

## Is Music Really the Medicine of the Soul?

An Interview with Renée Fleming and Francis Collins

BY JOANNA CROSS, NIMH

**WHAT HAPPENS WHEN YOU GET A** world-renowned scientist and a famous opera singer in the same room? A spontaneous rendition of “The Times They Are a-Changin’” and the establishment of an important collaboration. NIH Director **Francis Collins** and Renée Fleming, who met a few years ago at a dinner party, realized that they both were curious about how music affects our minds. And so the “Sound Health: Music and the Mind” initiative, an NIH–Kennedy Center partnership in association with the National Endowment for the Arts, was born.

Fleming visited NIH on May 13, 2019, as the featured guest at the annual J. Edward Rall Cultural Lecture, named for the former deputy director for intramural research. She and Collins discussed the creative process, the intersection of music and science, and the Sound Health initiative, which aims to expand our understanding of the connections between music and wellness.

Music has been part of our lives for millennia and may well predate speech. The earliest known surviving instrument is a bone flute from about 40,000 years ago, and our vocal mechanisms have hardly changed throughout the years. “Can you imagine a Neanderthal opera?” Fleming joked. Because music has been part of our society for so long, it follows that it must

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## Historical Medical Films at NLM

How a Unique Collection Started and Grew

BY MOHOR SENGUPTA, NEI



MOHOR SENGUPTA, NEI

The National Library of Medicine (NLM) has one of the world’s largest collections of medical films and videos. Shown: Several 35-mm films at NLM’s storage vault in Bethesda.

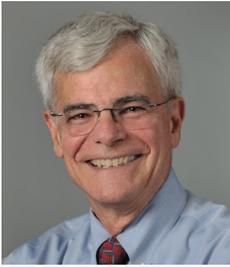
**ONE OF THE WORLD’S LARGEST COLLECTIONS OF MEDICAL FILMS AND VIDEOS IS AT THE** National Library of Medicine (NLM), which has been collecting and preserving them—and making them available to researchers—since the 1950s. Then-NLM-Director Colonel **Frank Bradway Rogers** set up a system to include audiovisuals as part of the NLM’s congressionally mandated mission to acquire a wide variety of materials pertinent to medicine. He hoped that such a repository would be a go-to place for visual information

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## Collecting and Interpreting NIH History

BY MICHAEL GOTTESMAN, DDIR

**THE NIH HAS A PROUD AND** intriguing history. Fittingly, we also have an Office of NIH History that documents, preserves, and interprets our many significant achievements. And the collections run deep.

Formally known as the Office of NIH History and DeWitt Stetten Jr. Museum of Medical Research (ONHM), the office captures the memory of who worked with whom, of when the work was conducted, and of what tools they used. The material heritage in its collections include instruments, objects, images, films, oral histories, notebooks, illustrations, and myriad documents (see its website at <https://history.nih.gov>).

These exhibits and displays that you see around the Bethesda campus—for example, the original Santiago Ramón y Cajal drawings in Building 35, the exhibits on **Christian Anfinsen** and **Michael Potter** in Building 10, **Al Kapikian's** Siemens 1-A electron microscope in Building 50, and the biotechnology showcase display in Building 31—all are curated by the ONHM.

The historical facts that you may hear sprucing up an NIH director's keynote address or read in a prominent NIHer's obituary are often provided by the ONHM. The ONHM also provides old photographs used in books and by the news media.

The ONHM focuses its research and collecting specifically on the NIH community. This focus differentiates the office from the NIH National Library of Medicine (NLM), which has a congressional mandate to collect, preserve, and make accessible the broad record of medical history from all times and places. The ONHM

works closely with NLM to ensure that important historical resources associated with the NIH are preserved and made accessible to interested researchers.

The ONHM builds its collection mostly through networking. The staff are happy to meet with those planning to retire, and they regularly interact with the NIH community through events such as the NIH Research Festival. They also meet with family members of deceased NIH staff to collect personal memorabilia such as private photographs and other treasured items that can provide extra charm and insight to historical exhibits.

The staff keep their eyes and ears open to planned moves or demolitions, too, and use these opportunities to ensure objects and documents of historical significance are not discarded. Some items, such as a set of handmade, early 20th-century manometers used by one of the founders of carbohydrate chemistry, **Claude Hudson**, were literally rescued from the trash.

The ONHM relies on a network of archivists and museum specialists to assess and interpret its collection, as well as on an NIH-wide collections committee to ascertain the past significance of now-obsolete equipment and to advise us what to collect to represent today's science for future historians. More than 95 percent of our collected objects are stored off-campus. Should we ever find space on campus for a physical museum, we would have enough objects to reconstruct an NIH laboratory from every decade dating back to 1900!

Given the limited space, we cannot keep most objects and documents. All are

assessed, though. Some documents are sent to the National Archives and Records Administration. Some are transferred to the NLM's History of Medicine Division.

Perhaps surprisingly given the age of the NIH—132 years as of August 2019, dated to **Joseph Kinyoun's** Hygienic Laboratory, our direct precursor—the ONHM was created only 33 years ago, in 1986, and moved into the Office of Intramural Research in 2006. The ONHM is now housed in historic Building 60, nicknamed the Cloister, formally designated as the Mary Woodard Lasker Center for Health Research and Education. **Chris Wanjek** is acting director of the office, which has a small staff consisting of a curator of collections (**Michele Lyons**), an expert in creating museum-quality exhibits (**Hank Grasso**), and an archivist (**Barbara Harkins**). Many helpful volunteers support our oral-history projects, the photo archives, and website updates.

The ONHM welcomes your engagement. Before you dispose of old equipment (especially from the early 2000s), reports, photographs, or even instrument manuals, contact the ONHM to see if it could be of historical value to the NIH story. Take charge of your own history by documenting your laboratories each year with a photograph. And identify each member for posterity...while your memory still serves you well.

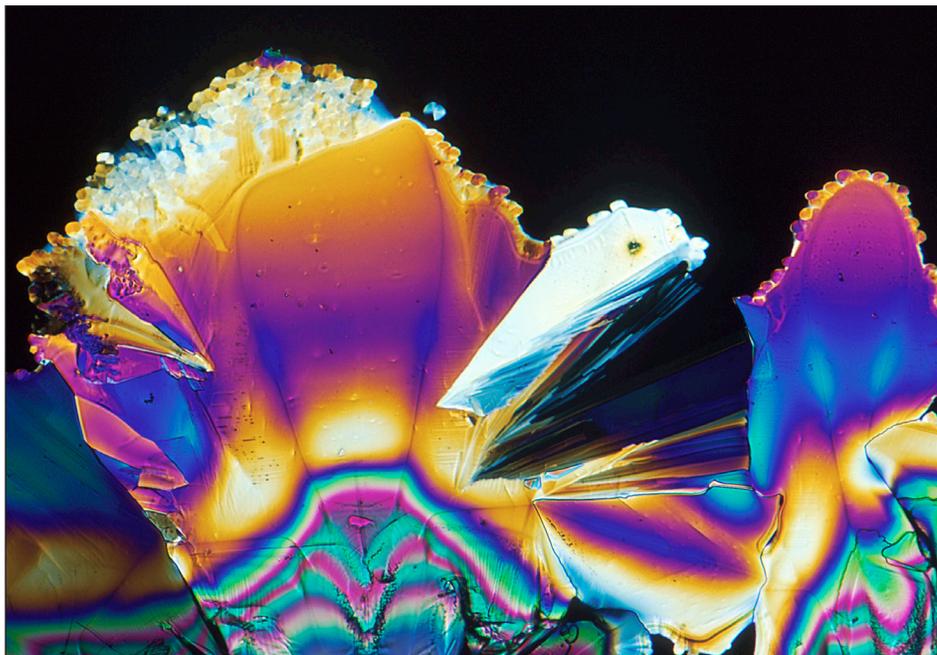
And most important, let's keep making history! ●

**Got history? Contact Michele Lyons, ONHM curator of collections, at [history@mail.nih.gov](mailto:history@mail.nih.gov).**

## Powerful, Condensed Matter

### The One-Day 2019 Research Festival

BY THE NIH RESEARCH FESTIVAL ORGANIZING COMMITTEE



LARRY OSTBY, NCI

Antiviral drug: Polarized crystals (photographed through a microscope) of the drug 2-3 dideoxyadenosine, also known as ddA, a drug that is closely related to AZT or azidothymidine. The antiviral effect of ddA against HIV was discovered at the National Cancer Institute.

**THE 2019 NIH RESEARCH FESTIVAL** will be as packed and energetic as a neutron star. Acting on your polite input from last year—that is, come on, guys, who has time for a three-day event?—we have condensed the Research Festival into one action-packed day on Wednesday, September 11.

You want hot topics? We got hot topics: combating pain, curing metabolic diseases, and highlighting cutting-edge homegrown intramural-research-program technologies.

You want prestigious NIH alumni? We got prestigious NIH alumni: 1998 Nobel Laureate **Ferid Murad**, who opens the festival with an inspiring talk about nitric oxide and cyclic guanosine monophosphate in cell signaling and drug development.

You want lightning talks? We got

lightning talks: 24 three-minute talks covering the breadth of NIH science. Posters? Yes, they're back but with a twist. There's only one session this year, which will remain up all day and include a selection of Fellows Award for Research Excellence winners, tenure-track investigators, the lightning-talk participants, and scientific directors.

You want food? We got food: food trucks on campus and plenty of drinks and light fare at receptions.

You want music? We got music: the NIH Director's band, a.k.a. ARRA, or the Affordable Rock'n'Roll Act, will play at an award ceremony at the close of the day.

You want dancing? Well, most of you didn't ask for that, but four of you did. Those four are free to dance to the

music, particularly on songs in which **John Tisdale** (National Heart, Lung, and Blood Institute) plays bass.

You don't want to lose parking spaces? No, we didn't pull that one off. That's because the Technical Sales Association (TSA) Vendor Tent Show is indeed back under the big top on September 12 and 13. This is a good opportunity to meet with hundreds of vendors.

