate student interning at the National Zoo in Washington, D.C., Catania was brought on to capture and bring back wild star-nosed moles. A team of researchers there wanted to study whether the mole’s curious looking nose, comprising 22 sensory appendages resembling a star, could detect electric fields. While these creatures are not endangered, they are extremely hard to find because they live underground in wetlands, usually under mud and dense vegetation.

Ready for the challenge, young Catania set out into the northern Pennsylvania wilderness in a van (in which he slept) with some traps, a map, and some jars of earthworms for baiting. He came upon an ecologically rich wetland surrounded by foothills where accumulated decaying vegetation and moist soil had allowed a huge diversity of invertebrates and other animals to thrive. Eventually, he caught five or six moles; the trip was considered a huge success! Back at the zoo, however, he didn’t find evidence for an electric sense—a mole’s nose was not, in fact, an electroreceptor. He surmised it must serve a different purpose.

Despite that early setback, Catania eventually cracked the case of the mole’s nose in graduate school. It turns out that the pink, fleshy tentacles surrounding the small mammal’s nose were exquisitely sensitive sensory organs. Compared to the human hand, which has 17,000 touch fibers, the star-nosed mole’s snout has an astounding 100,000, making it one of the most densely innervated skin surfaces of any mammal. This sensory organ enables the mole to navigate through underground tunnels and forage for food at unprecedented speeds, sometimes eating five separate prey items in a single second.

Through his experience with the star-nosed mole, Catania got a taste for solving biological mysteries and studying extreme adaptations in the animal kingdom that reveal new insights into how life evolved. He learned the benefits and challenges of tackling questions (and going on adventures) that few had previously considered. He has since applied those skills to learning more about other animals such as electric eels, tentacled snakes, water shrews, and parasitoids. Such creatures have advanced the field of science in unique ways. For example, the electric eel inspired Italian physicist Alessandro Volta to invent the battery in 1800 and allowed scientists to first identify acetylcholine receptors, which enable skeletal muscle contraction.

Catania also shared his process of discovery, which has gone hand-in-hand with failure in his own research. “As a rough rule of thumb, one in six ideas work and the rest fail,” he said, adding that he encourages young scientists to get comfortable with failure. “Learn not to get too attached to any one idea, and then move on quickly from those failures.”

The Porter Book Club is a new literary initiative at NIH aimed at gathering people and encouraging discussion about interesting books on the topics of science, health, and society. Keep an eye on your NIH email for the Daily Digest from the NIH Calendar of Events for future lectures.
What We’re Reading
Articles That Capture the NIH’s Role in History or Society

“TRUST IN US FEDERAL, STATE, AND LOCAL PUBLIC HEALTH AGENCIES DURING COVID-19”
Health Affairs
March 2023

“Scientific expertise was a more commonly reported reason for ‘a great deal’ of trust at the federal level, whereas perceptions of hard work, compassionate policy, and direct services were emphasized more at the state and local levels. It may be especially helpful to identify opportunities for creating complementary communication strategies at the federal, state and local levels, with more emphasis on scientific expertise at the federal level and more emphasis on compassionate direct services at the state and local levels.”

“NOAM CHOMSKY: THE FALSE PROMISE OF CHATGPT”
New York Times
March 8, 2023

“The human mind is not, like ChatGPT and its ilk, a lumbering statistical engine for pattern matching, gorging on hundreds of terabytes of data and extrapolating the most likely conversational response or most probable answer to a scientific question. On the contrary, the human mind is a surprisingly efficient and even elegant system that operates with small amounts of information; it seeks not to infer brute correlations among data points but to create explanations.”

“USING POPULATION DESCRIPTORS IN GENETICS AND GENOMICS RESEARCH”
NASEM
March 14, 2023

“In response to a request from the National Institutes of Health, the National Academies assembled an interdisciplinary committee of expert volunteers to conduct a study to review and assess existing methodologies, benefits, and challenges in using race, ethnicity, ancestry, and other population descriptors in genomics research. The resulting report focuses on understanding the current use of population descriptors in genomics research, examining best practices for researchers, and identifying processes for adopting best practices within the biomedical and scientific communities.”

