

## NIH and the 1918 Flu

### From Alice Evans's Memoirs

BY ALICE EVANS (SEPTEMBER 2 1963)

*The following is an excerpt from Alice Evans's memoirs, written in 1963, about her experiences during the 1918 influenza pandemic. Evans, a bacteriologist, was one of the first women scientists at NIH and worked there from 1918 to 1945. Her research led to the recognition of brucellosis as a public-health problem and the acceptance of the need to pasteurize milk.*

PERHAPS AN ACCOUNT OF HOW THE influenza pandemic of 1918 affected one member of the staff of the Hygienic Laboratory [the forerunner to NIH] will give [people]...whose knowledge of such epidemics is gained by reading, fortunately not by experience, an idea of the disruption that a serious epidemic may cause.

[The 1918 flu] struck Massachusetts in September and reached Washington [D.C.] in early October. Here war-time conditions favored a rapid spread of the disease, for the city was over-filled with dislocated people, the majority of whom were women who had come to do the vastly increased war-time work of the government departments. They were crowded in boarding houses with three or more persons commonly occupying one room as a result of the shortage of housing. When someone became ill and a threat to associates, she was apt to find herself very much alone, with no one to take care of her. Some landladies dismissed boarders coming down with the disease.

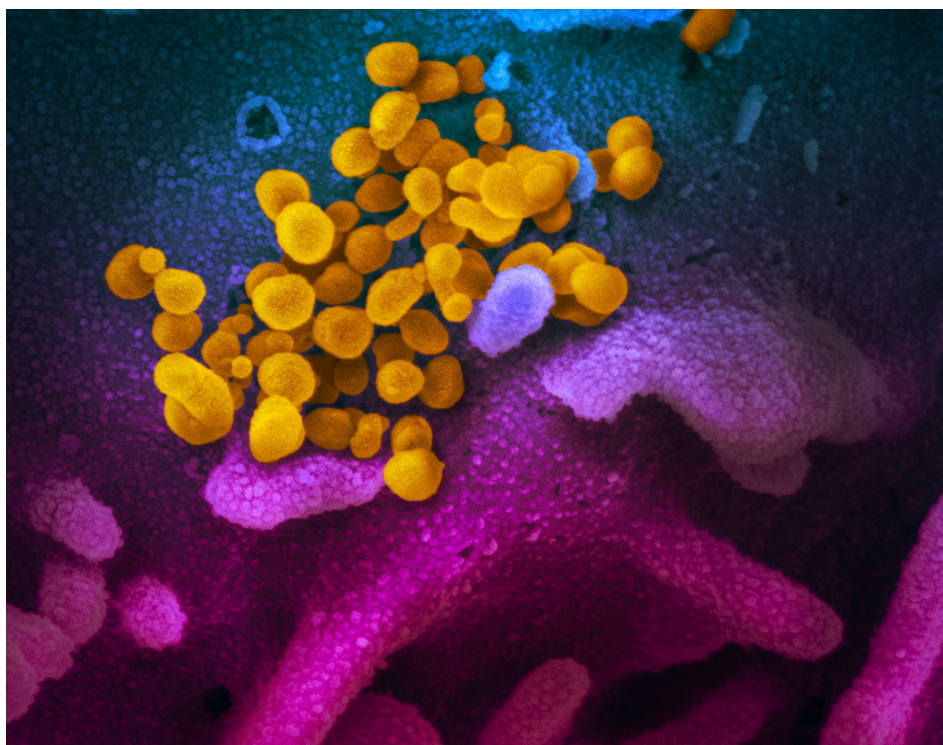
On October 1 [1918], Congress passed a resolution "to enable the Public Health Service to combat [the 1918 flu] and other

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## COVID-19 Timeline at NIH

### Highlights through April 30, 2020

COMPILED BY LAURA STEPHENSON CARTER



CREDIT: ROCKY MOUNTAIN LABS, NIAID

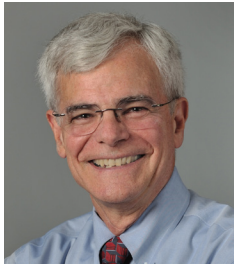
This scanning electron microscope image shows SARS-CoV-2 (yellow)—the virus that causes COVID-19—isolated from a patient in the United States. The virus is emerging from the surface of cells (blue and pink) cultured in the lab. The image was captured and colorized at NIAID's Rocky Mountain Laboratories in Hamilton, Montana.

THE COVID-19 PANDEMIC HAS UPENDED THE WAY WORK IS GETTING DONE AT NIH these days. Thousands of NIHers are teleworking, and all labs have minimal staffing to carry on essential research or maintenance operations. But many NIH scientists have been working around the clock trying to decipher the secrets held by the virus that causes the disease and to develop treatments and vaccines. The *NIH Catalyst* has compiled a timeline highlighting much of what is going on during this historic time (see page 11).

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## Working Together While Staying Apart

### Best Practices for “Virtual” Interactions

BY MICHAEL GOTTESMAN, DDIR

**ALL OF US HAVE BEEN EXPERIENCING THE** isolation, anxiety, and frustrations of dealing with the COVID-19 pandemic. For most of us this is a stressful period, yet we still must carry on our interactions with our colleagues, now physically separated from us, using communication tools that may be unfamiliar and at times add additional stress. It is especially important that we continue to interact with each other in a civil and respectful manner.

Most of you are now teleworking. For some of you, it is just a matter of figuring out how to do your regular job from home. For many of our bench scientists and trainees, it is a matter of finding new ways to contribute to the biomedical-research enterprise. I am impressed with the professionalism that all of you have shown in adapting to this new normal. As the Deputy Director for Intramural Research and a lab chief in the National Cancer Institute’s Center for Cancer Research, I am simultaneously dealing with both sets of challenges.

In my administrative role, I have been using multiple videoconferencing platforms with varying amounts of success. That said, I have observed a few promising practices for small group meetings (less than 15 people), such as staff meetings, in which there would normally be a lot of back and forth discussion. Civility and decorum are just as important online as they are in person. In my experience, civility and respect are practiced well at the NIH in the midst of this present crisis.

If bandwidth and privacy are not an

issue, appear in person on video wherever possible. Visual cues and feedback, such as perplexed looks, raising your hand, or nods of agreement, can be important for meeting flow. Avoid the temptation to be too casual in a videoconference for work. At least wear your good sweatshirt. Try to be on time for videoconferences. It is a sign that you respect the time of others and avoids embarrassing and disruptive beeps in the middle of someone speaking. Please mute your microphone

**During videoconferences, civility and decorum are just as important online, as they are in person.**

(or phone) when you are not speaking. Use a headset, if available, to reduce feedback and extraneous noise. When possible, have an agenda and stick to it. There should also be a clearly designated meeting moderator.

It is especially important during videoconferences that only one person speak at a time. Some videoconferencing systems automatically shift to the loudest voice. If this is a regular meeting, you should decide, as a group, the best way to ask a question. Options might include using the text or chat feature in your videoconferencing tool (highly recommended), using the raise-hand feature, or actually raising your hand, if you are sharing your video. When speaking for an extended period, pause every few minutes to check the text and chat messages and look at the people sharing their videos to see if

anyone has a question or comment. If you are building on someone else’s idea, be sure to give them credit.

Say when you have finished talking so that others know it is their turn, particularly in large groups with no visual cues. I’ve heard several people simply say “Over” like an airline pilot when finished speaking—that is pretty clear and helpful.

A wise person once told me that the difference between good people and great people is what they do during their down time. I have advised my lab staff and trainees to use this time to read scientific papers, take online courses, update their CVs, design experiments, develop research plans, and write manuscripts. If you have not recently looked at our list of Scientific Interest Groups (SIGs), or other affinity groups, now is a good time to do so. These groups are great resources for networking, information sharing, and finding out about career and collaboration opportunities. Some of them continue to host seminars and other events online. Recently created SIGs include one devoted to COVID-19 research.

In addition, teleworking time can be used to binge watch archived videocasts of lectures from the Wednesday Afternoon Lecture Series (WALS), Clinical Center Grand Rounds, Demystifying Medicine, and other lectures and conferences going back to 1993. Our Office of Intramural Training and Education (OITE) also continues to host online events on topics relevant to career development and wellness.

Speaking of wellness, it is important to take care of yourselves. Try to build some

physical activity into each day. Have regular breaks from screen time. Also remember that social distancing does not mean social isolation. Call friends or family just to say hello and let each other know how you are doing. I know how much a call from one of my children or grandchildren means to me.

Finally, if you need help, do not suffer in silence. There are many other groups at NIH (see list below) that are available to provide help with issues that might arise. We are all in this together, even if we are physically apart. ●

### Links

- **NIH Civil Program:** <https://hr.nih.gov/working-nih/civil>
- **Employee Assistance Program:** <https://www.ors.od.nih.gov/sr/dohs/HealthAndWellness/EAP/Pages/index.aspx>
- **OITE:** <https://www.training.nih.gov>
- **Occupational Medical Service:** <https://www.ors.od.nih.gov/Pages/home.aspx> (and click on OMS)
- **Division of International Services:** <https://www.ors.od.nih.gov/pes/dis/Pages/default.aspx>
- **Office of the Ombudsman:** <https://ombudsman.nih.gov>
- **NIH Guidance for Staff on Coronavirus:** <https://employees.nih.gov/pages/coronavirus>
- **Scientific Interest Groups:** <https://oir.nih.gov/sigs>
- **Other Affinity Groups:** [https://www.training.nih.gov/you\\_are\\_not\\_alone](https://www.training.nih.gov/you_are_not_alone)

### Archived videocasts

- **WALS:** <http://videocast.nih.gov/PastEvents.asp?c=3>
- **Clinical Center Grand Rounds:** <http://videocast.nih.gov/PastEvents.asp?c=27>
- **Demystifying Medicine:** <https://videocast.nih.gov/PastEvents?c=45>

## NEW SIG: COVID-19 Scientific Interest Group

**THE COVID-19 SCIENTIFIC INTEREST** Group was created in March 2020 in response to the COVID-19 pandemic. This interest group is intended for NIH scientists and HHS colleagues to exchange information concerning research on COVID-19 disease and the virus that causes it—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

In early 2020, as the world was just learning of a strange and alarming new virus infecting people in southeast China, NIHers already were at work investigating the nature of what would become known as SARS-CoV-2. Researchers at the National Institute of Allergy and Infectious Diseases (NIAID), in particular, were among the first in the United States to assess this emerging threat. NIH then combined this initial assessment with years of ongoing research on pandemics, in general, and on coronavirus, specifically, to inform other health authorities.