But here's the most important part: We want you. It doesn't matter whether your area of science doesn't match what is being presented. What matters is that you get out of the lab or office and interact with your colleagues, see new people, hear new ideas, and broaden your perspective. Encouraging these activities was the purpose of the first, single-day "Research Day" in 1986 and is the purpose of the 2019 Research Festival.

There will be some other highlights best kept out of print for now...but likely legal, they tell us. (Preliminary schedule at <https://researchfestival.nih.gov/2019/>.)

See you at the festival. ●

**The 2019 Research Festival is Wednesday, September 11, from 9:00 a.m. to 5:00 p.m. in Masur Auditorium, the FAES terrace, and other Building 10 locations. The corresponding TSA Vendor Tent Show is September 12-13 from 9:30 a.m. to 3:30 p.m. (Thursday) and to 2:30 p.m. (Friday) in Parking Lot 10H. Questions? Contact [ResearchFest@mail.nih.gov](mailto:ResearchFest@mail.nih.gov). The members of the NIH Research Festival Organizing Committee include Scientific Directors **John Gallin** (Clinical Center) and **Amy Newman** (National Institute on Drug Abuse) as well as Office of Intramural Research staff **Chris Wanjek** and **Jacqueline Roberts**.**



## From the Fellows Committee

Want to Improve Your Scientific Writing Skills? There's Training for That!

BY CRAIG MYRUM, NIA

**THE PRIMARY RESPONSIBILITIES OF** most NIH trainees include running experiments and analyzing data. But effectively reporting scientific findings is arguably an even more important task. Without adequate skills in writing, scientists are less likely to get grants or have their work published. Studies show that journal articles that are written in clear, accessible language were likely to receive more citations than less well-written articles (*Proc Nat Acad Sci U S A* **116**:341–343, 2016).

Despite the clear importance of skilled writing in scientific careers, many trainees have never gone through formal training to acquire these skills. Fortunately, the NIH intramural program offers several resources to improve writing skills including coursework in scientific writing, editing opportunities, and grant-writing workshops.

In a workshop offered by the Foundation for Advanced Education in the Sciences (FAES) titled “Writing and Publishing a Scientific Paper,” participants gain insight into the publishing process from a science journal editor’s perspective. Over the course of three weeks (including four classroom sessions), participants are guided through writing a complete paper based on their own data. In addition, attendees get tips on constructing figures and tables, writing cover letters, understanding the peer-review process, and responding effectively to reviewers’ comments. Trainees at every level of education and language ability can benefit from the course. “The greatest barriers to becoming a skilled scientific writer are not making an effort to improve (like taking writing courses or online tutorials) and not learning from mistakes,” said workshop instructor Maggie Meitzler, who has extensive science-journal editing experience.

“Every minute you spend learning about writing will pay off because it will lessen the time spent on writing projects, thus saving you valuable time in your research career.”

“I would recommend this course to others who are in the final stages of a project and are looking to put together a manuscript,” said postbaccalaureate fellow **Lynde Wangler** (National Institute on Aging), a recent workshop participant. “Through peer-review groups and instructor feedback, the workshop helped me to write more clearly and concisely, convey what the results mean to the field, and . . . better tell a ‘story’ when writing about our research.”

Meitzler offered a few key pieces of writing advice for trainees: “First, get started immediately. Allowing time for revisions is the key to a good scientific paper. Second, read every word of the Author Guidance section of your target journal. And lastly, writing a scientific paper is not a solitary sport. You have help from co-authors, collaborators, reviewers, and journal editors, plus the free editorial services at NIH.”

One of those editing services that Meitzler referred to can also be an excellent training opportunity. Intramural trainees can become members of the Fellows Editorial Board (FEB), which offers fellows a free, fast, and confidential scientific document editing service to other fellows. Members are immersed in the editing process right away and get to learn by doing, rather than by just observing or reading about English grammar.

FEB Senior Editor **Brandi Carofino** (National Cancer Institute) explained FEB’s win-win structure for editors and trainees submitting their manuscripts: “Through our tiered review system, the work of each editor is reviewed by several others. Help and feedback is provided when necessary. I

think this active-learning approach benefits both the editors and the fellows receiving the manuscript review service.” The experience also exposes editors to subjects outside of their expertise. “Sometimes it’s easier to spot holes in the storytelling when you are not an expert in the area being discussed,” said Carofino. “Most journals want the work to be accessible to a general audience, which is easy to forget when we are a bit close to the data.”

Echoing a piece of writing advice from Meitzler, Carofino commented, “A surprising number of authors do not format their manuscript according to their target journal’s requirements. It’s important to pay close attention to [these requirements] since some journals won’t even send your manuscript out for review if it doesn’t use the right template or have the correct organization of sections.”

Other resources are available for trainees seeking to improve grant-writing skills. The Office of Intramural Training and Education (OITE), for example, periodically offers grant-writing workshops. Several other NIH institutes and centers hold more in-depth courses and workshops; some workshops include written assignments and feedback on drafts of applications. ●

### RESOURCES

**FAES:** <https://faes.org/content/writing-publishing-scientific-paper-workshop>

**OITE:** <https://www.training.nih.gov/events/upcoming>

**NIH grant-writing workshops and courses:** [https://www.cc.nih.gov/training/resources/grant\\_writing.html](https://www.cc.nih.gov/training/resources/grant_writing.html)

**Fellows Editorial Board:** <https://www.cancer.gov/grants-training/training/resources-trainees/career-planning/submit-editorial-board>



MARLEEN VAN DEN NEST

Scientists gathered for the inaugural symposium, held on April 22, 2019, of the new Myeloid Malignancy Scientific Interest Group.

## New SIG: Myeloid Malignancy Interest Group's Inaugural Symposium

**THE NEW MYELOID MALIGNANCY** Scientific Interest Group celebrated its launch with an inaugural symposium on April 22, 2019. Myeloid malignancies, such as myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML), are rare, often highly fatal, cancers of the blood cells. The goal of this SIG is to intensify collaborations across the NIH communities and contribute to the ongoing growing momentum and interest in addressing these diseases and developing better treatments.

Myeloid malignancies are an area in which progress in cancer therapies has, until recently, been limited and survival outcomes remain dismal. Recent advances in understanding the genomics of these diseases, as well as tumor immunology, are opening unprecedented opportunities for more-rapid translation of new therapies into the clinic. The prominent unmet needs in

this field are MDS and secondary and therapy-related AML. These diseases are particularly suited for being studied in the NIH intramural research program (IRP) due to their inherited and acquired genetic defects, relative rarity, and frequently subacute disease trajectory.

### SYMPOSIUM

**Christopher Hourigan** (NHLBI), one of the founders of the new SIG, welcomed everyone and reported that there were already 73 people on the SIG's LISTSERV and that at least four institutes were represented as well as the FDA and extramural organizations. Deputy Director for Intramural Research **Michael Gottesman** explained the importance of having a program in myeloid malignancies—it's complicated; there are interesting animal and genetic models; scientists are getting closer to understanding the origins of the myeloid diseases; and there are multiple modalities for treatments. Gottesman, who's also the director of NCI-CCR's Laboratory of Cell Biology, spoke about his

research on the mechanisms of multidrug resistance in cancer. His lab identified the first ABC transporter and showed how it conferred multidrug resistance in cancer. The lab is trying to figure out the role of the transporters in AML.

**Steven Pavletic**, a senior clinician in NCI-CCR and also one of the SIG's founders, gave an overview of myeloid-malignancies research at NIH. He explained that the SIG aims to bring together NIH MDS and AML researchers, and intensify collaborations among them to cure, treat, and prevent these diseases. He pointed out that there was a session on myeloid malignancies at the 2018 Research Festival.

Several researchers presented their work. **Daniel Larson**, a senior investigator in NCI-CCR, gave a talk titled "Myelodysplastic Syndromes—From Lab to Clinic" in which he described some of his research. **Naoko Takebe** (NCI) discussed the rationale for a phase 1 clinical trial involving a combination treatment with clofarabine and bortezomib for patients with solid tumors, lymphomas, and other cancers. Case studies were presented by Takebe, Clinical Center investigators **Alina Dulau-Florea** and **Katherine Calvo**, and NHLBI investigator Hourigan. One of the cases highlighted was that of an 81-year-old man who had refractory MDS that evolved into AML. The patient participated in a combination drug trial of pembrolizumab and decitabine and showed marked improvement in six weeks (a reduction in myeloblasts, from 20 percent to less than one percent). ●

**For information about this SIG and instructions on how to join its LISTSERV, go to <https://oir.nih.gov/sigs/myeloid-malignancy-interest-group>. For other questions, contact Steven Pavletic ([pavletis@mail.nih.gov](mailto:pavletis@mail.nih.gov)).**

Read more at: <https://irp.nih.gov/catalyst/v27i4/the-sig-beat>.

## Richard Chadwick, NIDCD Scientist Emeritus and a New Catalyst Editor

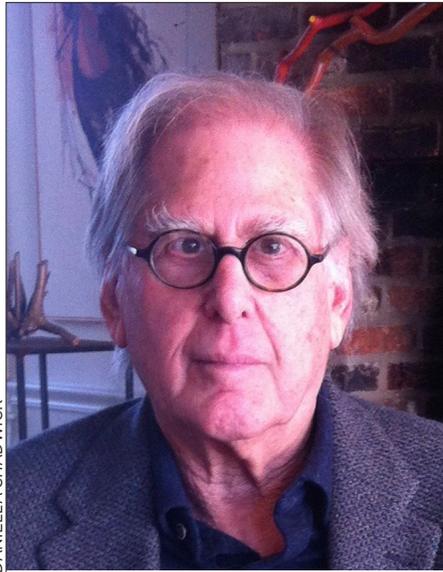
One of the First NIH Researchers to Study Bioengineering

BY LAURA MANELLA, NIDCD

**RICHARD CHADWICK PIONEERED** bioengineering technologies that have allowed researchers to study delicate tissues—such as those in the inner ear—without touching or damaging them. His work has led to a better understanding of how the inner ear works and how the structure of the cochlea enables it to amplify sound. Chadwick, who was chief of the Section on Auditory Mechanics in the National Institute on Deafness and Other Communication Disorders (NIDCD), retired in April 2019 after having spent 39 years at NIH, the last 23 of which were in NIDCD. He continues to serve NIH as a scientist emeritus and is also the new scientist-emeritus editor for the *NIH Catalyst*.