“AS SCIENTISTS EXPLORE AI-WRITTEN TEXT, JOURNALS HAMMER OUT POLICIES”
Science
February 22, 2023
https://www.science.org/content/article/scientists-explore-ai-written-text-journals-hammer-policies

“So far, scientists report playing around with ChatGPT to explore its capabilities, and a few have listed ChatGPT as a co-author on manuscripts. Publishing experts worry such limited use could morph into a spike of manuscripts containing substantial chunks of AI-written text.

One concern for journal managers is accuracy. If the software hasn’t been exposed to enough training data to generate a correct response, it will often fabricate an answer, computer scientists have found.

“Many journals’ new policies require that authors disclose use of text-generating tools and ban listing a large language model such as ChatGPT as a co-author, to underscore the human author’s responsibility for ensuring the text’s accuracy.

That is the case for Nature and all Springer Nature journals, the JAMA Network, and groups that advise on best practices in publishing, such as the Committee on Publication Ethics and the World Association of Medical Editors. But at least one publisher has taken a tougher line: The Science family of journals announced a complete ban on generated text last month.

The journals may loosen the policy in the future depending on what the scientific community decides is acceptable use of the text generators, Editor-in-Chief Holden Thorp says. “It’s a lot easier to loosen our criteria than it is to tighten them.”

“THE FAUCI PHENOMENON, PART 2”
New England Journal of Medicine
March 23, 2023

“In this episode of ‘Intention to Treat,’ Anthony Fauci sits down with host Rachel Gotbaum to discuss his long career in infectious disease and public health, what has motivated him, and the lessons he has learned and taught along the way.”

https://irp.nih.gov/catalyst 19
**Bang for the Buck**

Updated Website Showcases NIH’s Impact on Health, Science, and Society

BY RACHEL DIAMOND, IRA KUHN, SARAH RHODES, AND KELLY SINGEL, OD

**Did you know that in the 1950s and 1960s, intramural researchers at the NIH Clinical Center pioneered the field of chemotherapy, leading to the dramatic increases in cancer survival rates seen today; cracked the genetic code, launching the genetic revolution; and helped develop the automatic blood counter that is now used in everyday bloodwork around the world?**

Or that scientists in NIH’s Intramural Research Program created Matrigel, a specialized gel that promotes cell growth on a 3D surface and has been cited in more than 13,000 scientific publications? Or that, built on a foundation of NIH-supported research, the United States biomedical industry contributes over $69 billion to the nation’s gross domestic product annually and supports over 7 million jobs.

You can read all about these impacts of NIH research and more—including how NIH improves health, revolutionizes science, and serves society—on the recently refreshed and redesigned NIH Impact Pages.

The NIH Impact Pages are an important source of information on the long-term, real-world impact of NIH for many of NIH’s community members, including Congress, advocacy groups, and the public. With that in mind, the Office of Evaluation, Performance, and Reporting (OEPR) launched a concerted effort to revamp the Impact Pages with a focus on making the website interactive and accessible—and with new content to showcase.

Historically, the Impact Pages had minimal design elements, were text heavy, and had very few pictures. Thanks to a close collaboration with the Office of Communication and Public Liaison, OEPR was able to redesign the website into a more engaging flip card format while still referencing source materials. The pages feature content on the impacts of NIH research on health, science, and society in a way that is eye-catching and interactive and provides additional context with references should anyone want to dig deeper.

But that’s just the look and feel of the revamped pages. It also took a workgroup of more than 100 staff across NIH, including from the Office of Intramural Research, to gather new content for the website.

Today, the Impact Pages feature 130 flip cards illustrating how NIH improves health, revolutionizes science, and serves society, with a myriad of additional topics flagged for future inclusion as NIH’s impacts continue to grow.

OEPR would like to thank everyone who contributed to these pages in many ways, from staff who gathered content to patients who participated in the clinical trials and were featured in some of the images. We encourage everyone to view the pages and share with their personal and professional networks. This was truly a passion project, because with every new impact uncovered, our pride in working at NIH and contributing to these impacts grew. If you have an idea for a flip card to be featured on the NIH Impact Pages, please email Sarah Rhodes at Sarah.Rhodes@nih.gov.
I served as co–principal investigator of the Ghana Breast Health Study, where we are identifying risk factors for different subtypes of breast cancer to help inform public health strategies for prevention in Africa and African ancestry populations (Int J Cancer 147:1535-1547, 2020).