The NIH constitutes an exceptional pool of scientific talent. It's only natural, then, that so many of you have turned your focus to studying SARS-CoV-2 and COVID-19 in your respective discipline, be it immunology, virology, epidemiology, structure biology, computational science, bioengineering, pandemic modeling, animal modeling, or another. Coordinating these activities will be a major focus of the COVID-19 SIG.

### LISTSERV and MS Teams

• The COVID-19 SIG has launched a LISERSERV email newsletter, which is open to scientists and staff at NIH and HHS. Although the LISERSERV newsletter can only accept subscribers within

NIH and HHS, external scientists can view the archive of messages. For instructions, go to <https://oir.nih.gov/sigs/covid-19-scientific-interest-group>.

- Anyone can send messages to the list at [COVID19research@list.nih.gov](mailto:COVID19research@list.nih.gov).
- HHS staff also can join the Microsoft Teams group. Launch the Microsoft Teams program, search for “OD COVID-19 Scientific Interest Group,” and ask to join.

### Virtual Lecture Series:

Wednesdays, 3:00–4:00 p.m.

Videocast live and archived: <https://videocast.nih.gov>

For a full list, go to <https://oir.nih.gov/sigs/covid-19-scientific-interest-group>

- May 6: “Animal Models for COVID-19: A Critical Component of the Response to the Pandemic,” by **Emmie De Witt**, Ph.D., Chief, Molecular Pathogenesis Unit, Laboratory of Virology, NIAID
- May 13: “Adaptive Clinical Trial Design,” by **Lori Dodd**, Ph.D., Mathematical Statistician, Biostatistics Research Branch, NIAID
- May 20: “Infection Control in COVID-19,” by **Tara Palmore**, M.D., Hospital Epidemiologist, Clinical Center
- *More to be scheduled.*

The PIs who lead or moderate this new group were culled from a far larger list of volunteers and represent the scientific diversity of the NIH: **Mario Borgnia** (NIEHS), **Carson Chow** (NIDDK), **Michail Lionakis** (NIAID), **Vinay Pathak** (NCI), **Kaitlyn Sadtler** (NIBIB), **Pam Schwartzberg** (NIAID), and **Irina Sereti** (NIAID). The NIH Office of Intramural Research representative is **Charles Dearolf** ([dearolfc@mail.nih.gov](mailto:dearolfc@mail.nih.gov)). ●

**For more information about the COVID-19 Scientific Interest Group, go to <https://oir.nih.gov/sigs/covid-19-scientific-interest-group>.**

## From the Fellows Committee

### The Potential Path from Ph.D. to Medical Science Liaison

BY CRAIG MYRUM, NIA

**ARE YOU AS GOOD WITH PEOPLE AS YOU** are with a pipette? Can you cut down on scientific jargon to effectively communicate science with anyone? What about your leadership and critical-thinking skills? If you envisage a career outside of academia and these qualities seem to describe you, consider transitioning into a role as a Medical Science Liaison (MSL).

MSLs are not pharmaceutical sales representatives, but are scientific experts who are increasingly essential resources to colleagues within their own company and to physicians at academic medical institutions and clinics. In short, MSLs seek to connect health-care companies (such as pharmaceutical companies, biotech firms, and medical-device businesses) with health-care professionals who treat disease.

Now may be a good time to get into the field. According to a 2018 survey conducted by the Medical Science Liaison Society, 68% of MSL managers plan to expand their MSL teams. But how can trainees break into the field without experience?

“When I decided I wanted to pursue the MSL career pathway, the Office of Intramural Training and Education (OITE) was an invaluable asset,” said **Chris McNabb**, a former postdoctoral fellow at the National Center for Complementary and Integrative Health. “I recommend all aspiring MSLs look into the resources they offer.” McNabb, who is now a Senior MSL in oncology at Bayer Pharmaceuticals, found that the NIH Career Symposium and one-on-one meetings with career counselors were particularly valuable. Counselors can help with everything from writing your resumé to negotiating an offer.

For those doing clinical research, the transition to an MSL role may be smoother than for bench scientists who lack clinical

experience. But with sufficient preparation and understanding of MSL roles and responsibilities, opportunities will open up for bench scientists and clinicians alike. “First, convert your CV [into] a resumé,” McNabb suggested. “This will be necessary for a transition to industry. Summarize your qualifications by listing your experience presenting, teaching, mentoring, and working on teams. These are the most important skills for MSLs, and they’re exactly what hiring managers want to hear.”

You will also need to be thoroughly prepared for interviews. It’s key to prepare carefully for behavioral interviews (which are based on discovering how the interviewee acted in job-related situations). OITE can help you by providing opportunities for mock interviews and offering training on how to use the STAR interview format (situation, task, actions, and results) to answer the inevitable behavioral interview questions.

Aspiring MSLs should also be aware of several other key resources. First, fellows should use LinkedIn. The networking platform is of much greater importance for MSLs than for those in research—both for finding jobs and for fostering and maintaining professional relationships. The MSL Society, a nonprofit organization dedicated to advancing the MSL profession, can also be a valuable resource. It offers a host of tools for those interested in an MSL career including regular webcasts for skill development and annual salary surveys that are useful when negotiating job offers. Lastly, become familiar with recruiting firms and their talent-acquisition specialists, and connect with them on LinkedIn. “They are incentivized to place people just like you in the positions you’re looking for,” said McNabb. “They know the latest job postings, and they will serve as your advocate

in discussions with the hiring company.”

Here is some insight from McNabb’s five years of MSL experience: “People with advanced degrees are often conditioned to engage in chronic self-doubt, and I regularly find in my discussions with postdocs that self-doubt is a significant mental hurdle that needs to be overcome before the job search even begins. So let me assure you that you *do* have skills that are valuable outside of academic laboratory research. Your skills *are* transferable to a different career pathway. And if you assess your experience honestly and match it with a fitting career path, you *will* find a position that fulfills you. In other words, keep your head up, stay confident, and don’t count yourself out.” ●

#### Related Links

- **Medical Science Liaison Society:** <http://www.themsls.org>
- **OITE Events:** <https://www.training.nih.gov/events/upcoming>

### Frolicking Foxes



JAMIE SCHEITROMPF, NIDCR

These fox kits were playing outside their den next to the front doors of Building 30 when Jamie Schetrompf happened to walk by and snapped a photo with his cell phone. “They had run over by the benches and under the trash can playing with each other,” said Schetrompf, who works in the National Institute of Dental and Craniofacial Research’s Veterinary Resources Core and is on campus every other week during the COVID-19 pandemic.

## Rare Disease Day and the DADA2 Story

It Takes Detective Work to Diagnose Rare Diseases

BY CHARLESICE HAWKINS, OD



CREDIT: NCAATS

Vanderbilt University physician Chip Chambers (left), who has two children with the rare disease DADA2, and NIH pediatric rheumatologist Amanda Ombrello (right), who also has a child with a rare disease, shared their stories at NIH's Rare Disease Day in February.

**MANY ASPECTS OF SHERLOCK HOLMES'S** famous detective skills and eccentric mannerisms were modeled after one of Sir Arthur Conan Doyle's medical school professors, Dr. Joseph Bell. Bell was known for using close observation to diagnose diseases. He was reputed to be able to deduce a stranger's occupation and recent activities based on the greeting they chose and minute details such as the dirt on their shoes. If only Sherlock Holmes or Dr. Bell could closely observe patients with rare diseases today, perhaps it would shorten the years-long diagnostic odysseys that many of them face.

At the Rare Disease Day conference, held at NIH on February 28, 2020, health-care providers, patient advocates, and patients with rare diseases shared their remarkable stories. The day was filled with talks, posters, and panel discussions, including "Shortening the Diagnostic Odyssey," which emphasized how advances in genomics, medical informatics, and novel clinical approaches—as well as

collaborations among scientists, doctors, and the community—help to make progress toward quicker diagnoses of rare diseases.

"Rare stories," about the detective work required to find such diagnoses, were highlighted at the conference. One of the stories began on a hot summer day in 1999 in Nashville, Tennessee. Two-year-old Allie Chambers was playing outside when small nodules suddenly appeared on her legs. Allie's father—Chip Chambers, a physician at Vanderbilt University Medical Center (Nashville)—took her to a pediatric dermatologist for a medical exam, beginning her nearly 15-year-long diagnostic journey. The pediatric dermatologist suggested the girl had flea bites, but Chambers knew that wasn't possible since the family did not have a dog.

A few months later, a skin biopsy revealed that Allie had very inflamed vessels in her skin and unusual-looking cells surrounding the vessels. But no one could diagnose what she had. In 2010, she became very sick with her liver functions going awry and her platelet

count dropping. Chambers took her to the Mayo Clinic (Rochester, Minnesota) and even the doctors there couldn't figure out what might be wrong other than diagnosing her with immunodeficiency. That same year, Allie's younger brother Trey (age 6) developed nodules just like his sister's.

The Mayo physicians, suspecting a hereditary link, sent samples of the siblings' blood to Baylor College of Medicine (Houston) for then-cutting-edge whole-exome sequencing. Simultaneously, the doctors made a blog post about the case.

A doctor from Finland responded and suggested testing the children for adenosine deaminase 2 (ADA2) deficiency. At the time, there were no scientific journal articles on the disease so, in essence, the disease did not "really" exist. The Finnish doctor went on to describe that symptoms might include intermittent fevers, mottled skin discoloration, immunodeficiency, bone-marrow failure, and recurrent strokes that may begin in childhood.