“Dr. Chadwick was one of the first researchers to study bioengineering ...promoting it internationally to spark interest in the budding field before it was standard curriculum at universities,” said NIDCD Scientific Director **Andrew Griffith**. “His unique and extremely collaborative approach...has yielded fundamental discoveries about cell mechanics and fluid dynamics within the inner ear as well as other types of tissues and cells.”

Chadwick began his career in mechanical engineering, earning a bachelor’s and then a master’s degree from Cornell University (Ithaca, New York) in 1966. He went on to earn a Ph.D. in aeronautics and astronautics from Stanford University (Stanford, California) in 1971. He then joined the engineering faculty at the Technion-Israel Institute of Technology (Haifa, Israel) in 1971, where he began to study the mechanical properties of the cochlea. He moved back to the United States in 1975 to work as a research fellow in chemical engineering at the California



DANIELLA CHADWICK

Richard Chadwick, one of the first to study bioengineering, retired after 39 years at NIH and 23 years at the National Institute on Deafness and Other Communication Disorders.

Institute of Technology (Pasadena, California) before becoming an adjunct associate professor at the University of California at Los Angeles in 1977.

In 1980, he joined NIH’s Bioengineering and Instrumentation Branch, later leading the Biomechanics Group.

“When I first arrived at NIH, there was no perimeter gate; it was an open campus,” Chadwick said. “However, the campus was not open about mixing engineering, physics, and math with biology. There is much less resistance now. I hope I had something to do with it.”

After the NIDCD was established in 1988, Chadwick began collaborating with scientists there and re-entered the field of cochlear dynamics. In 1996, he transferred to the NIDCD as a senior investigator and chief of the Section on Auditory Mechanics.

Chadwick was integral to the development and use of atomic force microscopy (AFM). He described how to use AFM with modeling to gain insights into

soft tissues. He later pioneered a modified version of this technology called noncontact AFM, which allows researchers to study tissues without physically touching—and thus damaging—their delicate structures. This method has enabled Chadwick and his collaborators to gain insight into the behavior of tissues, such as the tissue necessary for sound detection in the inner ear.

Through an artful interweaving of mathematical, physical, and biological approaches, Chadwick’s work has increased knowledge of the hearing process. One of his many contributions was an insight into the structure of the cochlear spiral. The reason for the snail shape of the cochlea in mammals had been elusive. He and his collaborators used cues from famous architectural structures such as whispering galleries—where someone can hear another’s whisper from across a large enclosed space, typically an area with curved walls—to show that the spiral curvature is critical to amplifying sensitivity to low-frequency sounds.

At an April 10 symposium held in Chadwick’s honor, his collaborators and former postdocs praised his work as well as his mentoring, his advocacy for women in science, and his kindness.

“Being kind to those you supervise is not always easy. It is a choice,” said former postdoc **Núria Gavara**, who is now an associate professor at Queen Mary University of London (London). “In this regard, Richard has been making the right choices for 40 years.” ●

This article was adapted from one that was first published on the NIDCD website.

([https://www.nidcd.nih.gov/news/2019/richard-chadwick-chief-nidcd-auditory-mechanics-section-retires.](https://www.nidcd.nih.gov/news/2019/richard-chadwick-chief-nidcd-auditory-mechanics-section-retires))



## National Academy of Sciences

### Mini Symposium Held to Celebrate NIH's New Members

**CELL MIGRATION, ANTI-CANCER DRUG** resistance, dogs and their genes, and a gene discovery that led to a treatment for a congenital immune disorder were the topics presented by the four recently elected members of the National Academy of Sciences (NAS) at a mini symposium, held on Thursday, May 23, 2019.

#### **Clare M. Waterman, Ph.D., NHLBI**

Clare Waterman described her research on the “dance” of cell migration. She has made seminal contributions to the understanding of the molecular and biophysical mechanisms of cell migration in development and disease. She pioneered the direct determination of protein organization and motion in living cells. In addition, she invented and used novel light-microscopy methods to define nanometer-scale architecture and dynamics of the molecular assemblies that generate, organize, and transmit forces that drive cell movement.

#### **Michael Gottesman, M.D., NCI-CCR**

“Most effective therapies for cancer cease to work after awhile,” said Michael Gottesman who has conducted pioneering research into improving cancer treatments, especially against cancer cells resistant to chemotherapy. His lab identified and cloned the first human ABC transporter and showed that it conferred multidrug resistance by energy-dependent efflux of hydrophobic natural-product drugs. Subsequently, other members of this transporter family were shown to impart broad-spectrum multidrug resistance. During his talk, he presented recent data pointing to the clinical contribution of multidrug transporters to anti-cancer drug resistance.

#### **Elaine A. Ostrander, Ph.D., NHGRI**

Elaine Ostrander is a pioneer in the field of comparative genomics, having initiated the canine genome project in 1993. Each of the over 450 breeds of domestic dogs is characterized by morphologic and behavioral features as well as disease susceptibility. To understand the underpinnings of this enormous genetic diversity, Ostrander's lab has assembled and analyzed the largest and most diverse dataset of dog breeds to date. She has shown that most breed-defining traits, such as body size, and leg length, are controlled by small numbers of genes. Similar variants are observed in humans but present a very different scenario and can be associated with disease. For example, mutations in growth genes in dogs are associated with obesity in humans.

#### **Michael Lenardo M.D., NIAID**

Michael Lenardo's research is helping to define genetic diseases of the immune system. Genomics coupled with biochemical investigation has allowed the molecular definition of a growing number of new genetic diseases and reveal new concepts of immune regulation. Defining the genetic pathogenesis of these diseases has led to improved diagnosis, prognosis, genetic counseling, and, most importantly, new therapies. For example, in 2017, his lab identified a genetic cause and a possible treatment for CHAPLE disease, a rare and potentially fatal autoimmune disorder. He found that the drug eculizumab could reverse the disease—a “remarkable change from death's doorstep,” he said. ●

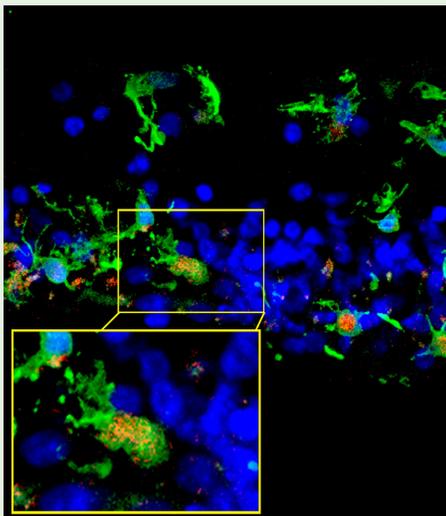
**To watch a videocast of the NAS Mini Symposium, held on May 23, 2019, go to <https://videocast.nih.gov/launch.asp?27568> (NIH only).**

#### NIH ABBREVIATIONS

**CBER:** Center for Biologics Evaluation and Research, FDA  
**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  
**FNIH:** Foundation for the NIH  
**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  
**NIHES:** National Institute of Environmental Health Sciences  
**NIHGS:** 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  
**OD:** Office of the Director  
**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



## Intramural Research Briefs



NEI

NEI: Retinal sections from a patient with retinitis pigmentosa show microglia (green) migrating into the photoreceptor layer (blue) after degeneration began. Inset shows microglia expressing C3 (red), which occurred in the context of photoreceptor degeneration. C3 is the central component of complement, and its absence made degeneration worse.

### NEI: IMMUNE SYSTEM CAN SLOW DEGENERATIVE EYE DISEASE

A new NEI study shows that the complement system, part of the innate immune system, plays a protective role in slowing retinal degeneration in a mouse model of retinitis pigmentosa, an inherited eye disease. This surprising discovery contradicts previous studies of other eye diseases—such as age-related macular degeneration—that suggest the complement system worsens retinal degeneration. Using the retinitis pigmentosa mouse model, the researchers found that the absence of the *C3* or *CR3* genes made degeneration worse. Further research is needed to complete the picture of how, and under what circumstances, complement activation has beneficial or harmful effects on photoreceptors and disease progression. (NIH authors: S.M. Silverman, W. Ma, Z. Wang, L. Zhao, and W.T. Wong, *J Exp Med* 2019; DOI:10.1084/jem.2019000)

### NIAID: SCIENTISTS DEVELOP “MINI-BRAIN” MODEL OF HUMAN PRION DISEASE

NIAID scientists at Rocky Mountain Laboratories (Hamilton, Montana) have used human skin cells to create what they

believe is the first cerebral organoid system, or “mini-brain,” for studying sporadic Creutzfeldt-Jakob disease (CJD). CJD is a fatal neurodegenerative brain disease of humans believed to be caused by infectious prion proteins. The researchers hope the human organoid model will enable them to evaluate potential therapeutics for CJD and provide greater detail about human prion disease subtypes than the rodent and nonhuman primate models currently in use.