In Scotland, using a socioeconomic index that integrated measures including income, health care access, crime, and education, we noted some inequities exist in breast cancer incidence and survival but differ depending on the molecular subtype of breast cancer (Breast Cancer Res Treat 194:463-473, 2022).

NEIL HANCHARD, M.B.B.S., D.PHIL., NHGRI
Senior Investigator, Center for Precision Health Research, National Human Genome Research Institute
Education: University of The West Indies, Kingston, Jamaica (M.B.B.S., which is equivalent to an M.D.) and University of Oxford (D.Phil., in human genetics and clinical medicine)
Training: Pediatric Residency, Mayo Clinic, Minnesota; Medical Genetics Residency and Fellowship, Baylor College of Medicine, Houston, Texas
Before coming to NIH: Clinical Research Fellow, Tropical Medicine Research Institute, University of the West Indies (Mona, Jamaica). Physician Scientist and Associate Professor in the Department of Molecular and Human Genetics at Baylor College of Medicine (Houston)

Come to NIH: In 2021

Outside interests: I watch (and sometimes try to play) sports of all kinds—tennis, swimming, baseball, and soccer. My children are heavily involved in one or more of these so there’s usually something to occupy my non-work time. Otherwise, I try to stay engaged with my church community and spend time with family and friends.

Research interests: My main research interests are to use human genetics to better understand complex childhood diseases. Early in my career, I indulged this interest by studying the population genetics of the mutation that causes sickle-cell disease and identifying novel genes in the development of congenital cardiovascular disorders and rare Mendelian disorders. More recently, I have tried to make inroads to our understanding of the pathogenesis of diabetic embryopathy (Genet Med 21:2453-2461, 2019), severe childhood malnutrition, and transfusion alloimmunization in sickle cell disease.

As head of the Childhood Complex Disease Genomics Section, I have continued much of the latter research, and we are currently working on three major projects. The first two are multi-omics
studies. One project focuses on severe childhood malnutrition, trying to answer the question of why some children get a severe form of malnutrition known as kwashiorkor (eBioMedicine 75:103791, 2022; Nat Commun 10:5791, 2019). The second project is about refining the mechanism underlying our previously described association between a genetic locus and an increased risk of transfusion-related alloimmunization in sickle-cell disease (Blood Adv 2:3637-3647, 2018). The third project is a study to identify the genes and pathways that underlie childhood-onset essential hypertension.

These disorders are all more common among individuals with recent African ancestry, and so all our studies are underpinned by efforts to use population genetics to better understand the complex genomes of individuals from those ancestries (Nature 586:741-748, 2020; Am J Hum Genet 102:731-743, 2018). In keeping with this, I am the Chair of the Genome Analysis Working Group of the H3Africa Consortium, Chair of the Diversity, Equity, and Inclusion Task Force of the American Society for Human Genetics, and a Distinguished Scholar at the NIH.

**ALEXANDER KELLY, PH.D., NCI**

*Senior Investigator, Laboratory of Biochemistry and Molecular Biology (LBMB), National Cancer Institute*

**Education:** Clark University, Worcester, Massachusetts (B.A. in biochemistry); University of California at San Francisco (Ph.D. in biophysics)

**Training:** Postdoctoral Fellow at The Rockefeller University (New York, New York)

**Before coming to NIH:** Research Associate at The Rockefeller University

** Came to NIH:** In 2012 as a Tenure Track Investigator in the NCI LBMB

**Outside interests:** Watching baseball; playing basketball; hiking; collecting modern furniture

**Research interests:** The faithful segregation of chromosomes is the key event of mitosis, and its dysregulation can lead to aneuploidy and genome rearrangements that drive tumor evolution and metastasis in cancer cells.