The Chambers children had most of the symptoms, but not strokes. Blood samples sent to Finland confirmed that the ADA2 enzymatic concentrations were virtually undetectable, which further supported the diagnosis. The children were subsequently found to have mutations in the *ADA2* gene.

While the Chambers family was undergoing their diagnostic odyssey, a seemingly separate and unrelated set of odysseys were ongoing at NIH in Bethesda, Maryland. In 2002, a 2-year-old girl presented to the NIH Autoinflammatory Disease Clinic for evaluation of her fevers, strokes, and rash. At the time, she did not exhibit any of the features of known autoinflammatory diseases.

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## Revolutionizing Science

### Two Nobel Laureates Wow WALs Audiences

BY MEGAN KALOMIRIS, NIAID, AND EMILY MEYER, NEI

**THE TWO NOBEL LAUREATES—FRANCES** Arnold and James Allison—who presented WALs lectures this winter were notable for their “firsts.” Arnold was the first American woman to receive the Nobel Prize in Chemistry. James Allison was the first to present a virtual WALs lecture in this historic time of the COVID-19 pandemic.



Frances Arnold

## Frances Arnold's Revolution of Evolution

BY MEGAN KALOMIRIS, NIAID

**IN 2018, THE NOBEL PRIZE IN** chemistry was awarded to an American woman for the first time—Frances Arnold, who's been at the California Institute of Technology (Pasadena, California) since 1986 and is currently the Linus Pauling professor of Chemical Engineering, Bioengineering, and

Biochemistry there. Her research involves using evolution to create enzymes that drive chemical reactions. The Wednesday Afternoon Lecture Series was proud to host her on February 25, 2020.

When Arnold joined Caltech, she began using DNA technology to engineer new enzymes that could be used to produce pharmaceuticals, plastics, and other chemicals. She hoped to create enzymes that would be a safe, sustainable alternative to the toxic chemicals currently used in the creation of everyday products. But after a couple of years of failed attempts of trying to “rationally” design new enzymes, Arnold realized she must take a different approach. “You can read, write, edit DNA,” she said, “but we don't know how to compose it.”

In the early 1990s, she pioneered “directed evolution” (a method that mimics the process of natural selection) to optimize existing enzymes and create new ones. In her first attempt, she engineered a new version of subtilisin—an enzyme derived from the bacteria *Bacillus subtilis*—that normally functions in the watery environment of a cell. Subtilisin is used in detergents and household cleaning products to remove proteinaceous deposits and stains.

Arnold introduced different mutations into the *aprE* gene that encodes for subtilisin and then inserted the mutated genes into separate colonies of bacteria to produce new enzymes. Arnold then picked the bacteria producing the best enzyme and started the process again with that mutated gene. After several rounds, she wound up with a version of subtilisin that was 256 times as active in dimethylformamide—a common solvent

in chemistry—as it is in its original form.

Arnold's lab uses directed evolution to create other enzymes that catalyze the production of pharmaceuticals, biofuels, and other chemicals we use regularly. The enzymes can replace toxic chemical compounds normally used in the catalyzation process. Her team starts with an enzyme, creates several genetic blueprints of it, each with a different mutation affecting the enzyme's site of activity. These genetic blueprints are then put into *Escherichia coli* bacteria to secrete the enzymes, and the researchers screen those to determine which mutation works best. The process can be repeated to accumulate beneficial mutations that optimize enzyme performance. Often after introducing only a few mutations, Arnold's team evolves well-functioning enzymes with capabilities beyond what is seen in nature, including the ability to catalyze reactions not known in biology.

Arnold continues to create enzymes as sustainable, environmentally friendly replacements for chemicals currently used in industry. “Let's use some of [the biological world's] best design tools,” Arnold said at the end of her talk. “Let's learn how to use evolution ourselves, so that maybe we can learn to survive on this planet, if not thrive.” ●

**The 2019-2020 WALs season was interrupted by the COVID-19 pandemic and lectures are being rescheduled. WALs is expected to resume in September 2020. Visit the WALs website for updates: <https://oir.nih.gov/wals>.**

CREDIT: JACQUELINE ROBERTS, OD



Nobel Laureate James Allison delivered his WALS lecture from an empty auditorium at MD Anderson Cancer Center in Houston to a small audience in NIH's Wilson Hall (Building One) while more than 1,000 people watched remotely.

## James Allison's Revolutionary Cancer Treatment

BY EMILY MEYER, NEI

**IN THE FIGHT AGAINST CANCER, THE** immune system may be a better drug target than the cancer itself. This was the vision presented, on March 11, 2020, by Nobel Laureate James Allison during NIH's first-ever virtual presentation for NIH's Wednesday Afternoon Lecture Series (WALS).

The WALS lecture was held virtually because of the COVID-19 pandemic and public-health concerns regarding nonessential travel and large group gatherings. Allison delivered his lecture from an empty room at the University of Texas MD Anderson Cancer Center (Houston), where he is the chair of the Department of Immunology. The NIH "audience" consisted of five people in NIH's Wilson Hall (Building One) including NIH Director **Francis Collins** and National Cancer Institute senior investigator **Steven**

**Rosenberg**, another cancer-immunotherapy pioneer, and more than 1,000 people who watched remotely.

Allison's research on T cells and checkpoint blockades revolutionized cancer treatment and won him a Nobel Prize in Physiology or Medicine in 2018. He and **Tasuku Honjo** (NIH fellow in the 1970s; Fogarty Scholar-in-Residence in the 1990s) shared the prize "for their discovery of cancer therapy by inhibition of negative immune regulation."

Allison described his work with two molecules—cytotoxic T-lymphocyte protein 4 (CTLA4) and programmed cell death protein 1 (PD-1)—that function as immune checkpoints. They downregulate immune responses by blocking the T cells' ability to attack cancer cells. To override the block, he developed an anti-CTLA4 antibody, which eventually became the drug ipilimumab. In 2011, the FDA approved the use of the drug to treat late-stage melanoma; it was the first drug to extend the survival of those with that cancer. (Survival used to be about four months from diagnosis, but with the drug more than 20% lived for at

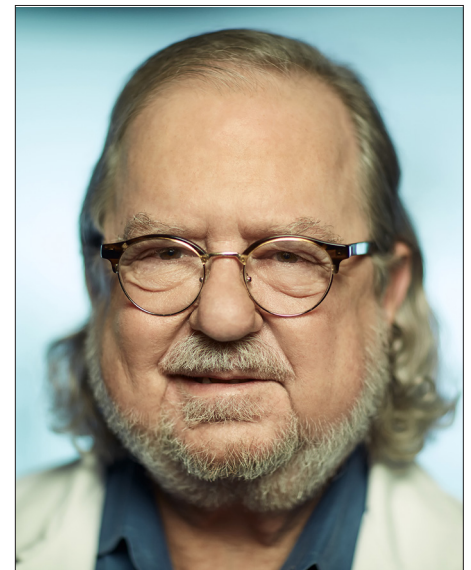
least three years and many lived 10 years and longer). In 2015, Allison won a Lasker Award in recognition of his achievements.

He is also exploring how another immunotherapy treatment with a PD-1 inhibitor drug, nivolumab, helps T cells fight cancer. PD-1 suppresses the tumor-killing activity of T cells and works via a different pathway than CTLA4 does. Nivolumab has shown promising results when used on many types of cancers including melanoma and lung cancer.

Allison explained how the drugs perform better together than alone and predicted that the future would bring more combinations of PD-1 and CTLA-4.

It used to be that the only way to fight cancer was to attack tumors and malignant cells directly. But Allison's immunotherapy approach—treating the immune system instead of the tumor—may one day defeat even the most untreatable cancers. ●

**To watch a videocast of James Allison's WALS talk, held on March 11, 2020, go to <https://videocast.nih.gov/watch=36081>.**

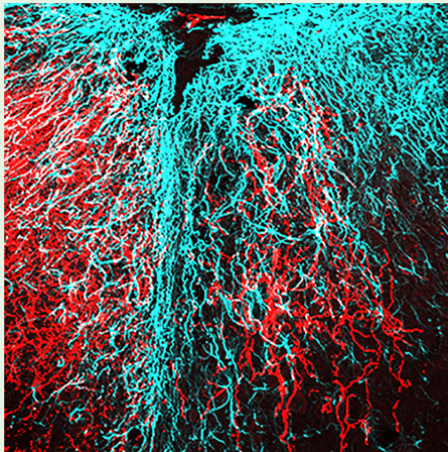


James Allison



## Intramural Research Briefs

Z.H. SHENG LAB, NINDS



NINDS scientists have found they can help spinal cord nerves regrow by enhancing mitochondrial axonal transport and increasing the energy supply to the damaged nerves. Shown: Spinal cord injury (black area at top); scar formed by glial cells (cyan) that surround neurons; undamaged nerves (red) to left of injury; nerves (red) that have regrown (to right of injured area).

### **NINDS: REPLENISHING NEURONAL MITOCHONDRIA LEADS TO SPINAL CORD REGROWTH**

After spinal-cord injuries, many patients have difficulty recovering due to the seemingly permanent damage to their axons, or nerve fibers. In studies conducted on mice, NINDS researchers and colleagues from the Indiana University School of Medicine (Indianapolis) have discovered potential mechanisms for axonal regrowth. They have identified impaired mitochondria as a key target.

The energy-generating mitochondria are critical for promoting axon growth. One of their primary functions is creating adenosine triphosphate, or ATP, our body's fuel source. But when the spinal cord axons are damaged, the nearby mitochondria are often damaged and lose their ability to produce ATP. Compounding the problem is that in adult nerves, damaged mitochondria can't be replaced because they are kept stationary by the protein syntaphilin.