In this study, the researchers infected five-month-old cerebral organoids with prions using samples from two patients who died of two different CJD subtypes, MV1 and MV2. Infection took about one month to confirm, and the scientists monitored the organoids for changes in health indicators, such as metabolism, for more than six months. By the end of the study, the scientists observed that seeding activity, an indication of infectious prion propagation, was present in all organoids exposed to the CJD samples. However, seeding was greater in organoids infected with the MV2 sample than in the MV1 sample; but the MV1-infected organoids showed more damage than the MV2-infected organoids. (NIH authors: B.R. Groveman, S.T. Foliaki, C.D. Orru, J.A. Carroll, B. Race, and C.L. Haig, *Acta Neuropathol Commun* 7:12, 2019; DOI:10.1186/s40478-019-0742-2)

### NICHD: BEING TEASED ABOUT WEIGHT MAY LEAD TO MORE WEIGHT GAIN AMONG CHILDREN

Youth who said they were teased or ridiculed about their weight increased their body mass by 33 percent more each year than a similar group who had not been teased, according to researchers at NICHD and the Uniformed Services University of the Health Sciences. The findings appear to contradict the belief that such teasing might motivate youth to change their behavior and attempt to lose weight. (NIH authors: N.A. Schvey, S.E. Marwitz, S.J. Mi, O.A. Galescu, M.M. Broadney, D. Young-Hyman, S.M. Brady, J.C. Reynolds, M. Tanofsky-Kraff,

S.Z. Yanovski, and J.A. Yanovski, *Pediatr Obes* May 29:e12538, 2019; DOI:10.1111/ijpo.12538)

### NIDDK, CC, NINR: HEAVILY PROCESSED FOODS CAUSE OVEREATING AND WEIGHT GAIN

People eating ultraprocessed foods ate more calories and gained more weight than when they ate a minimally processed diet, according to results from a study conducted by NIDDK researchers. This small-scale study of 20 healthy adult volunteers (10 males and 10 females) is the first randomized controlled trial to examine the effects of ultraprocessed foods (with ingredients such as hydrogenated oils, high-fructose corn syrup, flavoring agents, and emulsifiers). People on the unprocessed diet ate about 500 calories more per day, ate faster, and gained an average of two pounds compared to people on the unprocessed diet. (NIH authors: K.D. Hall, et. al., *Cell Metab* 30:1-11, 2019; DOI:10.1016/j.cmet.2019.05.008)

### NIEHS: SLEEPING WITH ARTIFICIAL LIGHT AT NIGHT ASSOCIATED WITH WEIGHT GAIN IN WOMEN

Sleeping with a television or light on in the room may be a risk factor for gaining weight or developing obesity, according to scientists at NIEHS who conducted a study involving more than 43,000 women. The research is the first to find an association between any exposure to artificial light at night while sleeping and weight gain in women. The results varied with the amount of exposure to artificial light at night. For example, using a small nightlight was not associated with weight gain, whereas women who slept with a light or television on were 17 percent more likely to have gained approximately 11 pounds or more over the five-year follow-up period. (NIH authors: Y.-M.M. Park, et.al., *JAMA Intern Med* 2019; DOI:10.1001/jamainternmed.2019.0571)

Read more briefs and longer versions at:  
<https://irp.nih.gov/catalyst/v27i4/research-briefs>.

## Our Brains Appear Uniquely Tuned for Musical Pitch

Speech and Music May Have Shaped Human Brain Circuits for Hearing

BY CHRISTOPHER THOMAS, NINDS

**IN THE ETERNAL SEARCH FOR UNDER-**standing what makes us human, scientists found that our brains are more sensitive to pitch, the “higher” and “lower” (or “deeper”) sounds caused by differences in wavelength (frequency), than our evolutionary relative the macaque (*Macaca mulatta*). The study, published in *Nature Neuroscience* and funded in part by NIH, highlights the promise of Sound Health, a joint project between the NIH and the John F. Kennedy Center for the Performing Arts, in association with the National Endowment for the Arts, that aims to understand the role of music in health. (See article on page 1 of this issue.)

“We found that a certain region of our brains has a stronger preference for sounds with pitch than macaque monkey brains,” said the study’s senior author **Bevil Conway**, who was a scientist at the Massachusetts Institute of Technology (MIT) in Cambridge, Massachusetts, at the time of the study, and who joined NIH as an investigator in the National Eye Institute in 2016. “The results raise the possibility that these sounds, which are embedded in speech and music, may have shaped the basic organization of the human brain.”

The study started with a friendly bet between Conway and Sam Norman-Haignere, a postdoctoral fellow at Columbia University’s Zuckerman Institute for Mind, Brain, and Behavior (New York) and the first author of the paper.

At the time, both were working at MIT (Norman-Haignere was a postdoctoral fellow there). Conway’s team had been searching for differences between how human brains and monkey brains control vision, only to discover that there are very few. Their brain-mapping studies suggested that humans and monkeys see the world in

very similar ways. But then, Conway heard about some studies on hearing being done by Norman-Haignere.

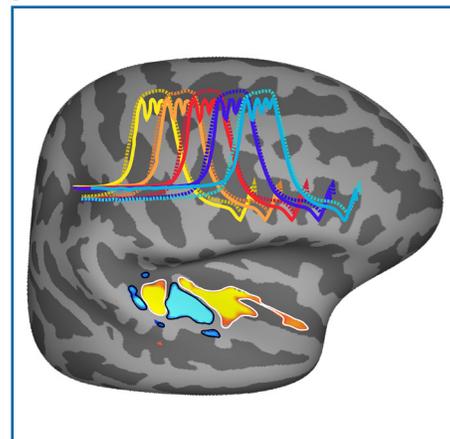
“I told Bevil that we had a method for reliably identifying a region in the human brain that selectively responds to sounds with pitch,” said Norman-Haignere. That is when they got the idea to compare the brains of humans with those of monkeys. Based on what he’d learned about vision, Conway expected to see no differences in the way the brains responded to sound.

To test their hypothesis, the researchers did two experiments in which they played a series of harmonic tones and noise sounds (sounds without pitch) to six healthy volunteers and five monkeys. The sounds in the first experiment were synthesized tones (such as broadband noise or simple ring tones on a cell phone). In the second experiment, the sounds were macaque vocalizations and versions of the vocalizations that had been put through an algorithm to render them pitch-less (much like whispering, which preserves the frequency range and temporal structure, but lacks pitch).

Functional magnetic-resonance imaging (fMRI) was used to monitor brain activity in response to the sounds. At first glance, the fMRI scans looked similar and confirmed previous studies. Maps of the auditory cortex of human and monkey brains had similar hot spots of activity regardless of whether the sounds contained harmonic tones.

However, when the researchers looked more closely at the data, they found evidence suggesting that the human brain’s auditory cortex was much more responsive than the monkey cortex to harmonic tones.

“We found that human and monkey brains had very similar responses to sounds in any given frequency range. It’s when we added tonal structure to the sounds that



BEVIL CONWAY LAB, NEI

Tuned for musical pitch: NIH-funded scientists found that our brains may be uniquely sensitive to the range of pitches (sound-wave frequencies) used in music and speech.

some of these same regions of the human brain became more responsive,” said Conway. “These results suggest the macaque monkey may experience music and other sounds differently. It makes one wonder what kind of sounds our evolutionary ancestors experienced.”

In the second set of experiments, fMRI scans showed that the human auditory cortex, compared to the monkey cortex, was much more responsive to the natural monkey calls than the pitch-less calls.

“This finding suggests that speech and music may have fundamentally changed the way our brain processes pitch,” said Conway. “It may also help explain why it has been so hard for scientists to train monkeys to perform auditory tasks that humans find relatively effortless.” ●

(NIH author: B.R. Conway, *Nat Neurosci* 22:1057-1060, 2019). The project received support from NIH extramural grants as well as from the intramural research programs at NEI, NINDS, and NIMH.

Read more online and see a video at <https://irp.nih.gov/catalyst/v27i4/our-brains-appear-uniquely-tuned-for-musical-pitch/>.

## Music

CONTINUED FROM PAGE 1

CHIA CHI CHARLIE CHANG



Opera singer Renée Fleming visited NIH in May as the featured guest at the annual J. Edward Rall Cultural Lecture. She talked about the Sound Health initiative, an NIH–Kennedy Center partnership in association with the National Endowment for the Arts, and had an on-stage conversation with NIH Director Francis Collins. Afterwards she and Collins sang Leonard Cohen’s “Hallelujah” and the spiritual song “How Can I Keep from Singing?”

have an identifiable impact. Indeed, it has been shown that exposing children to music can enhance reading proficiency and tends to lead to higher rates of career success.

Plato remarked that “Music is the medicine of the soul.” But why is it so beneficial? We understand how a piece of music can influence our emotions, but one study showed that rhythm may also be important in our development. Fleming showed a video of a study that demonstrated that when a stranger bounced in time with a baby, the infant was more likely to help the stranger complete a task afterwards than if the bouncing was out of sync. This study showed that even from an early age, music can bring us together, but to find out what happens in the brain, we need to be able to observe neuronal activity.

Bring in the magnetic-resolution-imaging (MRI) scanner. In 2017, Fleming experienced the feeling of being in such a scanner for herself. She chose the song “The Water Is Wide,” and her brain activity was measured as she spoke, sang, and imagined

singing the words. Interestingly, imagining the words produced the most striking brain activity, but she put this down to the fact that singing is natural to her; imagining the words was the hardest.

MRI studies have revealed the fascinating influence of music. Fleming described an experiment in which neuroscientist Charles Limb asked jazz piano prodigy Matthew Whitaker to undergo two tasks while in the scanner. First, Whitaker had to listen to a boring lecture and, unsurprisingly, very few areas of his brain showed activity. However, when he listened to his favorite band, his brain lit up like a Christmas tree. Although Whitaker is blind, even his visual cortex responded, indicating that music could have very potent therapeutic benefits.

One striking example, said Fleming, is the case of Forrest Allen, who was left in an almost lifeless state after a snowboarding accident in 2011 that caused a traumatic brain injury. Allen’s recovery was long and tough, surgeries to repair his skull catapulted him into comas, and he couldn’t speak for

two years. His childhood music teacher noticed a tiny movement in Allen’s pinkie finger when music was playing, as if he was tapping along with the rhythm. As part of Allen’s rehab, the teacher began using rhythm and melody to help his brain heal. Thanks to his doctors, surgeons, and physical therapists, Allen slowly recovered. Thanks to music therapy, he learned to talk again. Today, Allen is a college student at George Mason University (Fairfax, Virginia).

