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Brave New Imaging:

From the Cosmos to the Molecule

BY ANNE DAVIDSON, NICHD

"Today we are going to consider the ultimate bridge from the farthest reach of the cosmos to the smallest molecule," **Irwin Arias**, the organizer of the DeMystifying Medicine lecture series, told the crowd that had crammed into the Building 50 conference room on March 13, 2018. The featured speakers were NASA astrophysicist John Mather, who studies the stars, and former NIH senior scientist **Jennifer Lippincott-Schwartz**, who studies the inner workings of cells.

"We have two spectacular presenters to take us through the brave new world of imaging from the cosmos to the molecule," said NIH Director **Francis Collins,** who was on hand to introduce the speakers. "You are about to travel through 36 orders of magnitude. Put on your seat belts, and let's see where it takes us."

Imaging the Cosmos: Mather, a senior astrophysicist in the Observational Cosmology Laboratory at NASA's Goddard Space Flight Center (Greenbelt, Maryland), shared the 2006 Nobel Prize in physics (with George Smoot) for the "discovery of the blackbody form and anisotropy of the cosmic microwave background" using the Cosmic Background Explorer (COBE) satellite launched by NASA in 1989. This discovery is in essence the afterglow of the Big Bang 13.8 billion years ago that gave birth to the universe. Mather was a key figure leading the COBE space mission and

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The Jugglers

Balancing a Scientific Career with Raising a Family

BY MICHELLE BOND, LAURA S. CARTER, ANNE DAVIDSON, CLARISSA JAMES, AND EMILY PETRUS

CHRIS RYAN, *NATURE*

Reprinted with permission from Springer Nature: Chris Ryan, *Nature* 2015 (From: Powell, K.,"Work–Life balance: Lab life with kids," *Nature* **517:**401–403, 2015).

"It's hard to feel good at everything," senior investigator **Deborah Citrin** (NCI) concluded after talking about the inherent and unavoidable "work–life imbalance" of being a PI and a mother of three. Her husband, a surgical oncologist at Walter Reed National Military Medical Center, has been deployed five times. So she has the challenge of single-handedly holding down the home front while working at NIH and running a laboratory and clinical trials. And yet she and her husband have managed to successfully juggle their careers with family-raising responsibilities.

"Remember, everybody is struggling," she warns. Be wary of the "glossy image" of the working parent who seem to be excelling in all aspects of his or her life.

(See Citrin's and others' stories starting on page 10.)

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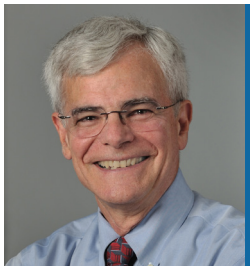

Parenting at NIH:
A Delicate Balance

BY MICHAEL GOTTESMAN, DDIR

Hanging in my Building One office is a reproduction of a Marc Chagall painting that shows a fiddler carefully poised on two rooftops, managing to stay upright and make beautiful music at the same time. This image represents the challenge of being a parent and a scientist at the NIH: How does one maintain equilibrium and productivity while juggling two such important responsibilities?

This issue of the *NIH Catalyst* addresses this question through a series of interviews with people who have been able to manage both parental and scientific responsibilities. Although not interviewed for this issue, my wife Susan and I fall into this category, so I will take the prerogative of the publisher of the *Catalyst* to offer my two cents about how we managed to survive our child-raising years. Here are some ways in which we maintained our careers and our sanity:

1. We always tried to have more adults than children involved in any activity. One on one is challenge enough; being outnumbered by children is risky. In fact, the more adults that can be brought into the equation, the better. Grandparents, aunts and uncles, friends, neighbors, and professional help are all highly recommended. If they don't directly help with child care, they can help in other ways: housework, errands, carpools, etc.

Single parents are at greatest risk and should do their best to engage other adults in the parenting process. I realize that many people are much better at managing children than we were, but for us, it took a village.

2. Choose a career with maximum flexibility of hours. You never know when a child will be sick and/or will require attendance at a performance, after-school activity, or help with homework. We are extremely fortunate at the NIH that some of the work we do offers this kind of flexibility, and when it does not (such as an experiment that absolutely must be harvested, or a clinical-care responsibility) then principle #1 applies (a second adult who can step in). Having two parents who both work at the NIH increases the likelihood of flexibility when it is most needed. One of the great recruiting arguments for the NIH is no teaching or grant-writing responsibilities, both of which are a drain on time otherwise spent with children.

3. Choose your partner carefully. Romantic attraction is a good start, but willingness for all partners to take on the responsibilities of child care is an absolute essential for any couple who is planning to have children together.

4. We always tried to set aside some time each day to listen to our children, hear what was on their minds, and give them our best direction. This is easiest to accomplish with a shared dinner time, but can come at bedtime (when we read to our children even through high school) or another relatively quiet time together.

5. Mentoring of our trainees and junior colleagues is very different from parenting our own children. Our mentees here seek our advice, try to follow our suggestions, and consider us to be role models. Teenage children do their best to ignore parental advice and seek alternative role models. So we tried never to confuse our children with our mentees; although in both cases we are vitally interested in the outcome of our efforts and want them to succeed, the relationship is very different.

6. With two scientists in the family, travel to scientific meetings can occasionally interfere with shared parenting. It is important for parents to realize that a scientific trip is an opportunity for one parent to get away from parental responsibilities and focus entirely on science. This can be accomplished by not overwhelming the traveling partner with unpleasant details of events at home or, if the family travels together, having the parent who is not an essential attendee at the meeting take over complete responsibility for the children.

7. One of the great pleasures in having a career in science and parenting children at the same time is that the children get to see how excited their parents are about their work and how rewarding it is to have a fulfilling career. They get to appreciate that it is possible to love your work and your family, and that the occasional inconvenience of having a parent who is late for dinner or occasionally out of town at a meeting is more than compensated for by having parents who are content with their lives.

8. We are at the stage now where our children have children, and as grandparents we try as best we can to be those extra helpful adults who can make parenting and a scientific career most rewarding for our children. Many scientists choose not to have children, but those who do develop coping mechanisms such as the ones described in this essay, with perfectly acceptable outcomes, not the least of which is the absolute joy of being a grandparent. ●

Clinical Center's New Chief Operating Officer: Pius Aiyelawo

ERNIE BRANSON, NIH

Pius Aiyelawo joined NIH, in April, as the Clinical Center's new chief operating officer.

Retired U.S. Navy Captain **Pius Aiyelawo** began his tenure on April 2, 2018, as chief operating officer (COO) of the NIH Clinical Center. Aiyelawo fills a role newly expanded to include management of most clinical as well as administrative areas. He reports directly to Chief Executive Officer **James K. Gilman**.

"Pius's tremendous health-care leadership experience is matched only by a positive energy and spirit that will inspire both patients and staff," said Gilman. "After a very competitive national search, I am convinced he is the right person to help us raise the bar ever higher in delivering safe, high-quality patient-centric care."

Aiyelawo held senior leadership positions in hospitals and large medical research programs throughout a distinguished military career spanning over 27 years. His most recent appointments included being assistant deputy director, Research and Development, U.S. Navy Bureau of Medicine and Surgery (Falls Church, Virginia) and COO/deputy commander of Naval Medical Research and Development Command (Fort Detrick, Maryland). He has also served as the commanding officer of the Navy's largest health-care facility—U.S. Naval Hospital (Okinawa, Japan)—where he led the successful planning, transition, and relocation to a new $650 million hospital complex.

Aiyelawo's awards include the Legion of Merit with two gold stars, Defense Meritorious Service Medal, Navy Meritorious Service Medal with two gold stars, Navy Commendation Medal with one gold star, Navy Achievement Medal, and service and unit awards.

After his retirement from the U.S. Navy in 2013, Aiyelawo served as a senior program director at General Dynamics Health Solutions (Silver Spring, Maryland). He has taught health-care courses throughout the world. Since 2014, he has served as an adjunct assistant professor of Preventive Medicine and Biometrics at the F. Edward Hebert School of Medicine, Uniformed Services University of the Health Sciences (Bethesda, Maryland).

Aiyelawo holds a B.A. in management science from Alaska Pacific University (Anchorage, Alaska) and an M.P.A. from the University of Alaska (Anchorage, Alaska). He is a fellow in the American College of Healthcare Executives, on the Board of Directors for HelpAge USA, and a member of the Society for International Development.

"I am grateful to the NIH senior leadership and Dr. Gilman for this opportunity and truly humbled to be selected as the chief operating officer of the finest and premiere research hospital in the world," Aiyelawo said. ●

Town Hall

With HHS Secretary Alex Azar

BY PATRICK WRIGHT, NINDS

Less than two months after he was sworn in as the United States Secretary of Health and Human Services (HHS) on January 29, 2018, **Alex Azar** visited the NIH Bethesda campus. On Tuesday, March 20, he met with institute directors and investigators, visited patients, and participated in a town hall meeting with NIH Director Francis Collins and the NIH community.

During the town hall, Azar, who is a lawyer and former drug-company executive, emphasized his four priorities as HHS secretary: reducing drug prices; fixing the health-insurance market to make it more affordable; using the power of Medicare to try to drive the value-based transformation of our health-care system; and tackling the opioid crisis.