The scientists observed, however, that—compared with control animals—syntaphilin-knockout mice show significantly more axonal regrowth after spinal-cord injury. In further experiments, the mice were given creatine,

which enhances the formation of ATP. The knock-out syntaphilin mice showed the most robust axon regrowth in the injured area. These findings suggest that enhancing mitochondrial axonal transport by depleting syntaphilin and increasing the energy supply within the injured spinal-cord nerves could promote regeneration and functional restoration after spinal-cord injuries. (NIH authors: Y. Xie, N. Huang, K.A. Chamberlain, and Z.H. Sheng, *Cell Metab* 31:623–641, 2020; DOI:10.1016/j.cmet.2020.02.002)

[BY EMILY MEYER, NEI]

### **NEI: TOOTH-ENAMEL PROTEIN MAY BE THERAPEUTIC TARGET FOR BLINDING DISEASE**

NEI researchers have discovered that the protein amelotin, which normally deposits mineralized calcium in tooth enamel, may play a role in the development of dry age-related macular degeneration (dry AMD). Dry AMD, for which there is no treatment, causes progressive loss of vision due to the death of the retinal pigment epithelium (RPE) and the photoreceptor cells. Deposits (some are called soft drusen) of cholesterol, lipids, proteins (including amelotin), and minerals accumulate at the back of the eye. Amelotin is responsible for the deposition of a calcium-containing mineral compound called hydroxyapatite (HAP), a key component in tooth enamel and bone, in the back of the eye.

The researchers discovered that if they starved cultured RPE cells for nine days, the cells began to deposit HAP. The nutritional stress upregulates amelotin protein expression, which augments HAP mineralization in RPE cell culture. Inhibiting amelotin expression in the RPE cells blocks this event. By examining human cadaver eyes, the researchers verified that HAP and amelotin occur only in eyes with dry AMD.

“Conceptually, you could see coming up with drugs that specifically block the function of amelotin in eye,” said Graeme Wistow,

senior author of the study. “This [blocking] might delay the progression of the disease. But we won't know until we try it.” (NIH authors: D. Rajapakse, K. Peterson, S. Mishra, J. Fan, J. Lerner, M. Campos, and G. Wistow, *Transl Res* 219:45–62, 2020; DOI:10.1016/j.trsl.2020.02.007)

[BY DIPTADIP DATTARROY, NIDDK]

### **NCI, NIA: HIGHER DAILY STEP COUNT LINKED WITH LOWER RISK OF DEATH**

Should one strive to take more steps per day? A recent observational study, conducted by NCI, NIA, and CDC investigators, found that higher daily step counts—but not the intensity of stepping—were associated with lower mortality risk from all causes.

The study was conducted through the CDC's National Health and Nutrition Examination Survey, allowing for data collection from a representative sample of U.S. adults aged 40 years and over. The participants wore accelerometers for seven days (2003–2006) so researchers could track step counts and step intensity (steps/minute). The participants were then followed for mortality through December 2015 via the National Death Index.

This study found that, compared with taking 4,000 steps, taking 12,000 steps per day (walking about six miles) was the healthiest option and associated with 65% lower risk of all-cause mortality. Taking 8,000 steps per day (walking about four miles) was associated with a 51% lower risk. The researchers were surprised that they didn't find an association between the intensity of stepping and all-cause mortality.

The findings confirm recommendations that to stay healthy, adults should be more physically active and sit less during the day. (NIH authors: P.F. Saint-Maurice, R.P. Troiano, B.I. Graubard, E.J. Shiroma, and C.E. Matthews; *JAMA* 323:1151–1160, 2020; DOI:10.1001/jama.2020.1382)

[BY CAROLINE DUNCOMBE, NIAID]





### NIEHS: AUTOIMMUNITY MAY BE RISING IN THE UNITED STATES

A group of NIEHS researchers has shown that autoimmunity appears to be increasing in the United States. They found that serum concentrations of antinuclear antibodies (ANAs)—a biomarker observed in most autoimmune conditions—have steadily risen over the last 25 years, particularly in males, non-Hispanic whites, adults 50 years and older, and most alarmingly in adolescents. The study included 14,211 participants, 12 years and older, in the U.S. National Health and Nutrition Examination Survey. Using immunofluorescence, a technique that uses fluorescent dye to visualize antibodies, the researchers examined the frequencies of ANAs in subjects from three time periods: 1988–1991, 1999–2004, and 2011–2012. Only 11% of participants in 1988–1991 had detectable ANAs in their serum, but ANA prevalence rose to 11.5% in 1991–2004 and to 15.9% in 2004–2012. Teenagers had the largest increases—from a twofold increase to a threefold increase over the three time periods. The scientists suggested that changes in lifestyles or the environment might be to blame. Further studies are needed to delineate possible causes and develop preventative measures. (NIH authors: C.G. Parks, C.R. Weinberg, D.C. Zeldin, and F.W. Miller, *Arthritis Rheum* 2020; DOI:10.1002/art.41214)

[BY SUNITA CHOPRA, NCI]

### NICHD, NIDCR: TARGETING A SIGNALING PATHWAY TO PREVENT TUMOR GROWTH

NICHD AND NIDCR scientists and colleagues at other institutions developed a way to stop tumors from growing new blood vessels (angiogenesis). Cellular signaling by growth factors such as vascular endothelial growth factor (VEGF) play a vital role in tumor angiogenesis. Anti-angiogenic therapies aimed at directly blocking VEGF are overwhelmed by the tumors' ability to produce more of this growth factor. The researchers found, however,

that they could thwart the tumors' response by disabling key enzymes in the VEGF signaling pathway.

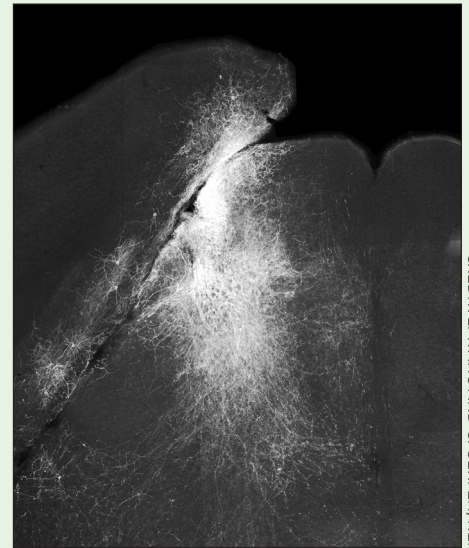
Interestingly, the downstream cellular pathway of these growth factors involves enzymes that convert the compound PIP2 into substrates that drive the process of angiogenesis. These substrates are converted back into PIP2 through a PI-recycling system that enables the angiogenesis process to continue. The researchers showed they could stop the growth of tumors by blocking any of the enzymes in this PI-recycling series.

The scientists showed that disruption of the PI-recycling system significantly decreased angiogenesis in zebrafish (*Danio rerio*) embryos and chemically treated human endothelial cells, and slowed the growth of pre-existing tumors in mice (*Mus musculus*). For the first two models, the researchers either disabled the genes for one or more of the enzymes or administered drugs that blocked the recycling enzymes. For the mouse model, they targeted the tumors with both genetic and chemical ablation of recycling enzymes. In their paper, the authors concluded that the “findings highlight the role that phosphoinositide recycling plays in tumor angiogenesis, and suggest that targeted inhibition of PI recycling may provide a useful anti-angiogenic modality for the treatment of cancer.” (NIH authors: A.N. Stratman, O.M. Farrelly, C.M. Mikelis, M.F. Miller, Z. Wang, V.N. Pham, A.E. Davis, M.C. Burns, S.A. Pezoa, D. Castranova, J.J. Yano, T.M. Kilts, J.S. Gutkind, and B.M. Weinstein, *Nat Commun* 11:article number 1204, 2020; DOI:10.1038/s41467-020-14956-z)

[BY KANCHAN GUPTA, NINDS]

### NEI, NIMH: VISUAL EVENTS HAVE 100 MILLISECONDS TO HIT BRAIN TARGET

NIH scientists have defined a 100-millisecond window that determines whether the brain notices or ignores visual events. The researchers used genetically modified mice in which the superior colliculus (SC)—a major



CREDIT: L. WANG AND C. GERFEN, NEI

NEI, NIMH: Slice of mouse brain showing neurons of the superior colliculus (white) highlighted on one side.

center in the brain for processing basic visual events—could be controlled via optogenetics. Optogenetics is the technique of using a beam of light to turn neurons on and off. Those mice were shown a Gabor patch (a pattern used as a visual stimulus) and trained to lick a spout when they perceived a change in the patch's orientation.

When the researchers used optogenetics to temporarily turn off neurons in the SC, they found that the inhibition had to occur within a specific 100-millisecond interval after the visual event; if the inhibition was outside that 100-millisecond timeframe, the mouse's decisions were mostly unaffected. Understanding these mechanisms by which visual information is processed has implications for conditions that affect visual perception and attention, such as attention-deficit hyperactivity disorder. (NIH authors: L. Wang, K. McAlonan, S. Goldstein, C.R. Gerfen, and R.J. Krauzlis, *J Neurosci*, 2020; DOI:10.1523/JNEUROSCI.2642-19.2020)

[BY MEGAN KALOMIRIS, NIAID]

Read more briefs and longer versions of these at: <https://irp.nih.gov/catalyst/v28i3/research-briefs>.

## 1918 Flu Memoir

CONTINUED FROM PAGE 1

communicable diseases by aiding state and local boards of health or otherwise.”

Some of the medical officers of the Hygienic Laboratory were sent into the field. Those who remained laid aside their research projects to organize emergency hospitals, or to become practicing physicians caring for sick government workers. Due to the absence of the doctors, and to the illness of many others of the Laboratory personnel, only a few were left to carry on.

I presume that there may have been a demand that the government agency should attempt to find the cause of the epidemic. However that may be, about the middle of the month [Hygienic Laboratory Director] Dr. [George] McCoy asked me to drop my current problem and turn my attention to the subject of greatest concern.

At that time bacteriologists were considering whether the “influenza bacillus” of Pfeiffer (*Haemophilus influenzae*), which was found quite constantly in cases of influenza, was or was not the etiologic agent of this disease. In later years it was considered to be a secondary invader.