Given that music can affect us to such a degree, Collins asked Fleming how she manages singing professionally during emotional moments. She recollected two particularly emotional moments—singing “Danny Boy” at Senator John McCain’s funeral in Washington, D.C., in 2018, and performing “Amazing Grace” at the National September 11 Memorial in New York City in 2013. She said that it was all about mental preparation before the events. She had to keep reminding herself that she was singing for everyone else and not just for herself: The singing had to be right.

Regarding her dreams for the Sound Health program, she hopes music therapy will become more widely covered by insurance and that the arts will be increasingly involved in our general well-being. She concluded by saying that she had been privileged to work with so many amazing people and takes great delight in performing in all sorts of ways. At this, Collins picked up his guitar and they wrapped up this unique event in an unforgettable way. They joined their voices in harmony to Leonard Cohen’s “Hallelujah” and the spiritual song “How Can I Keep from Singing?” The audience sat spellbound as the music echoed around the room. ●

To view a videocast of the May 13 Rall Lecture featuring Renée Fleming (NIH only), go to <https://videocast.nih.gov/launch.asp?27524>.

## NIH Science in Orbit : Tissue Chips in Space

BY ANNE WRIGHT, NCATS

**BOTH INTRAMURAL AND EXTRAMURAL** NIH scientists are using the special environment of space to gather new insights into human health. Symptoms of accelerated aging and many health conditions, such as immune-system changes and bone and muscle loss, occur more rapidly in space due to the effects of microgravity (close-to-zero gravity). Microgravity facilitates studies that could take much longer to carry out on Earth.

“NIH scientists have an amazing opportunity to model diseases and investigate potential treatments for them at the International Space Station,” said **Lucie Low**, the NIH-NASA liaison point-of-contact and a scientific program manager at the National Center for Advancing Translational Sciences (NCATS). “NIH has a long history of collaborating with NASA, and I see lots of exciting opportunities for our researchers to continue doing so over the coming years.” NASA and NIH have been collaborating since the early 1960s. NIH’s role in the collaboration, which includes many institutes and centers, was first led by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, later by the National Institute of Biomedical

Imaging and Bioengineering (NIBIB), and today by NCATS.

To illustrate the usefulness of NIH science-in-space, here’s a quick look at the projects that NCATS and the National Cancer Institute (NCI) launched from Cape Canaveral, Florida, to the International Space Station U.S. National Laboratory (ISS National Laboratory) on May 4, 2019. The projects are now back on the ground, and researchers are analyzing the results.

### Tissue Chips in Space

NCATS sent up four miniature tissue-chip systems to better understand aging-related conditions and diseases, speed up the development of interventions to treat them, and enable wider use of tissue-chip technology on the ground.

Tissue chips, also known as organs-on-chip, are tiny, bioengineered three-dimensional models that mimic the structure and function of human organs such as the heart, kidneys, and lungs. Scientists use tissue chips to study diseases and test the possible effects of drugs on those tissues.

The projects on the May 2019 mission are part of the Tissue Chips in Space Initiative, a collaborative program involving NCATS, NIBIB, and the ISS National

Laboratory, which partners with NASA to use the U.S. portion of the space station for research.

This launch was the second time NIH-funded tissue-chip experiments flew on the ISS. The first was in December 2018 with immune-system tissue chips developed by researchers at the University of California, San Francisco. The NIH-funded projects on the May 2019 mission included kidney chips, bone and cartilage chips, lung and bone-marrow chips, and chips modeling the blood-brain barrier. Each project has direct clinical applications to health conditions we experience on Earth. For example, findings from the lung and bone-marrow chips will directly relate to how aging affects our ability to fight infection. Findings from the kidney-chip models could yield clues to the cause, prevention, and treatment of aging-related conditions affecting the kidneys. And the blood-brain barrier chips will enable researchers to look at neurodegenerative diseases.

To get the projects ready for the ISS, the scientific teams collaborated with engineers to shrink a roomful of lab equipment into “plug-and-play” shoebox-sized packages that could stand the stress of space flight and be operated by astronauts and pilots who don’t know the research.

Each tissue-chip project will fly into orbit twice. The initial group of tissue chips were aboard the ISS National Lab for about a month before returning to Earth. In 2020, the chips will be sent back to the space station so potential drug therapies can be tested on the biological processes observed during the first visit to the space. ●

For more information, go to <https://ncats.nih.gov/tissuechip/projects/space>. If you’re interested in sending a project into space, please email Low at [Lucie.Low@nih.gov](mailto:Lucie.Low@nih.gov).



NASA

Laboratory setup of the International Space Station U.S. National Lab’s Expedition 59 crew as they work with the NIH-supported research on tissue chips in space. The projects take advantage of how the microgravity of space accelerates the aging process and may provide clues to how neurodegenerative diseases develop.

## Historical Medical Films at NLM

CONTINUED FROM PAGE 1



NLM

A still from a 1938 film titled *Three Countries Against Syphilis*, which was produced by the U.S. Public Health Service and donated to NLM by Leroy E. Burney.

on aspects of medicine ranging from delivering an infant to how to treat battle wounds in the field. By 1962, NLM had acquired almost 700 titles (each title could have several associated items). Today the collection comprises nearly 40,000 titles and an estimated 8,000 catalogued film and video recordings considered historically significant. Some items are so rare that NLM has the only surviving copy.

In February 2019, NLM launched a new website—“Medicine on Screen: Films and Essays from NLM”—a curated, freely accessible portal presenting digitized historical titles from its audiovisuals collection.

Because many of the films that NLM acquired in the 1950s featured medical training and clinical procedures, Rogers realized that it would be more appropriate to house them in the audiovisual branch within the Communicable Disease Center (now the Centers for Disease Control and Prevention, CDC) in Atlanta. Thus, the collection resided there from 1962 through the early 1980s.

This period saw a large addition of films to the initial collection. During this time, the National Medical Audiovisual Center (NMAC) was established in Atlanta and its mandate was to produce public-health, clinical, training, and other medical films on behalf of the United States government. NMAC, which started as a branch of CDC’s predecessor—the Office of Malaria Control in War Areas—in the 1940s, was integrated into NLM in 1967 and was physically moved to NLM’s Bethesda campus in the 1980s.

At first, the film collection was managed by NLM’s General Collection, which started loaning some of the 16-mm films to patrons. In 1988, all films that predated 1970 were transferred to NLM’s History of Medicine Division (HMD), which also accepted transfers and donations from other sources. Today, HMD holds a wide variety of material in audiovisual format including educational and instructional titles, animations, documentaries, and films of live surgeries and counseling sessions. The films provide a peek into medical knowledge and practices of a bygone time. There are thousands of post-1970 titles in the collection

as well. The audiovisual materials at NLM, whether housed in HMD or in the General Collection, are considered as one collection, now numbering about 40,000 titles.

### Where did the films come from?

Many of the titles in the collection were transferred to NLM from other government agencies. Advocacy organizations such as the American Dental Association (ADA) or hospitals including the former Western Psychiatric Institute in Pittsburgh also have contributed large numbers. Besides NMAC (which transferred about 1,600 films), all branches of the military and other government agencies have given films to NLM, as have other NIH institutes such as the National Institute for Mental Health. The Office of NIH History often coordinates NIH-related film transfers to NLM.

In the 1940s, making medical documentaries and short films related to the battlefield was common. These films were intended to inform soldiers and citizens about such health hazards as malaria, dysentery, and yellow fever. Films on psychiatric illnesses, such as post-traumatic stress disorder (then called shell shock or combat fatigue), were declassified before being donated to NLM. And, as the Cold War (1947–1991) intensified in the 1950s, the military produced dozens of films about public preparation and response to nuclear attack.

Donations also came from state health



SARAH EILERS, NLM

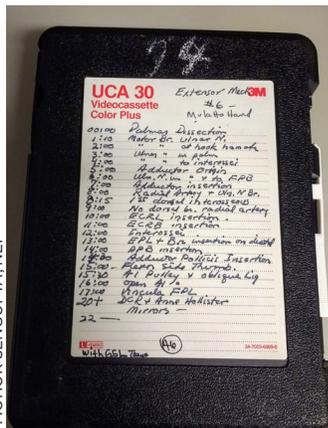
This film, *Surviving Under Atomic Attack*, was made during early years of the Cold War.



authorities including New York State’s Department of Health and the State Psychiatric Institute, hospitals, and academic institutions. Among the films donated were several collections on psychiatric problems and their societal implications. Medical and advocacy organizations such as the ADA mentioned above, the American Cancer Society, and the National Tuberculosis Association donated films that typically had been produced for circulation in schools and community organizations.

Pharmaceutical, surgical-equipment, and medical-device companies donated more than 1,000 films. Films made by doctors and scientists are in the collection, too. For example, NLM holds a set of World War II-era films on wound ballistics and decompression research made by Princeton physiologist Edmund Newton Harvey (1887–1959), who studied decompression sickness and tissue damage caused by high-velocity missiles. Donations also come from the unlikelyst of places. One set of films on childbirth education was discovered in a dumpster in Jacksonville, Florida, 15 years ago and donated to NLM in 2016.

The History of Medicine’s most recent acquisition came in February 2019. Grafton County Senior Services, a small organization in New Hampshire, donated about 30 VHS



MOHOR SENGUPTA, NEI

U-matic tape at the NLM vault in Bethesda.

tapes and audiocassettes on dementia, Alzheimer disease, and elder-care.