He also answered questions that had been submitted in advance by members of the NIH community. He commented on how HHS is better prepared to handle a health crisis than it was post-9/11; that the latest research is needed to address the opioid addiction problem; and that his job is not to solve a crisis but to have a team that can. It's like conducting an orchestra, he said—getting the musicians to perform their best and act as a team. ●

To watch a videocast of the town hall (HHS and NIH only), go to https://videocast.nih.gov/launch.asp?23769.

Read the full article about the HHS Secretary's visit at https://irp.nih.gov/catalyst/v26i3/news-briefs

From the Fellows Committee

The Perks of Mentoring Summer Interns

BY CRAIG MYRUM, NIA

You're likely to soon see a flux of young, energetic new faces in your laboratory. That's because it's time for summer internships. For eight weeks between May and August, approximately 1,300 students—from high schools, community colleges, and four-year universities as well as from professional and graduate schools—will join the NIH community, where they will attend lectures, participate in workshops, conduct research, and present their findings at Summer Poster Day on Thursday, August 9, 2018, in the Natcher Conference Center (Building 45). Interns will be able to develop professional connections, learn new skills, and gain insights into whether graduate school is for them. So what's in it for the mentors—most of them postdocs—who train them?

"Mentoring interns is your chance to pay it forward," said **Lori Conlan**, director of Postdoctoral Services and Career Services at the Office of Intramural Training and Education (OITE). "Many scientists say that their first research experience was a key influence early in their career."

Indeed, nearly every researcher has benefitted from good mentorship. Most of the summer students will come to NIH with little to no research experience, but they will leave with a wealth of fresh knowledge and newfound confidence. Seeing that happen can be an extremely rewarding experience for the mentor.

Having a strong mentoring track record can have a profound effect on your career and be an influential factor when you're later applying for positions post-NIH regardless whether that is in academia, industry, or another career.

Being an effective mentor takes practice, so taking in summer interns provides excellent opportunities to hone critical mentoring skills. Mentoring requires a tailored approach for each student. Some require extensive one-on-one time, whereas others need minimal direction with only gentle nudges and encouragement along the way. Being able to properly assess skill levels and adjust accordingly can be instrumental in creating a positive experience for both the mentor and mentee.

> Mentoring summer interns can be a win-win for everyone. Mentees get hands-on experience in answering real-life research questions, and mentors refine mentoring skills.

"Learning the elements of a good research project is also critical," said Conlan. In just eight weeks, students must take an idea, generate data, and present their findings. Mentors can help students learn the important skills of getting the scope of the research question right and developing realistic projects that can be completed within a finite amount of time. Those skills can later come in handy for anyone who will mentor or supervise people in the future.

Supervising a summer intern can also push mentors to understand a project on a new level. Teaching mentees about a research project is an excellent way to practice all-important science communication skills. It requires being able to balance a description of the big picture of a research question with the provision of the necessary details. Throughout our careers, we will need to be able to communicate our work with experts and novices alike, so developing communication and storytelling skills now can be valuable. And expect questions from the students—lots of them. Discussing background literature or project data can result in challenging, insightful, and maybe even stumper questions. In these ways, mentoring can deepen an understanding of a mentor's own research and enable us to think about it in new ways.

Mentoring summer interns can truly be a win-win for everyone. Mentees get hands-on experience in answering real-life research questions, and mentors refine mentoring skills that will serve them throughout their careers.

Whether you are new to mentoring or need a refresher, OITE offers resources and courses:

- 2018 Summer Research Mentor Training: May 15 and 23, 2018, Building 60 (Cloisters), Lecture Hall Room 142 (10:00 a.m.–noon each day). To register go to http://bit.ly/2HcPQqa
- OITE Careers Blog, for lots of mentoring advice and other information: https://oitecareersblog.wordpress.com/category/mentoring-2/
- OITE also offers training for the summer interns: https://www.training.nih.gov/trainees/summer_interns
- Institute Training Directors: Check with them for more information. ●

NIH's Top-Ranking Supercomputer

The Computational Behemoth, Biowulf

BY BRANDON LEVY, OIR

BEN CHAMBERS, OIR

Combined, Biowulf's 10 high-performance storage systems, two of which are pictured here (each occupies two racks), provide more than 25 petabytes of storage capacity.

Tucked away behind the nondescript walls of Building 12 lies a computational behemoth known as Biowulf. The state-of-the-art supercomputer enables scientists in the NIH Intramural Research Program (IRP) to analyze massive data sets and attempt projects whose sheer scale would make them otherwise impossible.

Although the intramural community has harnessed the power of supercomputers since 1986, Biowulf itself was first launched in 1999. The size and complexity of scientific data sets were growing rapidly then, in no small part due to the massive amounts of data being produced by the Human Genome Project. More recently, modern scientific endeavors in fields such as biochemistry, microbiology, molecular dynamics, genomics, and biomedical imaging have once again dramatically increased scientists' computational needs.

To meet the demand, in 2014 the NIH embarked on a five-year initiative to dramatically enhance Biowulf's already considerable computing power. Four years in, the supercomputer has become a world-class resource used by more than one-third of the thousand-plus IRP research labs.

In 2017, Biowulf became the first machine completely dedicated to advancing biomedical research to break into the top 100 of TOP500.org's list of the most powerful supercomputers in the world, landing at number 66 in the rankings. Since 2014, the number of active Biowulf users has doubled (from 640 to 1,276), and jobs submitted have increased more than 800-fold (from 3.7 million to 32.1 million). More than 2,000 journal articles have been published based on data analyzed using Biowulf.

With Biowulf at their service, intramural researchers can process large-scale data sets much faster than would be possible with standard computational equipment. The revamped supercomputer has been a boon to researchers all across the NIH, contributing to publications on topics ranging from how the time of day affects the brain's water content, to how genes influence sleep duration in fruit flies, to a hunt for antibiotic-resistant bacteria in hospital plumbing.

The system is also being used to aid machine-learning projects, as researchers attempt to develop algorithms that can rapidly and accurately trace the borders of cells in a microscope image or diagnose illnesses by looking at magnetic-resonance-imaging scans or other scans. Overall, about a third of Biowulf's computing power is used for computational chemistry, a third for structural biology, and 20 percent for genomics, with dozens of other areas of biomedical inquiry using the remainder.

Biowulf's ascendance represents remarkable progress for both the NIH and scientific research generally, said **Andy Baxevanis**, Director of Computational Biology for the NIH Office of Intramural Research. "High-performance computing is a critical element of modern-day biomedical research and a vital resource for the intramural community," he said. "Biowulf's expansion is a sign that the NIH recognizes the importance of investing in state-of-the-art technologies to permit our scientists to remain at the forefront of their fields."

The High-Performance Computing (HPC) Group at NIH's Center for Information Technology (CIT) manages Biowulf and supports its users. The name "Biowulf" is a play on words combining "biology" with the name of a specific type of HPC system called a Beowulf cluster (Beowulf was named after the hero in the Old English epic poem, who had "thirty men's heft of grasp in the gripe of his hand.") NIH's HPC Group first learned about the Beowulf-cluster approach to supercomputing from its creator, then–NASA Goddard Space Flight Center Senior Scientist and current Indiana University Professor Tom Sterling, at a 1997 conference in San Jose, California. Each cluster is composed of several low-cost computers, called nodes, connected to one another and to other clusters via a centralized network and loaded with open-source software. By connecting enough nodes together, Beowulf systems can generate immense computing power for a relatively low cost.

Today, Biowulf is composed of more than 4,200 nodes collectively containing 97,000 cores, each of which can independently run program code. The computer system provides over 25 petabytes of primary storage to accommodate the large

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Brave New Imaging

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the principal investigator for the far-infrared absolute spectrophotometer on COBE.

"The sky is filled with at least 100 billion galaxies," said Mather. Each galaxy "is 100 billion stars orbiting a common center pulled together by gravity." And the universe is expanding. Astronomers can measure this expansion based on the wavelength of the light emitted from distant stars.

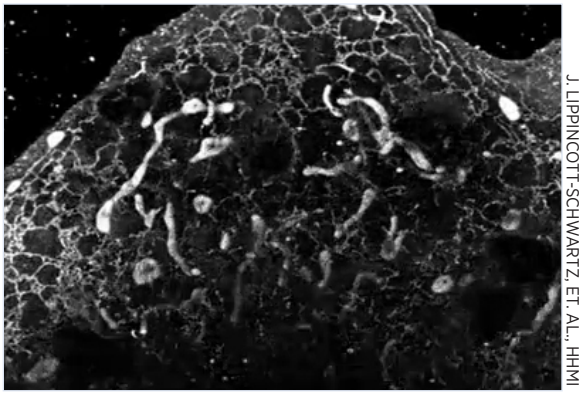
The Hubble Space Telescope, which was launched into low Earth orbit (at an altitude of 340 miles) in 1990, was intended to help astronomers "see the first galaxies forming," said Mather. But it wasn't strong enough. So now NASA, in collaboration with the European and Canadian space agencies is building the James Webb Space Telescope. (Mather is the senior project scientist.) This large infrared telescope has a mirror that is in 18 hexagonal segments and measures 21 feet in diameter, about 2.5 times as long as Hubble's mirror, folds up to fit in a rocket, and will take two weeks to unfold. It is scheduled to launch in 2020 and will be about 930,000 miles beyond Earth. Astronomers are excited that the Webb telescope will be used to study galaxies as they are forming, understand the formation of stars and planets, and directly image novas and planets outside our solar system.