My first thought was that I would examine the sputum of patients and tissues taken at autopsy to find the dominating bacterial species. That study would require a special culture medium. As our media maker was ill, I went to the media-room to make it myself.

Things were not going well, and I knew that I was not skillfully undertaking this job of making media to which I had long been unaccustomed. Gradually I realized that there was something the matter with me, more than the feeling of helplessness on being assigned unexpectedly to an enormous task. Finally I guessed it—I was coming down with the flu. I put away utensils and ingredients and went home. A little more than a month later I returned to work.

It was during those weeks when I was

confined to my room that Washington experienced a very serious epidemic. Dr. McCoy became a part-time physician, taking care of the Laboratory’s personnel who were ill with uncomplicated influenza, in addition to his administrative work. Dr. [James] Leake took care of government workers who were seriously ill with pneumonia in temporary hospitals.

Years later: I heard a minister say that during the worst days of those weeks, burial services in Washington cemeteries had to be curtailed in order that each funeral cortege could move along promptly to make room for the next.

When I returned to the Laboratory, I resumed my studies on meningococci, for the war was over, the peak of the epidemic in Washington had passed, and conditions were more favorable for clear-headed thinking. It was recognized that the search for the etiologic agent of influenza was not a problem for a lone investigator. It became a major project of study in more than one institution (but not at the Hygienic Laboratory), and about fifteen years later a team of investigators in a London laboratory discovered that the causal agent is a virus. ●



CREDIT: NATIONAL LIBRARY OF MEDICINE

Alice Evans, one of the first women scientists to work at NIH (1918–1945), did research that led to the recognition of brucellosis as a public-health problem and the acceptance of the need to pasteurize milk.

## About Alice Evans (1881–1975)

**ALICE EVANS WAS ONE OF THE FIRST** women scientists to work at NIH. Her research led to the recognition of brucellosis as a public-health problem and the acceptance of the need to pasteurize milk. She received her B.S. in bacteriology from Cornell University (Ithaca, New York) in 1909 and her M.S. from the University of Wisconsin (Madison, Wisconsin) in 1910. She never did earn her Ph.D., which caused a delay in the acceptance of her research findings on brucellosis and milk. Male scientists and milk manufacturers found it hard

to believe a woman without a degree. Evans began her federal civil-service career in 1910 with the U.S. Department of Agriculture (USDA) in Wisconsin. In 1913 she moved east to Washington, D.C., to work in the newly completed laboratories of the USDA Dairy Division. In 1918, she inquired of the Hygienic Laboratory whether her services might be of use in connection with the wartime effort; she was hired as a bacteriologist. She joined a team working to improve the serum treatment for epidemic meningitis. Evans retired from NIH in 1945. ●



## NIH 2020 Timeline Highlighting Selected COVID-19 Activities

**January 23:** NIH officials discuss novel coronavirus that recently emerged in China

**January 29:** President Donald Trump announces the formation of the Coronavirus Task Force, which includes HHS Secretary Alex Azar and NIAID Director Anthony Fauci.

**February 13:** NIAID researchers publish paper showing that the experimental antiviral remdesivir prevents MERS coronavirus disease in monkeys. (*Proc Natl Acad Sci USA*, 2019; DOI:10.1073/pnas.1922083117)

**Feb 25:** The NIAID-sponsored the first clinical trial of remdesivir to treat COVID-19 begins at the University of Nebraska Medical Center.

**March 3:** President Trump visits NIAID's Vaccine Research Center to discuss coronavirus.

**March 6:** NIH launches its Coronavirus Response Team, which begins meeting daily. Co-chairs are NIH Principal Deputy Director Lawrence Tabak and NIH Director for Management Alfred Johnson.

**March 10:** CC starts deferring elective patients.

**March 12:** CC starts screening patients and visitors coming into Building 10.

**March 15:** NIH reports first known employee with COVID-19 infection.

**March 16:** Most NIH employees and trainees begin teleworking; telework is now extended through May 31.

**March 16:** Closure of all schools in Maryland, Virginia, and Washington, D.C., begins.

**March 16:** An NIH-funded clinical trial of an NIAID-developed investigational vaccine for COVID-19 begins in Seattle.

**March 17:** NIH establishes large-scale, centralized COVID-19 screening (and testing, if needed) for employees.

**March 17:** NIAID's Rocky Mountain Laboratories scientists report that the virus that causes COVID-19 is stable for hours to days in aerosols and on surfaces. (*N Engl J Med* 382:1564-1567, 2020; DOI:10.1056/NEJMc2004973)

**March 18:** Many NIH campus services begin closing. The NIH childcare centers remain open until March 30 when all childcare centers in Maryland are ordered closed.

**March 18:** A new COVID-19 Scientific Interest Group is established.

**March 20:** NIH shifts non-mission-critical lab operations to minimal maintenance phase.

**March 20:** NIH holds its first virtual town hall meeting on the coronavirus response. More than 24,000 have watched the broadcast.

**March 23:** NIH announces launch of COVID-19 virtual-training site for frontline responders.

**March 23:** Maryland prohibits large gatherings and events and closes senior centers and all non-essential businesses.

**March 24:** Clinical Center (CC) enrolls first two participants in NIAID remdesivir trial.

**March 25:** The National Library of Medicine expands access to coronavirus literature through PubMed Central.

**March 26:** Screening of all staff members entering Building 10 begins.

**March 27:** An Atlanta site is added to the clinical trial of the NIAID's vaccine for COVID-19.

**March 27:** In the CC, surgical masks are required for everyone doing direct patient care.

**March 30-April 1:** Stay-at-home orders for Maryland, Virginia, and Washington, D.C., take effect.

**April 2:** NIDA Director Nora Volkow outlines the potential risks to people who smoke and use drugs during the COVID-19 pandemic. (*Ann Intern Med*, 2020; DOI:10.7326/M20-1212)

**April 2:** The NIH CC provides surgical masks to everyone who enters the building.

**April 9:** NHLBI begins a clinical trial in Nashville to evaluate the safety and effectiveness of hydroxychloroquine to treat COVID-19.

**April 10:** The NIH Office of Data Science Strategy has compiled COVID-19-related resources in one website location.

**April 10:** NIAID begins a serology study to determine how many adults not diagnosed with COVID-19 have antibodies to the virus.

**April 13:** Montgomery County, Maryland, requires that all shoppers wear face coverings in grocery stores, pharmacies, and elsewhere.

**April 15:** A study by investigators at NIAID's Rocky Mountain Laboratories validates

decontamination methods for re-use of N95 respirators. (non-peer-reviewed preprint server medRxiv, April 24, 2020; DOI:10.1101/2020.04.11.20062018)

**April 15:** NIDDK investigators report the results of a laser-light-scattering experiment that provided visual evidence of how speech-generated droplets moved through the air and that putting a damp cloth over the mouth decreased the number of droplets. (*New Engl J Med*, 2020; DOI: 10.1056/NEJMc2007800)

**April 17:** NIH announces a public-private partnership (called ACTIV)—including 16 biopharmaceutical companies, HHS, CDC, FDA, and the European Medicines Agency—to speed COVID-19 vaccine and treatment options.

**April 17:** NIDCR begins enrolling participants for a study to determine whether SARS-CoV-2 is in the saliva of asymptomatic individuals.

**April 17:** Early treatment with the experimental antiviral drug remdesivir significantly reduces clinical disease and damage to the lungs of rhesus macaques infected with SARS-CoV-2, according to NIAID scientists. (non-peer-reviewed preprint server bioRxiv, 2020; DOI:10.1101/2020.04.15.043166)

**April 17:** The NIAID-supported clinical trial of an experimental COVID-19 vaccine begins enrolling older adults. NIH is now a site.

**April 21:** Expert U.S. panel—including co-chairs H. Clifford Lane (NIAID) and Henry Masur (CC)—develops NIH treatment guidelines.

**April 22:** DDIR Michael Gottesman announces the Intramural Targeted Anti-COVID-19 (ITAC) funding program made possible by NIAID.

**April 23:** A new strategic plan from NIAID provides details for accelerating research to diagnose, prevent, and treat COVID-19.

**April 24:** Second NIH virtual town hall meeting.

**April 29:** NIH announces a \$1.5 billion initiative (called RADx) aimed at speeding innovation, development and commercialization of COVID-19 testing technologies.

**April 29:** NIAID clinical trial shows that remdesivir accelerates recovery from advanced COVID-19. ●

## You Are What You Eat

Profile: Emily Chew, M.D.

BY EIMEAR HOLTON, NIAID

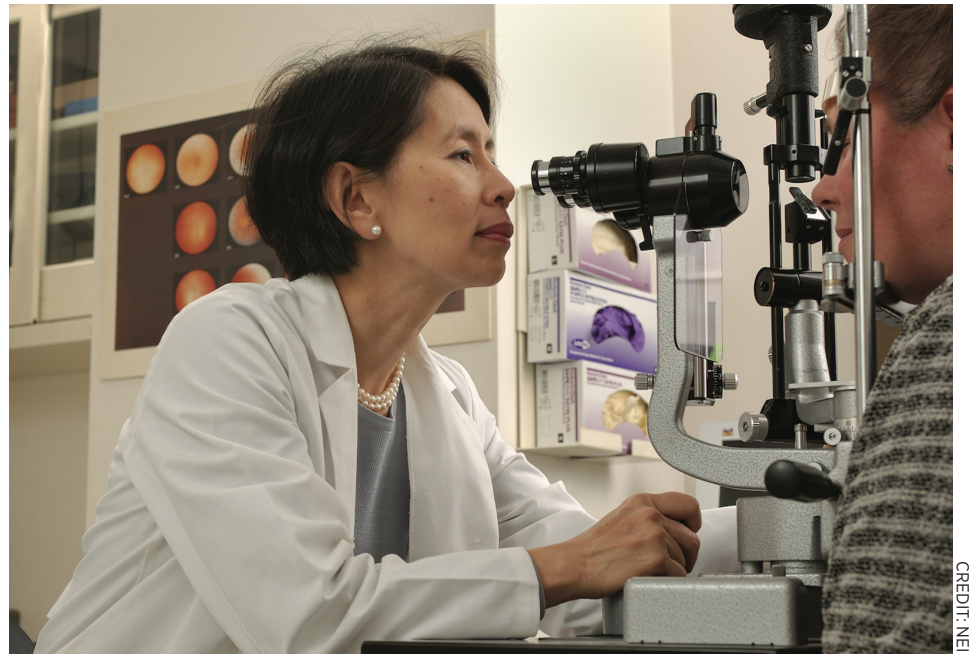
**EMILY CHEW UNDERSTANDS THE POWER** of nutrition, and she has the data to back herself up. Eating fish as “brain food” before taking an exam and consuming goji berries to achieve better eyesight were some of the many wisdoms she learned when growing up in a Chinese immigrant family in British Columbia (Canada).