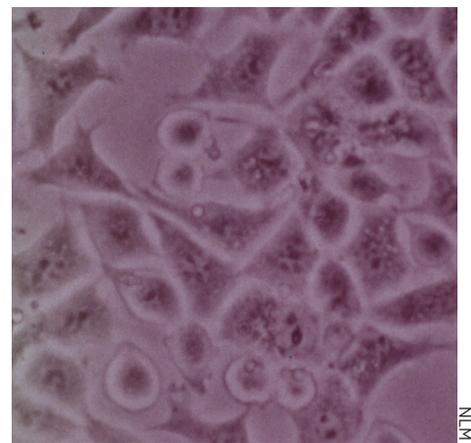
### Availability of the films

The films arrive at NLM in formats ranging from perishable U-matic tapes (common in the 1960s, 1970s, and 1980s) to the more stable 16-mm and 35-mm formats (used in documentary and feature films respectively). The original films and tapes are in cold storage and out of circulation, but DVD viewing copies are available for thousands of titles, and about 350 films are available for viewing in NLM Digital Collections. The NLM website “Medicine on Screen” takes viewers deep into selected rare films, with essays that provide context and commentary. All cataloged titles can be found via LocatorPlus.

Some of the collection is stored onsite in a basement vault at NLM. Sarah Eilers, NLM’s Historical Audiovisuals Program Manager, showed this writer around the vault, where hundreds of titles in various formats (U-matic tapes, Betacam SP formats, 16-mm and 35-mm films, and VHS tapes) are stored. Eilers and her colleagues at NLM are preserving and digitizing these rare and unique historical formats to protect them from the ravages of time.

About 80 percent of the collection is stored offsite in two vaults that NLM leases at the Iron Mountain facility, a former limestone mine in western Pennsylvania.

A “cool vault” stores magnetic tapes and microfilms at 55 degrees Fahrenheit and a “cold vault” stores films at 35 degrees Fahrenheit. Underground at the facility, temperature and humidity are ideal for long-term film storage. The Internal Revenue Service and Warner Brothers Pictures are some of the other corporations leasing space at Iron Mountain. Newly acquired films are shipped to the facility and wait their turn to be processed at the Bethesda campus. On the other end, older films requested by



NLM

A still from the 1968 film produced by National Educational Television and Radio Center and titled *Drugs Against Cancer*. This was one of the three films in the NLM collection used in the making of *Cancer: The Emperor of All Maladies*.

documentary producers for high-resolution copies are recalled from the facility to be digitized and shared.

### Managing historical audiovisuals

“I’m responsible for intellectual and physical control of the collection,” Eilers said. New material arrives regularly, and, to make it valuable and available for research, staffers must assess, inventory, and store the items, then catalog and digitize them as resources permit. About five percent of the collection has been digitized so far. The sound quality of older films can be poor, making it harder for them to be transcribed and subtitles added. Older films also have outdated



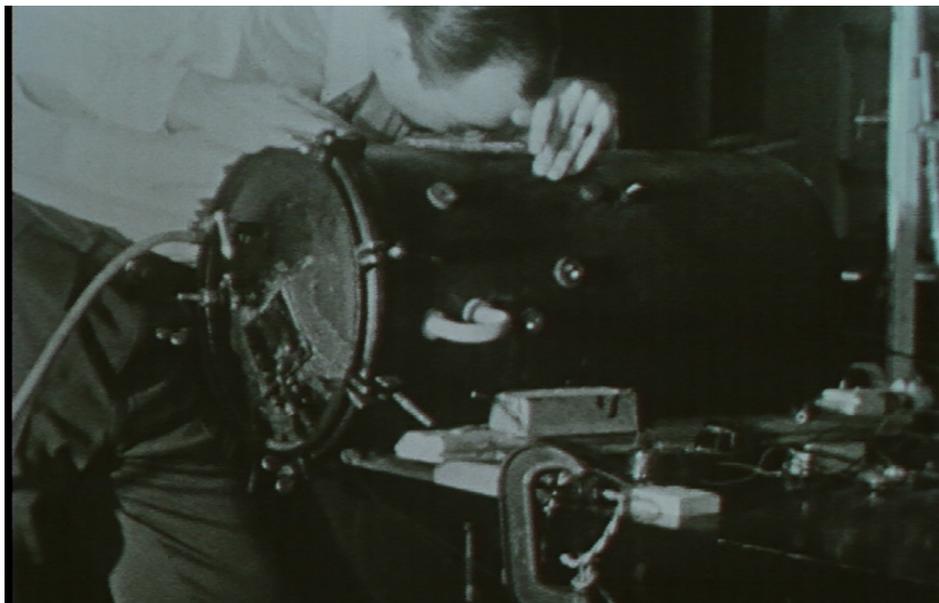
NLM

A still from a 1940 film titled *Choose to Live*, which is about early detection of and treatment for cancer. Depicted here are radium tubes used for cancer treatment. The film was produced by the U.S. Public Health Service and donated to NLM by former U.S. Surgeon General Thomas Parran Jr., who served from 1936 to 1948.

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## Historical Medical Films at NLM

CONTINUED FROM PAGE 13



NLM

NLM holds a set of World War II-era films on wound ballistics and decompression research made by Princeton physiologist Edmund Newton Harvey, who studied decompression sickness and tissue damage caused by high-velocity missiles. Shown: Screen capture from Harvey's 1949 silent film *Decompression Sickness Project*, in which he is peering into a decompression chamber in his lab.

medical terms that may be unfamiliar to the transcriber or viewer. “We don’t change them,” Eilers noted. “We just capture exactly what’s being said.”

NLM often gets requests for digital copies from individual patrons and documentary-film makers. For example, the production company that made the

Ken Burns film *Cancer: The Emperor of All Maladies* (adapted from the Pulitzer prize-winning book by Siddhartha Mukherjee) used three films from NLM’s collection. The company arranged—and paid—to have the films digitized by a vendor used by NLM; NLM provided the original films to the vendor.

Eilers, along with project consultant Oliver Gaycken of the University of Maryland (College Park, Maryland), is responsible for decisions about which titles appear in “Medicine on Screen.” Rarity or uniqueness of a film and patron demand are factored into the selection process. “Medicine on Screen” highlights selected films from the NLM’s audiovisual collections along with expert commentary that sets the films in historical context. The essays explore “the social, cultural, and medical milieu of the work, as well as cinematic techniques, the agendas of directors or producers, and other contextual details,” according to the website (<https://medicineonscreen.nlm.nih.gov>). Eilers is formalizing procedures for

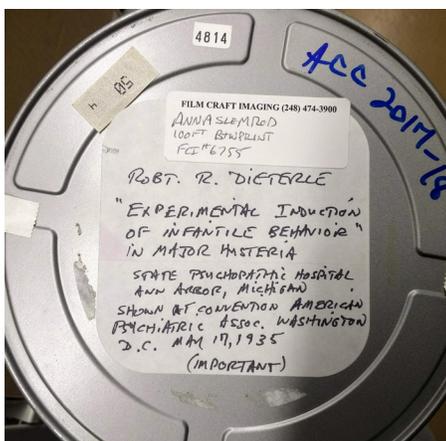
identifying potential contributors, guidelines for essayists, planning online-publication dates, and acquiring author permissions.

Finally, acquiring new titles is an ongoing task for the historical film curator. In one case, she tracked down and met with a family member of renowned psychiatrist Robert R. Dieterle (1896–1969) and secured the Dieterle-produced film titled *Experimental Induction of Infantile Behavior in Major Hysteria*. That film, along with a paper of the same name, was presented at a convention of the American Psychiatric Association in Washington, D.C., in 1935.

Eilers is also interested in constructing education and outreach programs for high-school and college students in order to promote films as one of the primary sources of information in educational settings.

Frank Rogers would be proud to see how the collection has grown and that it spans more than a century. More than 900 titles date from before 1950. The oldest film in the collection is a 1917 film showing a step-by-step procedure for performing a root-canal technique. Ouch! ●

To read more about the films and essays in NLM’s collection, go to <https://circulatingnow.nlm.nih.gov/2019/02/21/medicine-on-screen-films-and-essays-from-the-national-library-of-medicine>.



MOHOR SENGUPTA, NEI

Acquiring films for the NLM historical film collection can include meeting with family members of the films’ creators. NLM staff met with a family member of renowned psychiatrist Robert R. Dieterle and secured his film titled *Experimental Induction of Infantile Behavior in Major Hysteria*.



SARAH EILERS, NLM

About 80 percent of the NLM’s historic film collection is stored offsite in two vaults that NLM leases at the Iron Mountain facility, a former limestone mine in western Pennsylvania.

## Valerie Schneider: Diving Deep into Information Engineering

Highlighting the Work of Our Unique NIH Staff Scientists

BY KATHRYN MCKAY, NLM

**VALERIE SCHNEIDER DIVES DEEP**—whether it’s into the ocean or her work. Ironically, if it weren’t for a fish, this developmental biologist and deep-sea diver might not have rediscovered her love of genetics and landed a career as a staff scientist at the National Center for Biotechnology Information (NCBI) at the National Library of Medicine.

Now in her fourth-floor office at NIH, Schneider stays focused on what’s important for NCBI’s Information Engineering Branch.

### ALWAYS BIOLOGY

Schneider recalled that as a child she enjoyed seeing cicada wings under a microscope, studying Gregor Mendel, and creating Punnett squares. Naturally, she majored in biology, a popular major at Cornell University (Ithaca New York). There, Schneider had access to an array of biology classes. When she was introduced to the field of developmental biology and specifically embryology, she thought it was “the coolest thing.”

For Schneider, “Development is a natural read-out for understanding genes: Perturb a gene or gene interactions and you often can see the impact on the macromolecular level.”

Upon graduating in 1994, Schneider applied to graduate schools everywhere from Seattle to Boston and ultimately decided upon the Ph.D. program at Harvard Medical School (Boston). “There was amazing research going on and the people were down to earth and super friendly,” she said. She got her Ph.D. in 2001.

At Harvard, she studied *Xenopus laevis*, also known as the African clawed frog, which had embryos that were perfect for studying early development. The large size and minimal culture needs of frog embryos made it possible to perform all

types of experiments that altered the typical developmental program. By using microinjections to perturb gene expression and an eyelash knife to do embryonic surgeries, she could learn how different parts of the embryo interacted to give rise to a head or heart.