CFHT, COELUM, MEGACAM, ET. AL.

The Webb Telescope will study galaxies as they are forming, understand the formation of stars and planets, and directly image novas and planets outside our solar system. Shown, an image of galaxy NGC 474, captured by the Canada-France-Hawaii Telescope (CFHT), which is on the summit of Mauna Kea in Hawaii.

Imaging Within: While Mather is looking skyward, Jennifer Lippincott-Schwartz is looking inward—at the tiniest elements of cells. Before becoming a senior group leader at the Howard Hughes Medical Institute (HHMI) Janelia Research Campus (Ashburn, Virginia) in 2016, she was a senior investigator in the National Institute of Child Health and Human Development (NICHD). She and **George Patterson**, then a postdoc in her lab and now a senior investigator in the National Institute of Biomedical Imaging and Bioengineering, created a photoactivatable form of green fluorescent protein that can be switched on using flashes of light. She hosted **Eric Betzig** (now at HHMI) and his colleague in her NICHD lab so they could build a super-resolution microscope called photoactivated localization microscopy (PALM), for which Betzig won the 2014 Nobel Prize in chemistry.

Lippincott-Schwartz explained that light microscopes have resolution limits—based on the wavelength of light, refractive index of the medium, and angle of the converging spot—and can't image many cell details. Super-resolution microscopy, such as PALM and the lattice light-sheet microscope (also developed by Betzig), however, can image the molecular complexity of the subcellular landscape. In PALM, a fluorophore is used as a point source of light, which Lippincott-Schwartz compared to stars. She calls it "super-resolution by pointillism." She has begun using even more advanced super-resolution techniques to explore the inner workings of cells.



J. LIPPINCOTT-SCHWARTZ, ET. AL., HHMI

Super-resolution microscopy allows biologists to see deep inside of cells and produce images that rival those of the universe. Shown: The Lattice Light-Sheet Microscope can do single-molecule imaging of lipids in membranes.

Imaging Life and the Cosmos: Both scientists acknowledge the commonalities their two fields share. Mather said he's grateful for the work of biologists who push the boundaries of microscopy. Lippincott-Schwartz pointed out that high-resolution microscopy has benefited from innovations in telescopes such as deformable mirrors that compensate for wave-front distortions in light coming from stars.

"We share the common intellectual tools trying to understand instrumentation [and] the objects we're looking at," said Lippincott-Schwartz. Whether it's looking at fluorophores in PALM or stars in the solar system, "[we] use the same algorithms for trying to understand the distribution and behavior of these systems." ●

You can watch the March 13, 2018, videocast online at https://videocast.nih.gov/launch.asp?23753.

Under Your Skin: Molecules and Cells for Touch and Pain

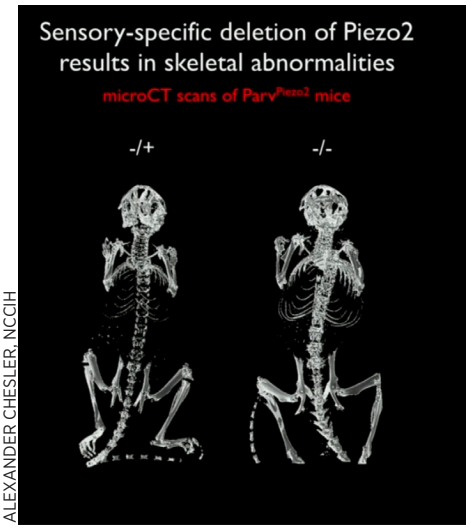
What Alexander Chesler Is Discovering about the Somatosensory System

BY HUSSAIN ATHER, NIDDK

She was a floppy baby, didn't stand until she was three years old, could walk at five—but only with assistance—and never ran or jumped. She developed difficulty grasping objects, poor balance and coordination, severe scoliosis, and joint contractures that caused her hands and feet to be abnormally shaped. She can't distinguish certain types of stimuli on her skin. And when she walks with her eyes closed, she loses her balance. But her brain is fine.

"She has absolutely no cognitive difficulties," however, said Stadtman Investigator **Alexander Chesler** (National Center for Complementary and Integrative Health) during a March 12, 2018, talk about his research. "In fact, there are no structural abnormalities in her brain, and she's incredibly bright. She's now in college studying engineering."

It turns out that the young woman (referred to as PS1) has two mutations in the *PIEZO2* gene. The discovery was made by National Institute of Neurological Disorders and Stroke senior investigator **Carston Bönnemann**, who studies the genetic basis for neuromuscular disorders in children. He introduced PS1 to Chesler because of her unusual phenotype. Chesler was intrigued that two mutations in a single gene could "result in this dramatic phenotype."



ALEXANDER CHESLER, NCCIH

Proteins encoded by the *PIEZO2* gene are expressed in tissues where mechanical forces influence biological processes such as touch and pain. Mutations in the gene not only wreak havoc with the somatosensory system, but when the PIEZO2 protein is selectively removed from proprioceptors, mice suffer from profound movement difficulties and skeletal abnormalities (right).

Chesler, who's been at NIH since 2013, is studying those *PIEZO2* mutations as well as other genetic and cellular mechanisms that underlie the somatosensory system (the system of neurons involved in the perception of touch, pressure, pain, temperature, position, movement, and vibration). His research focuses on mechanosensation, one part of the somatosensory system.

"Mechanosensation is required for our ability to sense things with our hands—like touch—and to warn us of potential dangers," explained Chesler. "It also enables us to know where our bodies are in space, called the sense of proprioception."

In 2010, investigators at Scripps Research Institute (San Diego, California) discovered that the proteins encoded by the *PIEZO2* gene are expressed in tissues where mechanical forces influence biological processes such as touch and pain. Chesler is trying to develop a deeper understanding of how mutations in this gene affect the mechanosensation system.

Working with mouse models as well as with human patients at the NIH Clinical Center, Chesler's lab examines the structure, neurochemistry, and function of the neurons underlying the somatosensory system.

In experiments with mice, his lab records the activity in neurons that are stimulated when a mouse's cheek is stroked or brushed or its hairs are pulled. Recording hundreds of neurons at a time, the lab can decode how different mechanical stimuli affect ensembles of neurons. Furthermore, Chesler's team has observed that upon removing the Piezo2 protein selectively from proprioceptors, mice suffer from profound movement difficulties and skeletal abnormalities.

Alexander Chesler was intrigued to learn that two mutations in a single gene cause dramatic problems in the sensory system.

After Chesler met PS1, he was inspired to study *PIEZO2* mutations in humans. He determined that the gene was required for identifying vibrations, distinguishing among types of touches, and creating sensations at joints. But the exact differences between *PIEZO2* function in mice and in humans is yet to be fully understood.

Chesler acknowledged that a better understanding of mechanosensation and proprioception could help scientists identify new approaches for helping people with movement difficulties as well as develop treatments for managing and treating pain. ●

To watch a video of Chesler's March 12, 2018, talk, go to https://videocast.nih.gov/launch.asp?23750.

To read the full version of this article, go to https://irp.nih.gov/catalyst/v26i3/under-your-skin-molecules-and-cells-for-touch-and-pain

Intramural Research Briefs

WEI LI, NEI

NIH scientists have uncovered cellular pathways that are critical for cold tolerance in hibernating mammals. Shown here, a hibernating 13-lined ground squirrel.

NEI, NINDS, CHI: STEM CELLS FROM HIBERNATORS MAY HAVE MEDICAL APPLICATIONS

Hibernating mammals can survive hypothermia without cellular injury at temperatures of less than 50 degrees Fahrenheit. This remarkable feat may hold significance for medical applications. But scientists don't yet understand the mechanisms that impart cold resistance. Using the first induced pluripotent stem cells (iPSC) line from a hibernating ground squirrel, NIH scientists uncovered cellular pathways critical for cold tolerance. Comparison between human and ground squirrel iPSC-derived neurons revealed differential mitochondrial and protein quality-control responses to cold. In human iPSC-derived neurons, cold temperatures triggered events that led to cell death. Manipulations of these pathways endowed cold stability on human iPSC-derived neurons as well as on rat (a non-hibernator) retina, preserving its light responsiveness after prolonged cold exposure. Furthermore, these treatments significantly improved microtubule integrity in cold-stored kidneys, demonstrating the potential for prolonging the shelf life of organs that will be used for transplant. (NIH authors: J. Ou, J.M.Ball, Y. Luan, T. Zhao, K.J. Miyagishima, Y. Xu, H. Zhou, J. Chen, D.K. Merriman, Z. Xie, B.S. Mallon, and W. Li, *Cell* **173**:1–13, 2018; DOI:10.1016/j.cell.2018.03.010)