Chromosome segregation is mediated, in part, via attachment of spindle microtubules to kinetochores, large proteinaceous structures that assemble on each chromosome at a site called the centromere. A major focus of my lab at the NCI is to understand how the kinetochore is assembled onto centromeres (Science 359:339-343, 2018; J Cell Bio 218:3237-3257, 2019), and how kinetochore-microtubule attachments are edited to ensure that the genome is divided equally (Dev Cell 42:640-654, 2017). We have a longstanding interest in how the mitotic kinase Aurora B, a cancer drug target that is part of the chromosomal passenger complex, regulates these processes. A key future question is how kinetochores and key kinases such as Aurora B are differentially regulated in distinct cell types and contexts (for example, embryonic versus somatic cells) to promote chromosome segregation.

Entry into mitosis also triggers dramatic structural changes in chromosomes that are necessary for their proper segregation. My lab is interested in how chromosomes are compacted into rodlike structures by condensin complexes, and what regulates condensin activity. We found that a part of the transcriptional initiation complex, the DNA translocase/helicase TFIIH complex, is required for both the establishment and maintenance of chromosome structure in mitosis through regulation of condensin function independently of transcription (eLife 11:e75475, 2022).

Going forward, we will determine the mechanism by which TFIIH regulates condensin in vertebrates and mammals, and use chromosome-capture and live-imaging approaches to examine the kinetics of condensation. In addition to shedding light on the regulation of chromosome condensation, our studies will also influence our work on kinetochores, as transcription and condensins play important but incompletely understood roles in centromere function.

**STEVEN MOORE, PH.D., M.P.H., NCI-DCEG**

*Senior Investigator, Metabolic Epidemiology Branch, Division of Cancer Epidemiology and Genetics (DCEG), National Cancer Institute*

**Education:** Williams College, Williamstown, Massachusetts (B.A. in psychology); Yale University School of Public Health, New Haven, Connecticut (M.P.H.); Yale University (Ph.D. in cancer epidemiology)

**Training:** Postdoctoral Fellow, Research Fellow, NCI, National Institutes of Health, Bethesda, Maryland

**Before coming to NIH:** Moore worked as a research analyst for the Connecticut Department of Public Health, and as a statistical analyst in the Division of Preventative Medicine at Brigham and Women’s Hospital in Boston.

**Came to NIH:** In 2005 as a predoctoral fellow in NCI-DCEG

**Outside interests:** Competitive masters running; board gaming; and spending time with family

**Research interests:** I research how physical activity, obesity, and diet are related to human carcinogenesis and health through analyses of large-scale consortium datasets and high-throughput molecular epidemiology studies.

In one study, my collaborators and I found that aerobic physical activity is associated with lower risk of at least 13 different types of cancer (JAMA Intern Med 176:816–825, 2016). I also found that weightlifting was associated with lower risk of colon cancer, particularly among men. In other studies, my collaborators and I found...
that as little as 10 minutes per day of activity was associated with a gain of almost two years of life expectancy—a surprisingly large gain for so little activity time (PLoS Med 9:e1001335, 2012).

I also investigate the biological mechanisms underlying the relation of physical activity and obesity to health. For example, my collaborators and I found that abnormal metabolism of branched-chain amino acids may increase risk of breast cancer in women with an elevated body mass index (J Natl Cancer Inst 110:588-597, 2018). To extend this work, I also have explored hundreds of metabolic factors and risk of other obesity-associated cancers such as renal cell carcinoma and endometrial cancer to determine whether similar “mechanistic mediators” are at play.

I evaluate biomarkers for diet that I have uncovered throughout my research career. I hope to evaluate whether specific food biomarkers exist for distinct types of processed foods and beverages like energy drinks. Metabolomics—the study of small molecule constituents of a biological system—has made it possible to study human physiology and metabolism as well as measure dozens, if not hundreds, of dietary biomarkers simultaneously, which can in turn be used as objective measures of diet in cancer etiology studies.

In 2013, I was named an Earl Stadtman Tenure Track Investigator and have since cofounded the Consortium of Metabolomics Studies (COMETS), a consortium comprising 65 international prospective cohorts that uses metabolomics to identify risk factors for chronic disease. My colleagues and I cocreated an online data analysis application named COMETS Analytics, which is used to conduct consortium-based analyses of metabolomics and other -omics data. I am a multiyear awardee of the DCEG Informatics Challenge for this work and other projects.