### FATE AND A FISH

She might have kept studying *X. laevis* as a postdoc, but fate and a fish intervened.

In 2001, her husband had accepted a position in the Philadelphia area, and the University of Pennsylvania had an opening for a postdoc in a lab for that was using the zebrafish (*Danio rerio*) as a model system.

Looking back, she said, “It was fortuitous because in the late 1990s, zebrafish as a model organism took off when Christiane Nüsslein-Volhard, who had won the Nobel prize for her work in fruit flies, decided to develop zebrafish as a model system for developmental biology.

“Working with zebrafish brought me back to that first love I had of genetics.”

She did both developmental biology and genetics at the University of Pennsylvania.

“It was the best of both worlds.”

Her work also aligned with what was going on in the greater scientific world.

“The Human Genome Project had released their draft version about 2001 when I got started,” she said. “As I was cloning this gene in zebrafish, there wasn’t a complete zebrafish genome yet, but there was a zebrafish genome project.”

### BUT WHAT WAS NEXT?

When her postdoc was over in 2007, Schneider wondered, “What’s next?” She could become a principal investigator. She could take a position in industry. She could leave the field entirely. She could teach. Or maybe she could do something else.



CHIA CHI CHARLIE CHANG

Coincidentally, at that time, NCBI was hiring more scientists.

She explained, “By 2007, the Human Genome Project was moving into a new phase and NCBI, which had been playing a role in a lot of the data management for the Genome Project, had joined this consortium to continue improving the reference. Just as I was finishing up my postdoc, there was a call for people to come curate the genome.”

She was intrigued. And working at NCBI would mean that she’d be able to find the time to enjoy her passion as a certified scuba-diving instructor while still pursuing her interest in genetics.

The leap from academia to government felt huge. “Stepping away from the bench into a bioinformatics environment would be quite a shift. I didn’t doubt I could do

CONTINUED ON PAGE 19 ▶

## Recently Tenured



KAPIL BHARTI, NEI



ASHISH LAL, NCI-CCR

SHALINI OBERDOERFFER,  
NCI-CCR

MADHAV THAMBISETTY, NIA



JOHN S. TSANG, NIAID

### **KAPIL BHARTI, PH.D., NEI**

*Senior Investigator, Unit on Ocular and Stem Cell Translational Research, National Eye Institute*

**Education:** Panjab University, Chandigarh, India (B.Sc. in biophysics); Maharaja Sayaji Rao University, Baroda, India (M.Sc. in biotechnology); Johann Wolfgang Goethe University, Frankfurt, Germany (Ph.D. in molecular cell biology)

**Training:** Research fellow, National Institute of Neurological Disorders and Stroke (NINDS)

**Came to NIH:** In 2004 for training; became staff scientist in NINDS in 2009; became Earl Stadtman Investigator in 2012

**Selected professional activities:** Scientific advisory board member for nonprofit patient-advocacy organizations: The Regenerative Outcomes Foundation (Nashville, Tennessee) and Choroideremia Research Foundation, (Springfield, Massachusetts)

**Outside interests:** Hiking; running

**Website:** <https://irp.nih.gov/pi/kapil-bharti>

**Research interests:** My lab is using induced pluripotent stem-cell (iPSC) technology to perform translational research on degenerative eye diseases. We are using this technology to develop in vitro disease models to study patient-specific disease processes, set up high-throughput drug

screens, and develop cell-based therapy for retinal degenerative diseases.

In particular, we are focused on the retinal pigment epithelium (RPE), a monolayer of highly polarized cells located in the back of the eye adjacent to retinal photoreceptors. The RPE performs several functions that are critical for the health and integrity of photoreceptors—regulating nutrient and metabolite flow, maintaining ionic homeostasis in the subretinal space, regenerating visual pigment, and phagocytizing shed photoreceptor outer segments. Dysfunctions in the RPE are thought to be the initiating events that lead to degenerative eye diseases. Therefore, a better understanding of the disease-initiating pathways in RPE will provide a basis for therapeutic interventions.

By culturing iPSC-derived RPE cells on biodegradable scaffolds, we are able to develop functional RPE tissue. We have modified the existing stem-cell-to-RPE-differentiation protocols to make them more compliant with current Good Manufacturing Practices. We are collaborating with the NIH Clinical Center's Department of Transfusion Medicine to develop iPSC-derived RPE tissue for cell-based therapy. Later, we plan to launch a clinical trial that uses this autologous iPSC-derived RPE tissue to treat patients with retinal degenerative diseases.

In collaboration with the NEI clinic, we are obtaining blood samples from patients who have clinically diagnosed degenerative eye diseases. These samples are being used to derive iPSCs. RPE cells differentiated from such iPSCs are used to study events that have led to disease initiation and progression. In collaboration with the National Center for Advancing Translational Sciences, we are combining a patient-specific iPSC approach with high-throughput screening assays to identify novel compounds that could act as potential therapeutic agents. Our work uses the most cutting-edge technologies in the field and aims to translate these technologies to a clinical use.

### **ASHISH LAL, PH.D., NCI-CCR**

*Senior Investigator and Head, Regulatory RNAs and Cancer Section, Genetics Branch, Center for Cancer Research, National Cancer Institute*

**Education:** Banaras Hindu University, Varanasi, India (B.S. in chemistry; M.S. in biochemistry; Ph.D. in biotechnology)

**Training:** Research Associate, Center for Cellular and Molecular Biology (Hyderabad, India); postdoctoral fellow, Laboratory of Cellular and Molecular Biology, National Institute on Aging; instructor of pediatrics, Immune Disease Institute, Harvard Medical School (Boston)



**Came to NIH:** From 2003 to 2007 for training; returned in 2010 as tenure-track investigator and head, Regulatory RNAs and Cancer Section, Genetics Branch, NCI-CCR

**Selected professional activities:** Editorial board member *Molecular and Cellular Biology*; associate editor *RNA Biology*; ad hoc reviewer for NIH and National Science Foundation study sections

**Outside interests:** Hiking; playing basketball, soccer, and ping pong

**Website:** <https://irp.nih.gov/pi/ashish-lal>

**Research interests:** Most of the eukaryotic genome is noncoding; only two percent represents protein-coding sequences. Among the several types of noncoding RNAs, microRNAs (miRNAs) and long noncoding (lncRNAs) have gained significant attention due to emerging evidence demonstrating critical roles of some miRNAs and lncRNAs in regulation of vital cellular processes.

Our goals are to define the molecular mechanisms by which noncoding RNAs such as lncRNAs function in the control of proliferation, apoptosis, and differentiation in the context of colorectal cancer, to gain insights into RNA biology, and to lay the foundation for future translational research.

Unlike miRNAs, which have been studied for more than two decades, the lncRNA field lags far behind. The lncRNAs were recently discovered. Their expression is often altered in cancer; they act via diverse mechanisms, are expressed at low concentrations, and are not well-conserved. The lncRNAs are therefore a source of investigation and debate.

To discover lncRNAs that may have a function, we use two approaches. The first approach involves identification and functional integration of lncRNAs regulated by *TP53*, the most frequently mutated gene in human cancer. We expect that this approach will enable us to better

understand how *TP53* and its regulated lncRNAs mediate tumor suppression.

The second approach relies on altered lncRNA expression in colorectal cancer and tissue specificity. We identify lncRNAs that are downregulated in colorectal cancer and select those that are expressed in an intestine-specific manner. We believe that a subset of these intestine-specific lncRNAs are expressed only in intestinal tissue because they have an important role to play in its biology. A deeper understanding of what restricts their expression in the intestine and the biology of these lncRNAs is critical in determining their potential in cancer therapy.

Using cell and molecular biological approaches to investigate lncRNA function and mode of action, combined with analysis of lncRNA expression in patient samples and in vivo studies in mice, we hope to better understand their role in cancer pathogenesis.

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**SHALINI OBERDOERFFER, PH.D., NCI-CCR**

*Senior Investigator, head, RNA Processing in Cellular Development Section, Laboratory of Receptor Biology and Gene Expression, Center for Cancer Research, National Cancer Institute*

**Education:** Bryn Mawr College, Bryn Mawr, Pennsylvania (A.B. in biology); Harvard University, Cambridge, Massachusetts (Ph.D. in immunology)

**Training:** Postdoctoral fellow, Immune Disease Institute, Harvard Medical School (Boston)

**Came to NIH:** In 2010 as tenure-track investigator, Center for Cancer Research, Frederick National Laboratory for Cancer Research (Frederick, Maryland); in 2012 became tenure-track investigator in NCI-CCR

**Outside interests:** Traveling; reading books; enjoying spicy foods

**Website:** <https://irp.nih.gov/pi/shalini-oberdoerffer>

**Research interests:** In my laboratory, we examine how DNA and RNA epigenetics regulate gene expression. The protein-coding capacity of human genes is diversified at every step, ranging from the copying of DNA into pre-messenger RNA (pre-mRNA), to processing of pre-mRNA into protein-coding mRNA, to the translation of mRNA into proteins. The net result is a staggering expansion in the coding potential of the human genome, wherein some 20,000 genes serve as a template for more than 1,000,000 proteins. Much of this diversity is achieved through epigenetic regulation (changes in gene expression that occur through nucleic acid modifications that alter the biochemical properties of DNA or RNA). In mammals, the “epigenome” is formed through methylation of the nucleobase cytosine in DNA. In contrast, in mRNA, modifications occur in all four nucleobases to generate the “epitranscriptome.”

To understand the archetype for epigenetic control within DNA, we examine how nucleic-acid modifications of cytosine influence gene expression at unexpected stages in the lifecycle of an mRNA. We ask how methylation of cytosine in DNA affects pre-mRNA splicing decisions, and how subsequent acetylation of cytidine in processed mRNA affects translation. We use a variety of tools to investigate the enzymatic regulation of cytosine modifications and their net impact genome-wide and at target genes. We are also developing methods to achieve base-resolution analysis of the modification landscape in single cells. Overall, we aim to uncover connections between the epigenome, epitranscriptome, and mRNA metabolism. Ultimately, we hope to understand how cytosine modifications contribute to the etiology of disease and to potentially identify avenues for novel therapeutic interventions.