NIAMS, NICHD: RESEARCHERS CRACK MYSTERY BEHIND RARE BONE DISORDER

Researchers in NIAMS and NICHD worked with 15 patients from around the world to uncover a genetic basis of "dripping candle wax" bone disease. The rare disorder—only 400 cases are known worldwide—is called melorheostosis and causes excess bone formation that on X-rays resembles dripping candle wax. The condition causes pain and bone deformity that can limit the function of bones. The study's results offer potential treatment targets, provide important clues about bone development, and may lead to insights about fracture healing and osteoporosis. Researchers compared samples of healthy and affected bone from each participant to look for differences in the exome, the portion of the genome that codes for proteins. The analysis revealed that eight of the 15 participants had mutations in the *MAP2K1* gene—which produces the protein MEK1 in the affected bone only. The gene was previously linked to some types of cancerous growths as well as to conditions that lead to abnormal blood-vessel formation in the head, face, or neck. In melorheostosis, all the identified *MAP2K1* mutations affect a region of the MEK1 protein that normally suppresses its activity. The bone growth is benign and does not spread to other parts of the body. (NIH authors: H. Kang, S. Jha, Z. Deng, W.A. Cabral, A. Ivovic, F. Meylan, E.P. Hanson, E. Lange, J. Katz, E.W. Cowen, R.M. Siegel, J.C. Marini, and T. Bhattacharyya, *Nat Commun* **9**:article 1390, 2018; DOI:10.1038/s41467-018-03720-z)

NCI: HIV USES NATIVE IMMUNE MOLECULES TO THWART THE BODY'S DEFENSES

NCI researchers have discovered that human immunodeficiency virus (HIV)–positive individuals with a specific set of immune-system genes have poorer outcomes because those gene variants allow the virus to inhibit the immune system. Molecules known as human leukocyte antigens (HLAs) allow the immune system to distinguish between healthy native cells and those contaminated by viruses or bacteria. There are multiple types of HLA proteins, each encoded by a different gene. The NCI team first observed that HIV-positive patients with a more active form of the *HLA-A* gene had more HIV virus in their blood, lower numbers of the CD4+ T cells that HIV infects, and a faster progression to AIDS. Moreover, a specific variant of the *HLA-B* gene magnified the negative effects of that *HLA-A* genotype. Further experiments revealed that those two genetic variations inhibit immune cells called natural-killer cells by boosting a type of HLA, called HLA-E, on the surface of the T cells that HIV infects. HLA-E, in turn, inhibits natural-killer cells via their cluster of differentiation 159 type A (NKG2A) receptors, thereby decreasing their ability to destroy T cells. A drug that prevents HLA-E from binding to the NKG2A receptor is being tested in clinical trials for rheumatoid arthritis and certain cancers. The NCI study suggests that the compound could potentially be repurposed to boost the body's immune response against HIV. (NCI authors: V. Ramsuran, V. Naranbhai, Y. Qi, M.P. Martin, Y. Yuki, X. Gao, J.J. Goedert, and M. Carrington, *Science* **359**:86–90, 2018; DOI:10.1126/science.aam8825.)

[BY BRANDON LEVY]

NHLBI: ADP PLATELET HYPERREACTIVITY PREDICTS CARDIOVASCULAR DISEASE

Platelet function plays a key role in arterial blood clots that underlie heart attack, stroke, and other cardiovascular diseases (CVD). But there's conflicting evidence about whether there's an association with CVD risk in healthy people. Some studies show a positive association, whereas others show a negative one. NHLBI investigators set out to resolve the conflict. In the largest study to date (2,831 participants)—with the longest follow-up surveillance (20 years)—NHLBI researchers demonstrated that platelet hyperactivity—specifically to ADP—predicts future heart

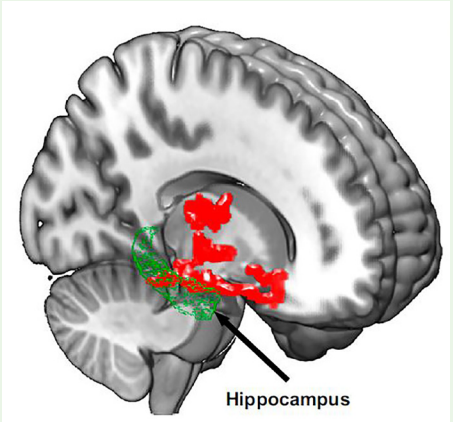
attack and stroke in individuals with no CVD. The study involved participants in the Framingham Heart Study.

Platelet reactivity was assessed by light-transmission aggregometry, using three different agonists that are contributors to the platelet activation process—ADP, collagen, and epinephrine. The researchers found that hyper-reactivity to ADP was associated with heart attack and stroke, whereas hyper-reactivity to the other two agonists was not. They were surprised, particularly because collagen plays an important role in initiating plaque formation.

"Data suggest that ADP reactivity in patients who have had a heart attack predicts worse outcomes and secondary cardiac events," said NHLBI investigator **Andrew D. Johnson**, who was the senior author on the study. "Similarly, mouse models indicate that ADP-reactive platelets form the outer shell of plaques in blood vessels, which rupture and burst to trigger heart attacks and strokes."

The data also suggest that ADP platelet hyper-reactivity could predict adverse cardiac events in healthy people and may potentially be a biomarker for CVD. (NIH authors: M.K. Puurunen, S.-J. Hwang, M.G. Larson, R.S. Vasan, C.J. O'Donnell, and A.D. Johnson, J *Am Heart Assoc* **7**:e008522, 2018; DOI:10.1161/JAHA.118.008522)

[BY CLAIRE MCCARTHY, NCI]



COURTESY OF PNAS

NIAAA: Brain imaging after one night of sleep deprivation revealed beta-amyloid accumulation in the hippocampus and thalamus, regions affected by Alzheimer disease.

NIAAA: LACK OF SLEEP MAY BE LINKED TO RISK FACTOR FOR ALZHEIMER DISEASE

Losing just one night of sleep led to an immediate increase in beta-amyloid, a protein in the brain associated with Alzheimer disease, according to a small, new study by researchers at the NIAAA. In Alzheimer disease, beta-amyloid proteins clump together to form amyloid plaques, a hallmark of the disease. The study is among the first to demonstrate that sleep may play an important role in human beta-amyloid clearance. Amyloid plaques harm communication between neurons. To understand the possible link between beta-amyloid accumulation and sleep, the researchers used positron-emission tomography (PET) to scan the brains of 20 healthy subjects, ranging in age from 22 to 72, after a night of rested sleep and after sleep deprivation (being awake for about 31 hours). The researchers found, in the sleep-deprived subjects, beta-amyloid increases of about five percent in brain regions including the thalamus and hippocampus, regions especially vulnerable to damage in the early stages of Alzheimer disease. The researchers also found that study participants with larger increases in beta-amyloid reported being in a worse mood after losing a night of sleep. Future studies are needed to assess the generalizability to a larger and more diverse population. (NIH authors: E. Shokri-Kojori, G-J. Wang, C.E. Wiers, S.B. Demiral, M. Guo, S.W. Kim, Kim, E. Lindgren, V. Ramirez, A. Zehra, C. Freeman, G. Miller, P. Manza, T. Srivastava, D. Tomasi, N.D. Volkow, *Proc Natl Acad Sci U S A* 201721694, April 9, 2018; DOI:https://doi.org/10.1073/pnas.1721694115)

NIDCD: USING GENOMICS TO SET SQUAMOUS-CELL CARCINOMAS APART FROM OTHER CANCERS

NIDCD researchers have uncovered molecular characteristics that link the genomic profiles of squamous-cell carcinomas (SCCs) from five areas of the body and that set these SCCs apart from other cancers. Using a robust dataset of SCCs from the head and neck, lung, esophagus, cervix, and bladder, the researchers also found defining characteristics in subtypes of SCCs associated with tobacco use or human papillomavirus infection. This research may lead to more effective diagnosis and treatment of these cancers by helping researchers develop tailored strategies for specific cancer subtypes. (NIH authors: J. Chen, H. Cheng, Z. Chen, and C. Van Waes, *Cell Rep* **23**:194–212.e6, 2018; DOI:10.1016/j.celrep.2018.03.063)

Read longer versions of these briefs online and others at https://irp.nih.gov/catalyst/v26i3/research-briefs:

- **NHLBI: New Technique Makes Heart-Valve Replacement Safer for Some High-Risk Patients**
- **NCI-DCEG: Get 150 Minutes/Week of Moderate Physical Activity: It Doesn't Matter How**
- **NICHD: Elevated Blood Pressure Before Pregnancy May Increase Chance of Pregnancy Loss**
- **NINDS: Neurodegenerative Disorders May Speed Up Aging Process**
- **NIDA: Study Changes Long-Held Concepts of Cell Decoding**
- **NCI: Normally Helpful Natural Bacteria May Also Trigger Lupus**
- **NICHD, NIAMS: Why Iron Can Worsen Malaria Infection**
- **NCI: Molecular Classification Revised for Most Common Type of Lymphoma**

The Jugglers

CONTINUED FROM PAGE 1

Everyone deals differently with how to balance raising a family with moving forward in a career, but they share common problems and use similar techniques in juggling the demands of family and research.