“All my life I’ve been aware [that] my whole family are foodies,” said Chew, who is a senior investigator at the National Eye Institute (NEI) and director of NEI’s Division of Epidemiology and Clinical Applications. Her family’s wisdom certainly proved useful. Chew’s 30-year career at the NIH has led to instrumental clinical studies to further our understanding of the influence of nutrition and genetics on blindness, especially in slowing the progression of retinal vascular diseases such as age-related macular degeneration (AMD).

### Influential Mentors

Chew’s pursuit of clinical research was inspired by influential mentors throughout her medical training. While at the University of Toronto, where she received her M.D., her mentor was Brenda Gallie, an ophthalmologist whose research focused on retinoblastoma (an eye tumor in children). “She was a wonderful role model,” Chew said. “She impressed upon me how you could do wonderful things clinically, one patient at a time. But to do research you really are affecting and impacting many more people.”

As a fellow at Johns Hopkins’ Wilmer Eye Institute (Baltimore), Chew began her work on macular degeneration. One of her mentors was the late Arnall Patz, who discovered that oxygen therapy could cause blindness in premature infants. Patz was



CREDIT: NEI

Emily Chew’s work has furthered the understanding of the influence of nutrition and genetics on blindness especially in slowing the progression of retinal vascular diseases such as age-related macular degeneration.

“incredible in the way he looked at life and how he approached patients,” said Chew. “And he is the humblest person you would ever meet.”

Chew has mentors even now. She talks to leaders throughout the NIH “who have been very kind, considerate, and generous with their time,” she said. “I’ve been very lucky; I think at every stage of your life one needs mentoring.”

Chew has been mentoring clinician–scientists herself for the past 30 years. As the director of the Medical Retina Fellowship program (2002–2017), she mentored some three dozen trainees who have gone on to work in eye-research programs across the United States and elsewhere.

“Right off the bat, [Chew’s] mentee is a new collaborator,” said **Wai Wong**, who completed a medical retina fellowship in 2007 and is now a senior investigator in NEI. “She allows the opportunity for each person to bring their best ideas to the table, and in that way, people feel inspired

about their project and contribute in the best way possible.” Wong has continued to collaborate with his mentor for the past 14 years.

Chew has also mentored medical students in NIH’s Medical Research Scholars Program as well as people in two former programs—the NIH–Howard Hughes Medical Institute Research Scholars Program and NIH’s Clinical Research Training Program.

She strives to instill in her mentees the importance of research and to nurture their curiosity, just as her mentors have done for her. She is delighted to see her mentees go on to do great things, pursue their passions, and value the importance of research.

She hopes to inspire future leaders in research to work with integrity above all. In doing so, she’ll have passed on a great deal to them. “You can be brilliant, work hard, but above all, [you need] integrity,” she said. “Unless we inspire these young people do these things it’s easy to lose them.”

## Eyes Wide Open

Chew's approach in each clinical trial is to enter with her eyes wide open and to see what the data tell her. The Age-Related Eye Disease Study (AREDS) group, of which she is a member, conducted a randomized clinical trial (AREDS) at 11 centers with 4,757 participants, aged 55–80 years, who had varying degrees of AMD. The trial demonstrated that a high-dose supplementation with vitamins C and E, beta-carotene, and zinc with copper reduced the risk of progressing to late-stage AMD. (*Arch Ophthalmol* **119**:1417–1436, 2001; DOI:10.1001/archoph.119.10.1417)

Based on AREDS data, the group found that there was a correlation between participants who ate green leafy vegetables and a diet rich in fish with a lower risk of developing AMD. They ran the AREDS2 study, which involved 82 clinical centers and 4,203 participants, age 50–85, who had bilateral intermediate AMD or advanced AMD in one eye. The study showed that replacing beta-carotene with lutein/zeaxanthin—found in green leafy vegetables—was 20% more beneficial in reducing the progression to advanced AMD; adding omega 3 fatty acids, however, was neither beneficial nor harmful (*Ophthalmology* **119**:2282–2289, 2012).

More data from both studies have shown the protective effects of the Mediterranean diet—high in vegetables, whole grains, fish, and olive oil—and the importance of fish consumption in AMD rather than just the intake of supplements.

In an April 2020 article published in *Alzheimer's and Dementia: the Journal of the Alzheimer's Association*, Chew and her group reported that a recent analysis of data from the AREDS and AREDS2 studies showed that adherence to the Mediterranean diet correlates with higher cognitive function and that dietary factors also seem to play a role in slowing cognitive decline. (*Alzheimer's Dement*, 2020; DOI:10.1002/alz.12077)

## Genetic Studies

In 2005, Chew's group conducted the first genome-wide association study done in the eyes. They identified the role of complement factor H (CFH) polymorphism as a genetic risk factor in the progression of AMD. The group noted a sevenfold risk of late AMD with the presence of CFH. This discovery and three other simultaneous studies with different methodologies came to the same conclusion. "It was a turning point in the field of AMD research [and] a banner year for AMD genetics." Chew notes that this discovery led to the exponential increase in genetic studies in AMD, increasing our knowledge of genetic pathways drastically. (*Science* **308**:385–389, 2005; DOI:10.1126/science.1109557).

Chew has since collaborated with many groups around the world to put the data together, showing genetic markers, and finding indicators of genetic pathways important for AMD. "With each accomplishment comes more challenges and new questions," she said. That's good because "We're never out of a job." She smiled.

Chew's current work focuses on the earlier stages of macular degeneration; she seeks to alter its progression. "If we can change the progression to the more intermediate late-stage AMD," her group would have done a great service to patients, she said. A 10–15% improvement in vision in the early stages of AMD can be monumental to patients' sight and in turn improve the quality of life. "It's quite clear that at every stage of macular degeneration you can make an impact [on] its progression through diet in some way," she said.

## Artificial Intelligence

Looking forward, the Chew lab is embracing the potential of artificial intelligence (AI) and deep learning on the detection and progression of AMD, coupled with further advancements in genetics and long-established clinical-trial principles. Her team

has shown that deep-learning methods can help physicians make more accurate predictions of the progression and risks of developing the later form of AMD. Chew is taking advantage of the technology evolution to enroll patients and even to predict what's going to happen in the study. "I think AI is going to be phenomenal for clinical research and for actual clinical care," she said. That "makes me very excited."

## Better treatments

Her group's work over the past three decades has resulted in dramatic changes in treatment for AMD. Treatments for blindness disorders range from injecting into the eye anti-angiogenic drugs that inhibit the growth of new blood vessels that can cause blindness; to using a hot laser to seal retinal blood vessels that are leaking in the wet form of AMD (but doing so can also accidentally destroy blood vessels and neighboring tissue); to implanting tiny telescopes in the eye to improve central vision. But Chew's research shows that making simple nutritional shifts in the diet can have a strong positive impact.

When speaking about her career in the NIH intramural program, Chew says that she "kind of grew up here." She values the collaborative atmosphere, especially among different research disciplines, but also among clinicians and basic scientists. "The beauty of NIH is that we have many wonderful colleagues who are very collaborative with similar goals," she said. She appreciates the ever-changing research environment in which there is always something new to learn. ●

**Emily Chew gave the Astute Clinician Lecture as part of the NIH director's Wednesday Afternoon Lecture Series on December 11, 2019. To watch a videocast of her lecture, entitled "We Are What We Eat: Nutrition, Genes, Cognition and Deep Learning in Age-related Macular Degeneration," go to <https://videocast.nih.gov/watch=35115>.**

## Discovering a Cure for Sickle-Cell Disease

The Journey of Physician–scientist and Musician, John Tisdale, M.D.

BY CAROLINE DUNCOMBE, NIAID



CREDIT: LEWIS SCHRAGER

When he's not conducting research on sickle-cell disease, John Tisdale (second from left) plays bass guitar in the NIH Director's Band. NIH Director, Francis Collins (fourth from left) is playing the red guitar.

**IF YOU WERE TO DISSECT THE ANATOMY** of the NIH director's band, you would find the supporting beat of **John Tisdale's** bass guitar. Although primarily a senior investigator and chief of the Cellular and Molecular Therapeutics Branch in the National Heart, Lung, and Blood Institute (NHLBI), Tisdale plays a secondary role as the resident bass guitarist for NIH musical ensembles. His skills—of applied creativity, supporting others from the backline, and healing the seemingly unfixable—span his vocations as a physician–scientist and musician and have helped him throughout his journey toward developing a cure for sickle-cell disease (SCD).

### Road to NIH

Tisdale's path to becoming a physician–scientist began when he was 8 years old, with an unfortunate accident involving a self-propelled lawnmower. While mowing the lawn he stumbled, still squeezing the

propelling handle, and accidentally directed the lawnmower toward his leg. He landed in the emergency room with a major knee injury. Physician after physician claimed they couldn't fix it.

Finally one physician asserted, "Yeah, I think can fix that." And after several surgeries and physical therapy, Tisdale's knee began to heal. Slowly, he regained the ability to walk and eventually to run. That physician's ability to mend the seemingly unfixable inspired Tisdale to become a doctor himself.