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## Recently Tenured

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### MADHAV THAMBISETTY, M.D., PH.D., NIA

*Senior Investigator and Chief, Clinical and Translational Neuroscience Section, Laboratory of Behavioral Neuroscience, National Institute on Aging*

**Education:** Government Medical College, University of Calicut, Kerala, India (Bachelor of Medicine and Surgery); University of Oxford, Green College, Oxford, England (D.Phil. in clinical pharmacology)

**Training:** Residency in neurology, Emory University School of Medicine (Atlanta); fellow and clinical associate in cognitive neurology and sleep disorders, Emory University School of Medicine

**Before coming to NIH:** Clinical Research Fellow, Alzheimer's Society Institute of Psychiatry, Kings College London (London)

**Came to NIH:** In 2007 as a staff clinician, Clinical Research Branch, NIA; in 2012 became investigator and chief, Unit of Clinical and Translational Neuroscience, Laboratory of Behavioral Neuroscience, NIA  
**Selected professional activities:** Adjunct professor of neurology, Johns Hopkins University School of Medicine (Baltimore); elected member of the American Neurological Association; board of trustees, McKnight Brain Research Foundation; associate editor, *Journal of Alzheimer's Disease*

**Outside interests:** He is an aspiring gourmand; enjoys cooking for his two boys aged 4 and 9 who have yet to provide informed consent to being unwitting consumers of his culinary experiments; enjoys writing and often rues a career path not taken—that of a cricket journalist.

**Website:** <https://www.nia.nih.gov/about/staff/thambisetty-madhav>

**Research interests:** I explore the disease mechanisms that operate in Alzheimer disease and am trying to identify novel biomarkers that can predict the disease

before the onset of clinical symptoms. I am also a practicing neurologist and care for patients with memory disorders at the Johns Hopkins Bayview Memory and Alzheimer's Treatment Center (Baltimore).

My research team uses multiple “OMICs” methods (metabolomics/proteomics/transcriptomics) to understand mechanisms underlying Alzheimer disease. We are also interested in relating genetic and environmental risk factors to changes in brain structure, function, and pathology during aging. The repeated failures of clinical trials of treatments for Alzheimer disease have highlighted the urgent need to identify novel targets for effective interventions.

Our work has added to growing evidence that Alzheimer disease is a pervasive metabolic disorder with abnormalities in many interacting biochemical pathways. These studies are leading to an emerging hypothesis that there may be multiple routes to Alzheimer pathology in the brain and the eventual expression of disease symptoms. This hypothesis in turn suggests that interventions targeting these metabolic abnormalities may be promising treatments. We are now testing whether commonly used medications for other illnesses may target metabolic abnormalities in Alzheimer disease.

I lead the Drug Repurposing for Effective Alzheimer's Medicines (DREAM) Study, which will test whether older individuals exposed to such drugs may be subsequently protected against Alzheimer disease. The DREAM study will analyze large real-world clinical datasets covering millions of older individuals to test this hypothesis. If we identify such drugs, they could then be rapidly tested in clinical trials. This is an exciting juncture in our work as we are beginning to translate enhanced knowledge about disease mechanisms into effective treatments for patients.

### JOHN S. TSANG, PH.D., NIAID

*Senior Investigator and Chief, Multiscale Systems Biology Section, Laboratory of Immune System Biology; Co-director, Center for Human Immunology (CHI), National Institute of Allergy and Infectious Diseases*

**Education:** University of Waterloo, Waterloo, Ontario, Canada (B.A.Sc. computer engineering; M.Math. computer science); Harvard University, Cambridge, Massachusetts (Ph.D. in biophysics)

**Before coming to NIH:** From 2008 to 2010, senior research scientist, Rosetta Inpharmatics, Merck Research Laboratories (Seattle and Boston)

**Came to NIH:** In 2010 as a tenure-track investigator and chief, Systems Genomics and Bioinformatics Unit in NIAID's Laboratory of Immune System Biology and CHI's Director of Computational Systems Biology

**Selected professional activities:** Member, steering committee, Human Immunology Project Consortium; member, steering committee, Human Vaccines Project; Co-organizer, Cold Spring Harbor Laboratory Inaugural Meeting on Systems Immunology (2019)

**Outside interests:** Enjoying jazz and classical music; playing tennis; traveling; hiking

**Website:** <https://www.niaid.nih.gov/research/john-tsang-phd>

**Research interests:** My laboratory works on systems and quantitative immunology. Immune responses involve complex molecular and cellular events occurring across space and time. They have been productively studied for decades at the level of individual molecules (such as major-histocompatibility-complex-encoded proteins), cells (regulatory T cells), or interactions (T cell–B cell cooperation). What is largely missing is a more quantitative and integrated understanding of how multiple interacting elements at several biological scales give rise to immune



responses. Attaining such a quantitative, predictive understanding of immunity has positive implications for furthering basic immunological understanding and advancing translational applications.

Toward these goals, my lab develops and applies systems-biology approaches—combining computation, modeling, and experiments—to study the immune system at and across the organismal, cellular, and molecular levels. One area of focus is human immunology. We use multiplexed technologies to assess the state of the immune system before and after both natural (disease and genetic variation) and experimental (particularly via vaccination) perturbations. We analyze and model the resulting multimodal datasets to 1) uncover biomarkers of immune responsiveness and health; 2) infer connectivities among components of the immune system; and ultimately, 3) understand how immune responses are orchestrated across spatial and time scales.

At the cellular level, we are particularly interested in understanding how immune cells adapt to the environment and in studying the functional consequences of cell-to-cell variations at both the network and cellular levels. We also aim to develop or turn internal toolkits into broadly distributed tools when it is apparent that they are useful in more-general settings. For example, we developed a free platform called Omics Compendia Commons, or OMiCC (<https://omicc.niaid.nih.gov/>). OMiCC uses a crowdsourcing approach to empower the broader biomedical research community to generate and test hypotheses using large, complex datasets.

Read more articles online at <https://irp.nih.gov/catalyst/v27i4>:

- Nobel Laureate Eric Betzig Shares “The Secret Lives of Cells”
- Fostering Stem Cell Research at NIH



## Schneider

CONTINUED FROM PAGE 15

it—but did I want it?” She did.

### DIVING IN AT NCBI

“I loved the lab—and still do—but what was more important to me was the scientific question and the process of getting an answer regardless of the specific topic, as long as it was good science and an interesting topic. It was...an alignment of the stars...that NCBI was looking for genome curators, and a favorite part of my postdoc work was the genome.”

When she arrived on campus 10 years ago, NCBI was focused on curating the human genome.

“This meant working a lot with the developers to figure out what kind of software tools we needed to manage the genome and what kind of database structures we would need,” said Schneider.

It helped that she had a mentor.

“I had an absolutely fantastic mentor when I started here. **Deanna Church** pushed me in lots of areas,” said Schneider. “After I’d been here a couple of years, she encouraged me to take the lead on a complete overhaul of NCBI’s Clone database.”

Then in 2013, Church left NCBI—and Schneider inherited a broad range of genome-associated tools and displays.

She called her mentor.

“I remember saying, ‘Oh my gosh, there’s so much going on and I have so many balls in the air,’” said Schneider. “I never forgot Deanna’s advice. She said, ‘You know what you learn in this job is not to be a perfect juggler; it’s knowing which balls you can let bounce. It’s prioritizing and understanding priorities and the dependencies between things.’”

Today as the program head for the Sequence Tools and Displays section (SeqView) in the Information Engineering Branch, Schneider still relies on that advice.

She’s constantly monitoring organizational-level priorities and

dependencies for the businesses in her program, which include BLAST, sequence display and analysis tools, and public-facing interfaces for many of NCBI’s sequence databases.

### COMMUNICATION AND BEING A FEMALE SCIENTIST

“NCBI works well because we have this mix of backgrounds, but sometimes communication can be challenging,” acknowledged Schneider. “It’s not that we speak different languages; we think a little differently. What one group might perceive as easy, the other may know is not so straightforward.”

In terms of gender, she said, “My perception of NCBI is that it’s pretty balanced, but when you dig into specifics, you find that more of the biologists are women and more of the developers are men, which means that as a biologist working with the development team I might be the only woman in the room even though there a lot of women in NCBI.”

No matter who she’s meeting with, Schneider said, “I know I need to bring my A-game to the table.” For her, this means being prepared and being fully present, not hesitating to ask questions, and speaking with confidence.

### DIVING DEEP—ON LAND AND SEA

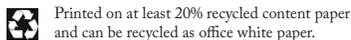
Part of the reason Schneider loves to dive is that “it’s amazing to see the other three-quarters of the planet.”

Part of the reason she enjoys being a scientific leader at NCBI is the opportunity to “really appreciate the breadth of knowledge that’s here.”

Whether she’s submerging herself in work or water, this scientific adventurer keeps investigating. ●

Adapted from an article in *NLM in Focus*: <https://infocus.nlm.nih.gov/2019/04/30/focus-on-valerie-schneider-diving-deep-into-information-engineering/>.

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## 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 e-mail: [catalyst@nih.gov](mailto:catalyst@nih.gov); fax: 301-402-1434; or mail: *The NIH Catalyst*, Building 60, Room 232.

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

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## ARTISTIC MOMENT



### “Crescendo”

The lush colors of crabapple and cherry blossoms bursting into bloom in New York City’s Riverside Park inspired artist Jon Friedman to create this painting, “Crescendo” in the 1990s. The painting now resides in a sunlit stairwell in Building 49 on the NIH Bethesda campus. Read more at <https://irp.nih.gov/catalyst/v27i4/artistic-moment>.



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