For this issue of the *NIH Catalyst*, we interviewed NIH scientists of all types, at all levels of their careers, and at all stages of raising their families—from having infants to having grown children.

The parents we interviewed appreciate all the resources NIH offers; the support, understanding, and sensitivity of their supervisors; and, in many cases, the ability to have flexible schedules and even being able to work from home at crucial times. The parenting resources include child-care centers; lactation rooms for breast-feeding mothers who need to pump milk at work; a LISTSERV; webinars and seminars; parenting coaches; and resource and referral services. In addition, the Intramural Research Program's (IRP) "Keep the Thread Program" offers postdoctoral fellows several options for increasing flexibility and temporarily reducing effort while remaining connected to their research during times of intense family needs. The tenure clock (normally six years; eight years for clinical or epidemiological research) was extended to seven years (nine for clinical or epidemiological research) to allow a person extended family or sick leave for childbirth, adoption, major illness, or family emergency.

But all agree that any trade-offs are worth it. Kids add so much fun to life, said senior investigator **Judith Walters** (NINDS), whose children are grown. A parent's love for their children is "uncomplicated" and makes all the lifestyle adjustments worth it.

The following are excerpts from the full interviews, which can be read in their entirety online at https://irp.nih.gov/catalyst/v26i3/the-jugglers.

The Stadtman Couple

BY EMILY PETRUS, NINDS

Two postdocs from rival labs meet at a conference, fall in love, get married, and have a beautiful daughter. It sounds like a science fairy tale, but for **Astrid Haase** (NIDDK) and **Markus Hafner** (NIAMS), it's just their story. Add some success with both being hired as tenure-track Stadtman Investigators, and you have a power couple pushing science and co-parenting to the limit.

Even while ramping up their labs, they knew they also wanted to be parents. So,

with the arrival of daughter Julia last year, they've found ways to be more efficient. The occasional afternoon coffee with leisurely scientific discussions have given way to more regimented and exact schedules, with the goal of finishing the day at a reasonable hour to allow for family time.

They attribute their sustained productivity to their cooperative teamwork style of parenting. Parental leave for them was more like working from home, with each parent taking turns being responsible for Julia while the other e-mailed the senior postdocs who ran each lab in their absence. Both of their scientific directors were extremely supportive, too.

Having children now is easier because their home budget isn't quite as tight as it was during their postdoctoral training and they have greater flexibility in running the lab remotely.

Use Your Village

BY LAURA STEPHENSON CARTER

"Being a single parent, you're dishwasher, chef, you clean, [and] you have to always be physically and emotionally present," said NCI Clinical Fellow **Patience Green**, who took a break from her surgical residency at Howard University Hospital (Washington, D.C.) to do a two-year fellowship at NIH. She has a 13-year-old son (Perry) and is the guardian for her 15-year-old sister (Stephanie).

In college, she had a scholarship but took out loans to cover child care. She had a great support system though: Her girlfriends loved babysitting Perry and her mom provided emotional support, encouraging her to pursue her dreams. She returned to her hometown of Atlanta to attend Morehouse School of Medicine and to be near family who could help with then six-year-old Perry. In 2014, she started her surgical residency and found it "very draining" especially when she was dealing with very sick patients and didn't always have time to emotionally process what she was dealing with at work.

When Patience's 12-year-old sister came to live with her, life became more of a juggling act, but she loved having both children. It was especially nice that Stephanie and Perry were like brother and sister.

She's found NIH's parenting resources helpful. She also suggests joining a support group; planning mommy dates with other moms; organizing play dates; and taking care of yourself. Most of all, "Use your village." Reach out to other people—you never know who's willing to help.

Be Sure to Have Balance

BY LAURA STEPHENSON CARTER

"Don't make work your whole life," NIA Scientific Director Dan Longo told **Michele Evans** (NIA) in 1995 shortly after she married **Charles Egwuagu** (NEI), who was the single parent of a 12-year-old daughter, Jemeh. "You need to be sure you have balance."

Michele and Charles took that advice to heart and succeeded in raising Jemeh and a daughter they had together, Emeka, while working full-time at NIH. But the way wasn't always easy. Charles had been a single parent since he was a graduate student; Jemeh was six when he came to NEI in 1987 as a staff fellow. Charles's lab chief and colleagues were very supportive and didn't mind when he had to leave early for child-related activities.

Luckily, Michele and Charles had the help of a nanny as well as Charles's mother from Nigeria. Even with child-care help, balancing home life with work can be challenging, especially for women. It took Michele longer to achieve tenure than Charles because she was usually the one who took time off to deal with family matters.

Jemeh (now 37) is working in Nigeria to help prevent and treat mother-to-child transmission of HIV-AIDS. Emeka (now 22) is headed to law school in the fall. "Nothing is more fulfilling than seeing your kids get out on their own and pursue their own life goals," said Michele.

How Much You Love Your Kids

BY LAURA STEPHENSON CARTER

Balancing a career and raising a family can be difficult for any couple, but postdoc **Andrew Kehr** (NIDDK) and his wife **Jacqueline** (NIAMS) faced extraordinary challenges when their daughter Elna was born. She aspirated meconium at birth and suffered severe respiratory problems that sent her to the hospital three times. Luckily their bosses, who are strong women scientists with children of their own, have been supportive and allowed the couple to modify their work schedules so they could attend to their daughter's needs. And they've had help from their family and friends, too—their parents have come from Indiana to stay for awhile to help.

And they take advantage of the many parenting resources NIH has to offer.

Although postdoc schedules can be erratic with long hours, Andy makes it a point to get home early every night so he can help with dinner, bath time, and reading stories to Elna. Then, around 8:00 p.m., he's back to work—usually on the computer at home, writing papers and doing other work related to his research.

What surprised them the most was how unprepared they were for "just how much you love your kids," said Andy. "I don't sleep [or] hang out with friends. But when [Elna] giggles…it doesn't matter."

Energetic and Efficient

BY EMILY PETRUS, NINDS

Clockwise from top left: Amy, Nigel, Josh (8; now 26 and starting a residency in neurology soon), Katelyn (6; now 24 and a journalist focusing on environmental and health science), and Kelly (10; now 27 and a strategist at a children's hospital).

Amy Newman (NIDA) and Nigel **Greig** (NIA) are principal investigators working at NIH's Baltimore campus. They seem to have made science and parenting fit together seamlessly. Having three kids while Amy was on the tenure track in the 1990s was full of challenges, but the couple approached running their family the same way they run their labs—energetically and efficiently.

Amy and Nigel remember the early years with their family fondly and count their blessings for all the help they received—a dedicated, reliable nanny and Amy's parents who provided child care in the summers. They always tried to provide the kids with all the opportunities they could even if it meant leaving the lab early to chaperone a field trip. And, no matter how late anyone returned home from work, school, or extracurricular activities, dinner was a shared family experience.

Although some view being a scientist as a family-unfriendly option, Amy and Nigel praise the flexibility of science—being able to set your own schedule and work remotely, and having the ability to adapt to unforeseen circumstances that being a scientist requires.

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The Jugglers

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Take the Free Stuff

BY LAURA STEPHENSON CARTER

Kate Brown (NCI), a visiting fellow from England, was diagnosed 34 weeks into her pregnancy with preeclampsia—a potentially life-threatening pregnancy complication—and put on modified bed rest for three weeks. Her baby, Orson, was delivered by caesarean section. Luckily, her P.I. allowed her to work from home so she was able to keep up with her responsibilities. Kate also feels fortunate that postdocs have eight weeks paid leave after the birth of a child. In addition, she and her husband Alex have help from both their families who travel from England to stay for extended periods.

When Kate returned to the lab, Alex was a stay-at-home dad and worked part-time from home. Orson recently started in a child-care program in Bethesda.

Kate discovered NIH's parenting resources such as the "amazing" NIH Parenting LISTSERV (she's gotten some secondhand clothes and toys). Her advice: "Take as much free stuff as you can." The hospital may offer diapers, diaper wipes, formula, and other items. If your friends throw you a baby shower, register at stores for gifts because you'll get welcome packets that include everything from coupons to different brands of baby bottles.

Live Your Life

BY CLARISSA JAMES, NIMH

Adam Messinger (NIMH) has had children during each stage of his career: his first son was born while he was in graduate school, his daughter when he was a postdoc at NIMH, and his second son when he was just about to become a staff scientist. There are challenges with every stage, he said. When you are a graduate student, your colleagues and PI expect you to be single and are less accommodating when you need to take time off for your children. As a postdoc, having children is more typical, so there are more resources. When you're starting a new job, it can be difficult to juggle the responsibilities of also having a baby.

The Messinger family (left to right): Adam, Lylah (14), Micah (10), Kira, and Jonah (19).

Adam's wife Kira is an advanced practice nurse and though her schedule is more rigid than his, they have found ways to balance the duties of parenting. She leaves for work early and comes home early so Adam gets the children to school and she's home in the afternoons. Both of them were able to take family leave when each of their children were born; Adam is grateful that his PI was very supportive. They put their first into child care when he was about six weeks old and hired a nanny for their next two.

He offers this advice: "You need to live your life…Do what makes sense for you [and] let the chips fall where they may."