As he navigated the path to becoming a physician, music remained a constant in his life. While pursuing his B.A. in chemistry at the College of Charleston (Charleston, South Carolina) and an M.D. from the Medical University of South Carolina (Charleston), he played cover tunes with his friends and fellow band members at local bars and earned enough to help pay his tuition. He decided to do his residency at Vanderbilt University School of Medicine in

Nashville partly because he hoped to play his bass guitar in the "Music City." But residency was so time consuming that he was forced to place his musical career on perpetual hold.

It was during his residency (1990–1994) that Tisdale first encountered SCD, which was, at the time, a disease without a cure. Here was something seemingly unfixable that he wanted to fix.

SCD, which affects about 100,000 people in the United States and millions worldwide, is an inherited blood disorder caused by a single-nucleotide mutation in the gene encoding the beta chain of the hemoglobin protein. The resulting abnormal hemoglobin gene triggers the production of distorted, sickle-shaped, red blood cells that block circulation and cause anemia, agonizing pain, and organ damage. Most people with SCD have a life expectancy of 42–47 years.

During Tisdale's residency, the standard treatment for patients with SCD was pain medications. The opportunity to address this issue as a physician–scientist is what brought him to NIH as a hematology fellow in 1994. He became a clinical tenure-track investigator in 1998 and a tenured investigator in 2006. With only a single-nucleotide mutation as the culprit, Tisdale believed SCD to be a curable illness.

### Fine-tuning Sickle-Cell Treatments

To Tisdale, both music and science are creative endeavors, with the skillset required of one naturally lending itself to the other. Now, as a senior investigator, Tisdale is embodying that expertise in the laboratory and the clinic to produce curative therapies that cover all SCD patients.

Nowadays, SCD can be treated with two types of bone-marrow stem-cell transplants: allogeneic (from a donor) and autologous (from oneself). In 2009, Tisdale

and his colleagues optimized a low-toxicity method of performing allogeneic transplants in which healthy hematopoietic stem cells from a matching donor (usually a sibling) are infused into the sickle-cell patient. But first, the patient's immune system had to be suppressed using chemotherapy to destroy the bone-marrow stem cells. The method, however, is too toxic for adults who have had years of accumulated organ damage. Tisdale's group developed and tested a new regimen that involved only partially replacing the bone marrow and using low-dose whole-body radiation to suppress the immune system and two drugs (alemtuzumab and sirolimus) to prevent rejection of the donor bone marrow. In a study with 10 patients, this new method reversed severe cases of SCD in nine of them. (*NEnglJMed* 361:2309–2317, 2009; DOI:10.1056/NEJMoa0904971)

In a 2014 study that included patients from the 2009 work, Tisdale and colleagues showed that their method reversed SCD in 26 out of 30 patients, and half of them were able to safely stop immunosuppressant medications. (*JAMA* 312:48–56, 2014; DOI:10.1001/jama.2014.7192)

Over the past 22 years, the Tisdale lab has been optimizing engineered viral vectors as a way to deliver the correctly encoded beta-globin gene. One of his latest iterations of viral vectors, when tested in animal models, was up to 10 times as effective as conventional vectors. With clinical trials underway, Tisdale's team is working toward substantiating gene therapies as a viable method for stem-cell transplantations, even in the case of severe SCD. (*Nat Commun* 10:Article number 4479, 2019)

Thanks to Tisdale's gene-therapy approach, so far several people—in a multicenter clinical trial that will have an estimated 50 participants—have been

apparently cured of SCD. The trial is expected to be completed in 2022.

But that cure is not widely available. “We need simpler, less toxic ways to get the therapy to work,” he said. With recent advancement with CRISPR-Cas9 gene editing, the prospect, while far off, now seem possible, according to Tisdale.

### Backline Approach to Mentorship

As a bass guitarist, the backline is where Tisdale is comfortable, placed toward the back of the stage, helping those around him shine while holding the song together with a steady rhythm. He takes a similar approach to mentoring the next generation of sickle-cell researchers. Tisdale has overseen the training of many fellows and students. “What I like to do is to find people who are internally motivated, who have the passion to do something to help humanity,” he said. “[I] just get out of their way.”

As mentees become collaborators, they are becoming part of a well-developed NIH consortium—that Tisdale helped establish—dedicated to addressing the challenges still facing sickle-cell treatment. Together, Tisdale and his colleagues are working toward expanding treatment to everyone with SCD.

Former mentee **Courtney Fitzhugh** (now a Lasker Clinical Research Scholar in NHLBI) is implementing clinical trials involving half-match bone-marrow donors—such as a parent, child, or half-matched siblings—as a way to use allogeneic stem-cell transplantation to treat SCD.

### Restoring the Seemingly Unfixable

To Tisdale, “The most satisfying thing is to go to a clinic, to see a patient through follow-up who has been through an experimental protocol and see their life totally changed.” Perhaps what music and medicine



John Tisdale

CREDIT: CHIA-CHI CHARLIE CHANG

have in common is the ability to heal people and ease their pain through either a soothing rhythm or a curative therapy.

Tisdale enjoys restoring other seemingly unfixable things. At the end of the interview, he showed this writer a video of the product of one of his hobbies—restoring pianos from the late 1700s and early 1800s. The deep buzz of a recently restored 1786 Longman and Broderip piano reverberated across the audio. The brass and steel strings effortlessly vibrated against the soundboard, a tribute to the care put in place by the person who sought to restore the seemingly unfixable piano, John Tisdale. ●

John Tisdale gave a Philip S. Chen Jr. Distinguished Lecture on Innovation and Technology Transfer, entitled “The Long and Winding Road toward Molecular Cures of the First Molecular Disease,” on November 8, 2019. To watch a videocast, go to <https://videocast.nih.gov/watch=35155>. He and his sickle-cell work were also featured in the Discovery Channel's *First in Human* documentary (aired in August 2017) that was filmed at the NIH Clinical Center: <https://www.youtube.com/watch?v=tnF4UYKzVbQ>.

## Recently Tenured



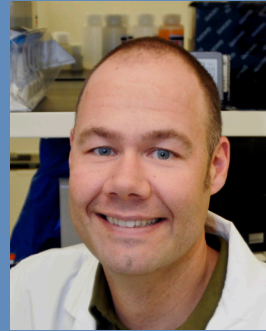
DANIEL BARBER, NIAID



MICHAEL B. COOK, NCI-DCEG



PAMELA GUERRERIO, NIAID



VINCENT MUNSTER, NIAID



ADAM PHILLIPPY, NHGRI

### DANIEL BARBER, PH.D., NIAID

*Senior Investigator, T-Lymphocyte Biology Section, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases*

**Education:** Rider University, Lawrenceville, New Jersey (B.S. in biochemistry); Emory University, Atlanta (Ph.D. in microbiology and immunology)

**Training:** Postdoctoral fellow and research fellow, Immunobiology Section, Laboratory of Parasitic Diseases, NIAID

**Came to NIH:** In 2006 for training; became Earl Stadtman tenure-track investigator in 2012

**Outside interests:** Motorcycling; collecting fountain pens

**Website:** <https://irp.nih.gov/pi/daniel-barber>

**Research interests:** My lab's major interest is in the CD4 T-cell response against *Mycobacterium tuberculosis* (Mtb) infection, the leading cause of infectious-disease death worldwide. CD4 T cells are critical for the control of Mtb, but they also drive tissue damage. We don't know exactly how they do either. Our goal is to identify the protective mechanisms of CD4 T cells and to understand the immunoregulatory molecules that prevent T-cell-mediated immunopathology in mice, nonhuman primates, and humans.

Early in my career, I led a study that

defined a new and critical role for the inhibitory pathway of programmed cell death protein 1 (PD-1)—which was known to regulate immune responses to self-antigens—in modulating T-cell function during chronic viral infection. (*Nature* **439**:682–687, 2006; DOI:10.1038/nature04444).

While at the NIH, I have shown that PD-1 is required to prevent CD4 T-cell-driven fatal disease during Mtb infection. The findings may have major implications for individuals being treated with PD-1-targeting drugs as cancer immunotherapy. My lab and I are investigating the mechanisms of immunopathology in this setting in both mice and nonhuman primates.

Our other major interest is in the mechanisms of immune protection against Mtb infection. We have shown that only a specific subset of CD4 T cells can migrate to the lungs and protect, and we are working to understand the cues that drive the generation of these protective T cells. We are also trying to identify novel T-cell-derived effector molecules that are required for the control of Mtb infection.

For example, my lab has shown that CD153 (expressed by CD4 T cells) is required for the control of Mtb infection, and we are currently studying the mechanisms of this novel antitubercular axis.

### MICHAEL B. COOK, PH.D., NCI-DCEG

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

**Education:** University of Nottingham, Nottingham, England (B.Sc. in genetics); University of Leeds, Leeds, England (Ph.D. in epidemiology)

**Training:** Postdoctoral fellow and research fellow, NCI-DCEG

**Came to NIH:** In 2007 for training; became a tenure-track investigator in 2011

**Outside interests:** Spending time with his wife and daughter; playing golf; cycling; camping; brewing beer

**Website:** <https://irp.nih.gov/pi/michael-cook>

**Research interests:** I am interested in the epidemiology and pathogenesis of esophageal adenocarcinoma and prostate cancer.

Esophageal adenocarcinoma has dramatically increased in the United States. Although we understand that gastroesophageal reflux disease promotes the development of esophageal metaplasia (Barrett's esophagus), which increases the risk of esophageal adenocarcinoma, there is much to be learned. I am using both classical and molecular epidemiological approaches to better understand 1) the pathogenesis and progression of this disease; 2) how obesity is associated with an increased risk of this malignancy; 3) why Barrett's





esophagus and esophageal adenocarcinoma are more prevalent in men than in women; and 4) what biomarkers can be used for diagnosis and risk prediction. I am pursuing studies of sex-steroid hormones, systemic inflammation, microRNAs, and other circulating and tissue-based markers to answer these questions. My hope is that we can develop evidence-based primary and secondary interventions to prevent esophageal cancer as well as diagnose this malignancy at earlier stages.