Manu Omar Platt, Ph.D., NIBIB
Director, Biomedical Engineering Technology Acceleration (BETA Center), and Associate Director, Scientific Diversity, Equity and Inclusion at the National Institute of Biomedical Imaging and Bioengineering (NIBIB)

Education: Morehouse College, Atlanta (B.S. in biology); Georgia Institute of Technology (Georgia Tech) at Atlanta and Emory University, Atlanta (Ph.D. in biomedical engineering)

Training: A postdoctoral fellowship in biological engineering at the Massachusetts Institute of Technology (MIT), Cambridge, Massachusetts

Before coming to NIH: Platt was a Professor and Associate Chair of Graduate Studies in the Walter H. Coulter Department of Biomedical Engineering at the Georgia Institute of Technology and Emory University. He also was Georgia Research Alliance Distinguished Cancer Scientist, Deputy Director of the Interdisciplinary Bioengineering Graduate Program at Georgia Tech, and Wallace Coulter Distinguished Faculty Fellow.

Came to NIH: In February 2023

Outside interests: I love movies, music, and television. I also enjoy theater, art, and lively conversations with my friends and family. Origami is also one of my hobbies so if there are other folders out there, look me up!

Research interests: In my lab, we study diseases of tissue remodeling and the mechanisms involved in going from healthy tissue to diseased tissue, which involves experimental and computational approaches.


Now I am the director of the NIH-wide Center for Biomedical Engineering Technology Acceleration (BETA Center), housed within the NIBIB Intramural Research Program. The BETA Center serves as a model to bring a focused engineering approach to NIH researchers across disciplines to accelerate the development, validation, and dissemination of innovative technologies. At the BETA Center, we work to expand opportunities for biomedical engineering training and professional growth, including supporting individuals from diverse backgrounds.

As a nationally recognized leader in expanding diversity and inclusion in science, technology, engineering, and mathematics, it is an honor to serve as NIBIB’s associate director for Scientific Diversity, Equity, and Inclusion. I am a fellow of the Biomedical Engineering Society and the American Institute for Medical and Biological Engineering and have served as the Diversity Director for the National Science Foundation’s Center on Emergent Behaviors of Integrated Cellular Systems (EBICS). I also cofounded Project ENGAGES: Engaging New Generations at Georgia Tech through Engineering and Science, which provides paid research lab experiences at Georgia Tech for Atlanta area African American high school students.

I directed the Georgia Tech Enhancing Science, Technology, Engineering, and Math Educational Diversity grant program, which is an NIBIB-funded training program to increase and support diversity at the undergraduate level. Some accolades earned from this service include the NIH Director New Innovator award, an American Association for the Advancement of Science Mentor award, and the Biomedical Engineering Society Diversity Award.
CATALYTIC REACTIONS?

**If you have a photo or other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation or confession that scientists might appreciate and that would be fit to print in the space to the right, why not send it via email: catalyst@nih.gov; or mail: *The NIH Catalyst*, Building 1, Room 160.**

Also, we welcome “letters to the editor” for publication and your reactions to anything on the Catalyst pages.


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PHOTOGRAPHIC MOMENT

New Surgery, Radiology, and Lab Medicine Wing

![Image of the new SRLM wing](https://irp.nih.gov/catalyst/31/3)

**Shades of things to come. The famed model of the Building 10 complex that sits in the Clinical Center atrium has been updated to feature the new Surgery, Radiology, and Lab Medicine (SRLM) wing, seen here in orange. Nestled into the northwest corner of the NIH Clinical Center, the 11-story SRLM—that’s nine high with two underground—will house state-of-the-art facilities for numerous clinical activities when completed in 2028. And a note, too, about shades of things that have come to pass. The Clinical Center will celebrate its 70th anniversary with a special Grand Rounds Lecture on June 28, followed by activities through July. For details, refer to https://clinicalcenter.nih.gov/ocmr/history/70thanniversary.html**