Unexpected Challenges

BY CLARISSA JAMES, NIMH

Lara Abramowitz (NIDDK) had both of her children while working as a postdoctoral fellow. One of the most important considerations for her was knowing that she and her husband John—who is an engineer—could share child-raising responsibilities equally. Luckily, they both have flexible schedules, and John can sometimes work from home. Additional support from family members has been invaluable, too. Both her parents and her husband's parents have been a huge help.

There are many unexpected challenges that arise when you have a baby such as how often children get sick. The limited availability, years-long wait lists, and expense of child care was another unanticipated challenge. Lara found the lactation rooms to be very helpful. She also welcomes advice from other scientists who have children.

Putting their passion for research on hold and leaving the work force is not a viable choice for many scientists. "You find ways to have a great home and professional life, too."

Lara's family (from left): Lara, Eli (2 and a half), Paige (7 months), and John.

Don't Be Afraid to Ask for Help

BY CLARISSA JAMES, NIMH

It can be difficult for scientist parents to gauge when they should have children. "Just as long as you're ready, you'll have the same experience," regardless of what stage of your career you're in, said research fellow **Xiaomin Yue** (NIMH), who is optimistic about being able to balance raising a family with doing research. His first son was born during his postdoctoral training at Massachusetts General Hospital in Boston; his second soon after he came to NIH.

Xiaomin and his wife Rosemary, who works at a wealth-management firm, took parental leave when each of the children were born. His parents came from China for about three years to help. Xiaomin is happy that his PI has been so accommodating in allowing a flexible work schedule and that NIH has great parenting resources, especially the parenting LISTSERV and the NIH Child Care program.

Xiaomin's advice to parents: Take care of your children first and foremost (basing your research schedule on their schedules) and don't be afraid to ask for as much help as possible.

Xiaomin Yue's family (from left): Rosemary, Benjamin (8), Darius (6), and Xiaomin.

Hard to Be Good at Everything

BY ANNE DAVIDSON, NICHD

"It's hard to feel good at everything," **Deborah Citrin** (NCI) concluded after talking about the "work–life imbalance" of being a PI and a mother of three. Her husband, Matthew, a surgical oncologist at Walter Reed National Military Medical Center (Bethesda, Maryland), has been deployed five times, giving Deborah the unique challenge of single-handedly holding down the home front while running a laboratory and clinical trials.

Deborah relies on child care for her little girl and before-and-after school care for her two boys. She has had to learn to be more efficient to meet the child-care center "deadlines" (when it closes). She stays more task-focused at work and more productive at home, using the evenings to review data and research papers once the kids are asleep.

Deborah Citrin's children (from left), Rachel (3), Ethan (10), and Benjamin (6).

"Remember, everybody is struggling," said Deborah. "We appear put together, but it's not abnormal to feel stretched thin and like you are doing the best you can but, somehow, still feel inadequate."

Having kids is great, she said. They provide a humbling perspective, too. One time when she was driving four-year-old Ethan to NIH Child Care, they passed a playground on campus. Ethan asked if that is where she and her NIH friends played all day.

Kids Force You to Be Involved

BY ANNE DAVIDSON, NICHD

When asked what kind of sacrifices assistant clinical investigator **Jonathan Lyons** (NIAID) has made for his family, he joked that he had to sell his BMW for a family–friendly Mazda. But, in all seriousness, he accepts that sometimes there will be conflicts between spending time in his career and spending time with his family.

Fortunately, he and Christiana, who works from home as a proposal manager for a construction firm, make a great team. They have a nanny who comes during the workweek and when she is off-duty, they share tasks—Christiana takes care of bath time, Jon covers cooking and nap times, and they take turns handling other chores.

An important question for many young professionals is when to start a family. Jon reflected that having kids early means the parents have more energy, but having them later often means the parents are more mature and financially secure. Even though managing a family and a career can seem overwhelming at times, the trade-offs have been worth it. Jon describes being with his family as "refreshing" and caring for patients as a "gut-check" to put his own family's good health in perspective.

"Kids force you to be involved. They have to come first," Jon said. "And having your kid say, 'I love you' makes you feel important in a pure way."

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The Jugglers

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Cynthia's family (from left): Alexa (25; works in computer technology), Charlie, Cynthia, and Anna (23; is designing gap-year programs in Boston after college graduation).

Family Friendly

BY EMILY PETRUS, NINDS

Success in science involves lots of hard work but also some luck. **Cynthia Dunbar** (NHLBI) admits that she's had her fair share of both in becoming a senior investigator and the mother of two young children in the 1990s. She was lucky that by the time she and her husband Charlie—the father of two grown children from a previous marriage—had their children, he was no longer in a high-stress Wall Street job and was a public-school teacher and musician. He was also working from home by the time their daughters were in school. Having such a supportive husband and relatively easy and healthy children, Cindy could give as much of herself to work as was needed. She was still involved with family activities and, when the girls were older, even coached their soccer teams.

Several things have improved since the 1990s. For example, there are more child-care spots on campus and more work can be done remotely.

Most trainees don't see science as family friendly, to which Cynthia replies, "What could be more family friendly than being your own boss?"

Find Your Own Path

BY EMILY PETRUS, NINDS

When Linda and Richard Wyatt were raising children in the 1970s and 80s, Linda took 10 years off between two postdocs to support and nurture the children. "We operated on one income," said Richard, who is the Deputy Director of the OIR. He realizes, however, that the cost of living and other factors make being a one-income family much more difficult for today's generation of parents.

Linda, who already had two children when she came to NIH as a postdoc in 1974, was able to snag rare spots in NIH's nascent child-care program. "I had the best of both worlds," said Linda who's now a staff scientist in NIAID. "I got to be a stay-at-home mom and then came back to work" as a senior research fellow. Once she returned to work, the Wyatts hired an au pair and later a nursing student to help. Family time remained a priority for the Wyatts and they regularly had breakfast and supper together.

The Wyatt children in 1986 (from left) Grace (6), Greg (2), and Katherine (12), and Will (16).

"Now child-care issues are major for entry-level scientists," said Richard, who's a member of NIH's Child Care Board.

The Wyatts recognize that the way they balanced children and careers worked for them, but every scientist and parent needs to find their own path to success at work and at home.

Kids Add So Much Fun to Life

BY ANNE M. DAVIDSON, NICHD

There was no maternity leave when **Judith Walters** (NINDS) came to NIH in 1975. After she had her first child by cesarean section in 1977, she came back to work just two weeks later. She recalls how hard it was to leave her baby for the first time yet feeling guilty for wanting to stay at home longer. She felt indebted to the male-dominated culture that had given her the opportunity to do research. Judie, who is now a senior investigator, went on to have two more children and returned to work as soon as she could each time. She also felt lucky to have the help of a local woman who took care of the children during the week, did light housework, and helped with dinner. When the boys turned three, they began going to morning nursery school as well. Judie would even drive home to have lunch with her boys sometimes.

Today, Judie is a mentor for women scientists and particularly sensitive to the challenges faced by young working parents. As a member of one of the NIH Child Care Board's subcommittees, she works to improve child-care and other parent-friendly programs.

Kids add so much fun to life, she said. A parent's love for their children makes all the lifestyle adjustments worth it.

Judie's family in 1988 (from left): Gregory (now 37), Douglas (now 33), Jamie (now 40), and Judie.

Parenting Resources

BY MICHELLE BOND, NIDDK

The NIH provides a number of resources to support parents as they try to integrate and balance their careers and family. Many of the parenting resources are provided by the Office of Research Services (https://www.childfamilycare.ors.nih.gov) as well as by the NIH Office of Intramural Training and Education (https://www.training.nih.gov/). Resources include child-care centers, lactation rooms for breast-feeding mothers who need to pump milk at work; a LISTSERV; webinars and seminars; parenting coaches; and resource and referral services. In addition, the Office of Intramural Research (https://oir.nih.gov/sourcebook) offers the "Keep the Thread Program" to postdoctoral fellows so they can modify their work schedules during times of intense family needs. It also extended the tenure clock from six to seven years (from eight to nine years for clinical or epidemiological research) for reasons such as childbirth, adoption, major illness, or family emergency.

Parenting is a challenging and rewarding part of life. Cherishing family moments when juggling work and home can be difficult, but with a wise use of available resources, it can be a little bit easier.

For a list of resources, go to the full version of this article at https://irp.nih.gov/catalyst/v26i3/parenting-resources.

Meet the authors and their families (from top): Laura Carter with her husband and daughters (1980s); Anne Davidson (second from left) with her siblings, dad, and dogs; Clarissa James (center) and her parents; Emily Petrus and her husband and sons (2016); and (left) Michelle Bond with her son.

News You Can Use

CONTINUED FROM PAGE 5

numbers of simultaneous jobs and large-scale distributed memory tasks common in the biosciences. To put that into perspective, Biowulf's primary storage could hold the information found on roughly 12.5 trillion pages of standard printed text—the equivalent of more than 24 billion copies of Charles Darwin's *On the Origin of Species*. Additionally, Biowulf has 528 graphical processing units that accelerate data analysis by handling multiple computational tasks simultaneously. The system also supports over 600 scientific programs, packages, and databases, many of which are custom-built to support the biosciences.

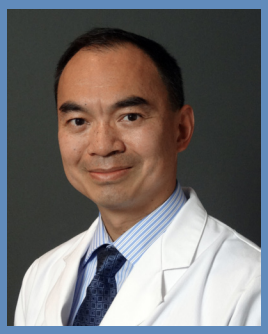
The HPC team was awarded the NIH Director's Award in 2017 for its incredible work in building up the Biowulf system. Yet, even with its astounding computing power, the supercomputer can barely keep up with the ever-expanding demands of IRP researchers. The fifth phase of the expansion effort, which will come online in July 2019, will add another 30,000 cores to the system.

Andrea Norris, director of CIT and NIH's chief information officer, looks forward to seeing more researchers realize the benefits of Biowulf. "We're very excited about the research that intramural scientists have been able to perform using Biowulf," she said. "NIH's strategic investments in high-performance computing, its high bandwidth network, and other key technology capabilities are enabling the intramural community to achieve scientific discoveries that were previously beyond its reach." ●

For more information on Biowulf, visit http://hpc.nih.gov or contact staff@hpc.nih.gov to see how Biowulf can help you advance your own research projects.

Recently Tenured


KENNETH D. ALDAPE, NCI-CCR


KONG CHEN, NIDDK


YAMINI DALAL, NCI-CCR


PAULINE MENDOLA, NICHD


GWENYTH REID WALLEN, CC

KENNETH D. ALDAPE, M.D., NCI-CCR

Senior Investigator and Chief, Laboratory of Pathology, Center for Cancer Research, National Cancer Institute

Education: Stanford University, Palo Alto, California (B.A.S., philosophy and biology); University of California at San Francisco (UCSF), San Francisco (M.D.)

Training: Residency and chief residency in anatomic pathology, UCSF; research fellowship, neuro-oncology, Preuss Laboratory for Molecular Neuro-Oncology, San Francisco; clinical fellowship, neuropathology, UCSF

Before coming to NIH: Faculty positions at MD Anderson Cancer Center, University of Texas (Houston), including chair and medical director, Department of Pathology (2001–2014); director, MacFeeters-Hamilton Brain Tumor Centre, and senior scientist, Princess Margaret Cancer Centre (Toronto, 2014–2018); associate member and director, Translational Genomics Laboratory, Ontario Institute for Cancer Research (Toronto, 2015–2018)

Came to NIH: in February 2018

Selected professional activities: Executive editor, *Neuro-Oncology*; international editor, *Brain Tumor Pathology*; on editorial review boards for several journals

Website: https://irp.nih.gov/pi/kenneth-aldape

Research interests: As a diagnostic and molecular neuropathologist, I focus on the genomics and molecular pathogenesis of primary brain tumors. I also work on the integration of new genomic and computational approaches to improve how cancer can be classified and treated. Cancer classification and treatment decisions will increasingly integrate these tools into clinical practice, and my vision is to contribute to this new paradigm in pathology.

In particular, my laboratory studies genomic and epigenomic alterations in brain tumors including glioma and meningioma. We characterize the biology of specific genomic alterations and how alterations contribute to the molecular pathogenesis and treatment resistance of aggressive brain tumors. We also use genomic signatures to identify clinically relevant subclasses. We hope that biologically based classification of brain tumors will lead to a greater understanding of why specific tumor subtypes may be more or less sensitive than average to therapeutics.

At the branch level, and as a diagnostic pathologist, I am passionate about the use of new technologies to improve how cancer is diagnosed. Although a light microscope is an effective tool for classifying most tumors, it's not very helpful when it comes to diagnosing ambiguous or difficult cases. The use of genomic, epigenomic, and computational modalities shows promise for improving the precision and accuracy of cancer diagnostics. The future of diagnostic pathology will increasingly rely on genetic and epigenomic alterations as well as on computational and image-analysis approaches to define and classify cancer. I hope to promote precision diagnostics of cancer by integrating these approaches and other technologies with our current standard of care.

KONG CHEN, PH.D., NIDDK

Senior Investigator, Diabetes, Endocrinology, and Obesity Branch; Director, Human Energy and Body Weight Regulation Core; chief, Metabolic Research Section, National Institute of Diabetes and Digestive and Kidney Diseases

Education: Tennessee Technological University, Cookeville, Tennessee (B.S. in mechanical engineering); Vanderbilt University, Nashville, Tennessee (Ph.D. in biomedical engineering; M.S. in clinical investigation)

Before coming to NIH: Assistant professor of medicine (primary), biomedical engineering, and surgery at Vanderbilt University

Came to NIH: In 2006

Selected professional activities: Associate editor of *European Journal of Clinical Nutrition* and of *Journal of Diabetes Science and Technology*; member of Organizing Commit-

tees, International Conferences on Recent Advances and Controversies in Measuring Energy Metabolism and Body Sensor Networks Annual Conferences

Outside interests: Used to dabble in oil painting, water colors, and pencil and charcoal drawings, now mainly admires them in the museums; taking photos of wildlife, architecture, and unique cultures when he travels; reading; cooking; playing sports

Website: https://irp.nih.gov/pi/kong-chen

Research interests: I am interested in understanding how energy metabolism and physical activity are regulated. Ultimately, my lab's goals are to develop safe and effective strategies for treating and preventing obesity in general populations and managing nutritional needs in patients with metabolic disorders.

As a biomedical engineer, I have designed and used whole-room indirect calorimeters (also called metabolic chambers) for measuring energy expenditure in people. I also do studies using wearable sensors for measuring people's physical activity, sedentary behavior, and sleep (in the lab and at home). As a clinical investigator, I focus on cold-induced thermogenesis, brown adipose tissue, muscle activities, heart rate and heart-rate variability, and body and skin temperature in response to subtle changes in environmental temperature. We are quantifying the capacity of cold-induced thermogenesis (how many extra calories are burned during tolerable cold exposures) to see what the differences are between lean and obese subjects, men and women, and young and old, and among different races. We are also quantifying, in humans, the amount, activity, and distribution of brown adipose tissue, which will allow us to better understand how it regulates body temperature and metabolism.

Our three custom-made metabolic chambers measure minute-by-minute energy expenditure for several hours to several days. In this well-controlled environment, we can also simultaneously measure movement and physiological parameters to determine the impacts of physical activity, diet, medications, and other stimuli on energy metabolism, heart rate, and hormonal responses. In addition, we can use a variety of techniques to quantify people's body composition.

Currently, we are working with intramural and extramural investigators to study energy balance in different populations such as people with diabetes, lipodystrophy, nonalcoholic fatty liver disease, inborn errors in metabolism, overgrowth, chronic fatigue syndrome, and certain cancers, as well as in a range of healthy volunteers (different ages and weights and in different geographic locations). We are also studying the effects of medications and dietary interventions on metabolism.

YAMINI DALAL, PH.D., NCI-CCR

Senior Investigator and Group Director, Laboratory of Receptor Biology and Gene Expression, Center for Cancer Research, National Cancer Institute

Education: St. Xavier's College, Mumbai, India (B.Sc. in biochemistry and life sciences); Purdue University, West Lafayette, Indiana (Ph.D. in cell and molecular biology)

Training: Postdoctoral fellow at Fred Hutchinson Cancer Research Center, Seattle

Before coming to NIH: Postdoctoral research associate, Fred Hutchinson Cancer Research Center, Seattle

Came to NIH: In September 2008

Selected professional activities: Affiliate professor, Department of Biological Sciences, University of Maryland (College Park, Maryland); Faculty of 1000 since 2010; editorial boards for *Public Library of Science*, *F1000 Research*, *Chromosoma*, and *Scientific Reports*

Outside interests: Reading historical fiction, science fiction, and popular science; appreciating archaeology and ancient languages; enjoying folk and Americana music; biking; hiking; spending time with family and friends

Website: https://irp.nih.gov/pi/yamini-dalal

Research interests: My research focuses on centromeres, which are essential for chromosome segregation during cell division. My lab studies proteins called histones, the main protein components of chromatin (made up of DNA and protein), which packages and orders DNA into nucleosomes (the building blocks that make up chromosomes). In cancer cells, certain chromatin regions are fragile and prone to chromosomal rearrangements. We use an interdisciplinary approach—combining chromatin biochemistry, computational modeling, single-molecule microscopy, genetics, genomics, and cell biology—to determine how specialized chromatin structures contribute mechanically and epigenetically to centromere function.

The principle challenges we have addressed in recent years are how the essential centromeric histone variant called centromere protein (CENP) A (CENP-A) determines where the centromere is in located every cell cycle; whether CENP-A and its complexes physically alter the chromatin fiber to support the mechanical stresses of mitosis; and whether such states can be inherited over several cell cycles.

In previous work, we documented that CENP-A nucleosomal and pre-soluble assembly structures are diverse and possess unique modifications and dynamics that make them intrinsically distinct from histone H3 (one of the five main histones involved in chromatin structure).

In a recent breakthrough, we used an adaptation of a very-high-resolution microscopy technique, called atomic force microscopy, to make nanoscale elasticity measurements of CENP-A nucleosomes

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Recently Tenured

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and compare them with nucleosomes that have different histone compositions. We found that CENP-A nucleosomes were surprisingly elastic, or "squishy," but adding kinetochore proteins made them rigid. (Kinetochores are where the microtubules attach during cell division.) Overexpression of CENP-C in human cells showed that a higher CENP-C/CENP-A ratio decreases the elasticity of the nucleosome and "closes" the chromatin fiber.

We speculate that the plasticity of CENP-A might be the key inherited feature conserved across the CENP-A of all species, and it is this feature that is uniquely recognized by centromere-binding proteins.

In our second project, we are focusing on the regulation and deposition of histone variants in normal and cancer cells. We were the first to report that in embryonic stem cells, naturally excess CENP-A is involved in chromatin repair and that error-free CENP-A assembly requires targeted and cell-cycle specific transcription.

We were also the first to demonstrate that in human colon-cancer cell lines and tumors, CENP-A invades transcriptionally coupled H3.3 pathways to deposit hybrid CENP-A:H3 nucleosomes at non-centromeric regions.

A significant question remains: How does non-centromeric CENP-A drive cancer progression? We have shown that CENP-A can drive chromosome instability by seeding large fragile domains outside of native centromeres. We have proposed that targeting cancer-specific CENP-A mis-interactions can potentially serve as a therapeutic target. We have worked on H3.3 pathways that are invaded by CENP-A, and recently we developed high-precision computational-prediction approaches to block these interactions.

RESEARCH WRITE-UP BY MOHOR SENGUPTA, NEI

PAULINE MENDOLA, PH.D., NICHD

Senior Investigator, Epidemiology Branch, Division of Intramural Population Health Research, National Institute of Child Health and Human Development

Education: State University of New York at Buffalo, Buffalo, New York (B.A. in social sciences interdisciplinary program; M.S. in epidemiology, social and preventive medicine; Ph.D. in epidemiology and community health)

Before coming to NIH: Chief of the Infant, Child, and Women's Health Statistics Branch, National Center for Health Statistics, Centers for Disease Control and Prevention (Hyattsville, Maryland, 2007–2011); health scientist and chief of the Epidemiology and Biomarkers Branch, National Health and Environmental Effects Research Laboratory, United States Environmental Protection Agency (Chapel Hill, North Carolina, 1997–2007)

Came to NIH: In 2011

Selected professional activities: President, American College of Epidemiology; associate editor, *Fertility and Sterility*; recipient of the President's Award from the Society for Pediatric and Perinatal Epidemiology

Outside interests: Enjoys spending time with her husband; visiting the amazing art galleries in the area; creating great meals to share with family and friends

Website: https://irp.nih.gov/pi/pauline-mendola

Research interests: Maternal asthma is the most common chronic disease in pregnancy. The burden of maternal chronic disease is high and continues to increase as advanced maternal age and overweight become more prevalent. My research is focused on the interplay of immune function (asthma, allergy, and maternal-fetal tolerance), oxidative stress, and air pollution in relation to preterm delivery, restriction of fetal growth, and other complications of pregnancy.

I am the principal investigator of the B-WELL-Mom study (Breathe-Wellbeing, Environment, Lifestyle, and Lung Function (B-WELL-Mom) study. B-WELL-Mom examines changes in asthma symptoms and control of asthma over the course of pregnancy and during the postpartum period. The study also compares lung function and immune markers for asthmatic and non-asthmatic women in relation to air pollution, dietary antioxidants, and allergies. Our research 1) assesses whether atopy (predisposition to allergic hypersensitivity) status—measured by total immunoglobulin E at the time a person enrolls in the study—predicts variability in asthma control during pregnancy; 2) evaluates whether atopy status is associated with additional decrements in lung function and increased inflammation in pregnancy among women with asthma; 3) evaluates the impact of regulatory T-cell concentrations on asthma control variability during pregnancy; and 4) evaluates changes in lung function and inflammation in all women exposed to poor ambient air quality (traffic, commuting, and ambient measures) and potential mediation by dietary antioxidants.

If you have been recently tenured, *The NIH Catalyst* will be in touch with you soon to do an article about you on these pages.

GWENYTH REID WALLEN, R.N., PH.D., CC

Senior Investigator and Clinical Nurse Scientist; Chief Nurse Officer; and Chief of Nursing Research and Translational Science, NIH Clinical Center

Education: University of Maryland, Baltimore (B.S.N. in nursing); Central Michigan University, Mt. Pleasant, Michigan (M.A. in management and supervision/business management); University of Maryland, College

Park, Maryland (Ph.D. in public health/health education)

Training: Postdoctoral research associate, Department of Family Studies, University of Maryland (College Park, Maryland); Bravewell Fellow in Integrative Medicine, University of Arizona (Tucson, Arizona)

Before coming to NIH: Clinical nurse specialist, Neonatology, Washington Hospital Center (Washington, D.C.)

Came to NIH: In 2001 as section chief, Office of Research and Outcomes Management, Nursing and Patient Care Services, NIH Clinical Center; chief of the Research and Practice Development Service, NIH CC (2005–2009); and chief, Nursing Research and Translational Science, NIH CC (2010 to present)

Selected professional activities: Adjunct associate professor, Behavioral and Community Health, University of Maryland, School of Public Health (College Park, Maryland); adjunct assistant professor, Graduate School of Nursing, Uniformed Services University of the Health Sciences (Bethesda, Maryland); reviewer for several journals; vice chair and member of the NICHD's institutional review board since 2001

Outside interests: Travelling; gardening; swimming; kayaking; boating; snorkeling

Website: https://clinicalcenter.nih.gov/about/SeniorStaff/gwenyth_wallen.html

Research interests: My clinical research focuses on health behaviors and health disparities. My team and I are especially interested in the methodology and measurement in end-of-life care, integrative health, and vulnerable populations. We are testing the feasibility of health-behavior-change interventions that improve sleep quality, physical activity, and nutrition, particularly in patients with chronic diseases.

One of my earliest projects was with the NIH Clinical Center's Pain and Palliative Care Service, studying how to provide the best possible care to cancer patients at the end of life. In a collaborative study with National Institute of Arthritis and Musculoskeletal and Skin Disease researchers, I worked with an urban community clinic that helps people with arthritis, lupus, and other rheumatic diseases. We determined that, for Hispanic patients, involving family members and spouses in the plan of care could facilitate health promotion and chronic disease management.

I am collaborating with **Tiffany Powell-Wiley** (National Heart, Lung, and Blood Institute) to examine cardiovascular risk assessment in people from under-resourced communities. In a recently completed project, my team explored the effect of severe alcohol-use disorder (AUD) on sleep. AUDs are often accompanied by comorbid physiologic and psychosocial conditions such as anxiety, depression, post-traumatic stress disorder (PTSD), and sleep disturbances, which are associated with an increased risk of relapse to drinking after detoxification and rehabilitation.

In following up with patients who had undergone inpatient alcohol rehabilitation, we used a statistical method called latent class analysis (LCA) to see whether any group was at a higher risk of sleep disturbances. Our study showed that LCA may provide clinicians with insight into the integrative tailoring of interventions that meet the varied needs of individuals with AUDs, accompanying comorbidities, and sleep disturbances.

In addition to doing my own research, I am helping to provide more formalized fellowship opportunities for scientists from diverse backgrounds to enter and stay in the field of health-disparities research.

RESEARCH WRITE-UP BY MOHOR SENGUPTA, NEI

ABBREVIATIONS

CC: NIH Clinical Center
CCR: Center for Cancer Research, NCI
CIT: Center for Information Technology
DCEG: Division of Cancer Epidemiology and Genetics, NCI
DIPHR: Division of Intramural Population Health Research, NICHD
FAES: Foundation for Advanced Education in the Sciences
FARE: Fellows Award for Research Excellence
FelCom: Fellows Committee
FDA: Food and Drug Administration
FNL: Frederick National Laboratory
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCATS: National Center for Advancing Translational Sciences
NCBI: National Center for Biotechnology Information
NCCIH: National Center for Complementary and Integrative Health
NCI: National Cancer Institute
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: Eunice Kennedy Shriver National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OITE: Office of Intramural Training and Education
OIR: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women's Health
OTT: Office of Technology Transfer

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FROM THE ANNALS OF NIH HISTORY

Two NIH Greats Remembered

OFFICE OF NIH HISTORY AND STETTEN MUSEUM

Christian Anfinsen and Michael Potter grace the halls of the NIH Clinical Center once again. In May 2018, the Office of NIH History and Stetten Museum is scheduled to open twin historical exhibits in tribute to these two NIH legends. Potter (second from left, left picture) won the 1984 Albert Lasker Award for Basic Medical Research for his elegant studies of plasma-cell tumors, which led to the development of monoclonal antibodies. Anfinsen (right, right picture) shared the 1972 Nobel Prize in chemistry for "work on ribonuclease, especially concerning the connection between the amino acid sequence and the biologically active conformation." The exhibits, in the great corridor of Building 10 leading to Masur Auditorium, are funded by the National Cancer Institute, the National Heart, Lung, and Blood Institute, and the National Institute of Diabetes and Digestive and Kidney Diseases.

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