I am also studying prostate cancer to explain its etiology and discover prognostic biomarkers that can help predict the course of disease. I am trying to 1) describe and understand the basis of racial differences in prostate cancer; 2) understand the etiologic roles of sex steroid hormones and reproductive factors; and 3) discover and validate tissue biomarkers that will help predict whether the malignancy is indolent or aggressive. In addition, I am assessing whether computational-pathology algorithms of prostate biopsy or radical prostatectomy samples may improve diagnostic and prognostic algorithms of prostate cancer.

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**PAMELA GUERRERIO, M.D., PH.D., NIAID**

*Senior Investigator and Chief, Food Allergy Research Unit, Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases*

**Education:** University of Iowa, Iowa City, Iowa (B.S. in biology); Johns Hopkins School of Medicine, Baltimore (Ph.D. in human genetics; M.D.)

**Training:** Residency in pediatrics and fellowship in pediatric allergy and immunology, Johns Hopkins Hospital (Baltimore)

**Before coming to NIH:** Assistant professor, Pediatric Allergy and Immunology, Johns Hopkins Hospital

**Came to NIH:** In 2014

**Outside interests:** Running; hiking; biking; engaging in other outdoor activities

**Website:** <https://irp.nih.gov/pi/pamela-guerrerio>

**Research interests:** My group aims to understand the key genetic, immunologic, and biochemical pathways that lead to the development of food allergies and how they can be manipulated for therapeutic benefit. We are using a multifaceted approach involving both patients and mouse models. Our current focus is on genetic diseases associated with food allergies and other allergies; environmental and immunologic factors that influence the development and severity of food allergies; and novel therapies for the prevention and treatment of these allergies.

In our genetic research, we have recently shown that patients with the connective-tissue disorder Loeys-Dietz syndrome (LDS) caused by mutations in genes encoding the receptor for transforming growth factor beta exhibit a high prevalence of food allergy, asthma, eosinophilic esophagitis (a chronic, allergic inflammatory disease of the esophagus), and other allergic conditions. By studying LDS and other genetic disorders that predispose one to food allergies, we can achieve greater insight into the key cellular and signaling pathways that regulate allergic inflammation. This information may have tremendous therapeutic implications for those who suffer from allergic diseases.

We are also investigating how genetic and environmental factors may interact in the development of food allergies. Why do some patients who have immunoglobulin E antibodies to foods experience an allergic reaction when they eat the food while others don't?

We are also identifying immunologic markers that can predict the severity and persistence of food allergies.

By achieving a greater understanding of the key environmental, immunologic, and biochemical pathways that drive the development of food allergies, we will be able to develop novel interventions that are based on a refined understanding of disease pathogenesis.

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**VINCENT MUNSTER, PH.D., NIAID**

*Senior Investigator and Chief, Virus Ecology Unit, Laboratory of Virology, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases*

**Education:** Utrecht University in Utrecht, Netherlands (M.Sc. in molecular biology); Erasmus University Rotterdam, in Rotterdam, Netherlands (Ph.D. in virology)

**Training:** Postdoctoral research fellow in virology at Erasmus Medical Center (Rotterdam); postdoctoral fellow in disease modeling and transmission, Laboratory of Virology, NIAID's Rocky Mountain Laboratories

**Came to NIH:** In 2009 for training; in 2013, established the Virus Ecology Unit as an independent tenure-track investigator

**Outside interests:** Cycling; skiing; hiking; wildlife; triathlons; cooking; reading; traveling; and gardening

**Website:** <https://irp.nih.gov/pi/vincent-munster>

**Research interests:** Emerging viral diseases—such as the Ebola virus, Middle East respiratory syndrome coronavirus (MERS-CoV), and the new coronavirus (COVID-19) that emerged in China in 2019—are a major challenge to public health. We know very little about the origin of these viruses and how they interact with their natural hosts (fruit

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## Recently Tenured

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bats for Ebola; dromedary camels for MERS-CoV; likely bats and pangolins for COVID-19) or how genetic or ecological changes (such as deforestation and climate change) would increase the frequency of outbreaks in humans.

To enhance our understanding of what drives pathogen spillover from animals to humans, my lab is combining field research in places where these outbreaks occur (in the Republic of the Congo for Ebola and Jordan for MERS-CoV) with controlled experiments in the lab. In the Republic of the Congo, we are collaborating with the Wildlife Conservation Society and the Laboratoire National de Santé Publique in Brazzaville (the capital of the Republic of the Congo) to conduct field studies on Ebola. We are doing long-term studies on the role of fruit bats in Ebola virus spillover to humans. We are also strengthening the diagnostic capacity for these pathogens to ensure rapid and safe detection. In Jordan, we are trying to understand the risk factors associated with MERS-CoV transmission by looking at the human-animal interface between camel herders and the dromedary camels.

In the lab, we try to link the information obtained in the field with detailed experimental studies on the mechanisms of pathogenicity and transmission. We are also working with several academic and industry partners to develop vaccines against MERS-CoV as well as against two other zoonotic viruses—Nipah virus and Lassa virus. As of January 2020, my lab has become directly involved in NIAID's response against the newly emerged 2019-nCoV; we are focusing on the rapid development of diagnostics, vaccines, and antivirals.

### ADAM PHILLIPPY, PH.D., NHGRI

*Senior Investigator and Head, Genome Informatics Section, Computational and Statistical Genomics Branch, National Human Genome Research Institute*

**Education:** Loyola University, Baltimore (B.S. in computer science); University of Maryland, College Park, Maryland (M.S. and Ph.D. in computer science)

**Before coming to NIH:** Senior principal investigator, Genomics, National Biodefense Analysis and Countermeasures Center (Frederick, Maryland)

**Came to NIH:** In 2015

**Outside interests:** Practicing lacrosse with his younger daughter; going to horse trials with his older daughter; spending time with his wife and family; and mountain biking solo

**Website:** <https://irp.nih.gov/pi/adam-phillippy>

**Research interests:** The Genome Informatics Section develops and applies computational methods for the analysis of massive genomic datasets with a focus on the challenges of genome sequencing and comparative genomics. For example, reference genomes are the foundation of all genomic research, but sequencing and assembling a genome is a difficult process that can leave many gaps and errors that, in turn, affect the accuracy of downstream analyses. To this day, even the human reference genome remains unfinished and incomplete. My research aims to improve such foundational processes and translate emerging genomic technologies into practice.

My past experience includes developing novel sequence-analysis methods that were essential for the FBI's investigation of the 2001 anthrax letter mailings, and later founding a

bioinformatics group—for the genomic investigation of biocrimes—at the National Biodefense Analysis and Countermeasures Center at Fort Detrick (Frederick, Maryland). My group has since developed high-impact bioinformatics tools and pioneered the use of single-molecule and nanopore sequencing for the automated reconstruction of complete genomes. Most recently, we released the first complete sequence of an entire human X chromosome, and we aim to finish sequencing the remaining chromosomes within the next few years.

Recent sequencing-technology advances also create an enormous opportunity to combat infectious disease. As sequencing technologies become smaller and more affordable, clinical and environmental pathogen sequencing will become routine, generating millions of microbial genomes. We aim to develop computational methods that will enable this new scale of data sharing and analysis, ultimately forming a worldwide sensor network of genomic data that can inform outbreak detection and response.

If you have been recently tenured, the *NIH Catalyst* will be in touch soon to include you on these pages.



## Rare Disease Day

CONTINUED FROM PAGE 5



CREDIT: NCATS

Rare Disease Day was filled with talks, posters, and panel discussions. Shown: **Michaela Cortes** of the National Institute of Neurological Disorders and Stroke, explained her poster on “Progressing Research and Improving Care in Neurofibromatosis Type 2,” a hereditary condition associated with benign tumors that occur on the nerves for balance and hearing.

In 2011, a 6-year-old girl—also with fevers, recurrent strokes, and rash—was referred to NIH’s Undiagnosed Diseases Program. Pediatric rheumatologist **Amanda Ombrello**—who works for the National Human Genome Research Institute (NHGRI) and, coincidentally, followed the other little girl in clinic, and, even more ironically, also has a child with a rare disease—recognized the similarities in their cases and sent blood samples from the young girls for whole-exome sequencing. Both girls had mutations in the *ADA2* gene.

In 2014, Ombrello’s group and colleagues in Jerusalem simultaneously published articles in the *New England Journal of Medicine* describing for the first time the disease (*N Engl J Med* **370**:921–931, 2014; DOI:10.1056/NEJMoa13073620). NHGRI Distinguished Investigator **Dan Kastner** and his team named the disorder deficiency of adenosine deaminase 2, or DADA2, which can lead to inflammation in the walls of blood vessels and interfere with blood flow to the brain, resulting in strokes as well as varying immunodeficiencies and bone-marrow abnormalities (*N Engl J Med* **370**:911–920, 2014; DOI:10.1056/NEJMoa1307361).

These diagnostic odysseys, at one time so separate, converged later in 2014 when the Chambers children’s diagnosis was confirmed by the Kastner group.

In 2016, Chambers launched the DADA2 Foundation to accelerate a search for a cure, working closely with Ombrello and Kastner. Ombrello and colleagues recently demonstrated that anti-tumor-necrosis-factor agents reduce the risk of stroke in patients with DADA2 (*N Engl J Med* **380**:1582–1584, 2019; DOI:10.1056/NEJMc1801927).

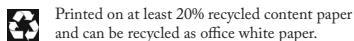
The well-known-phrase, “When you hear hoofbeats, think of horses not zebras,” may not resonate well with people who have, or who are trying to diagnose, rare diseases. The quote from Sherlock Holmes, however, “When you have eliminated the impossible, whatever remains, however improbable, must be the truth” may resonate more with the rare-disease patients whose stories are far from elementary.

**NIH’s Rare Disease Day is sponsored by the National Center for Advancing Translational Sciences and the NIH Clinical Center. To see a videocast of Rare Disease Day, on Friday, February 28, 2020, please visit <https://videocast.nih.gov/watch=34608>.**

## 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
- FNH:** 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
- NIAD:** 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

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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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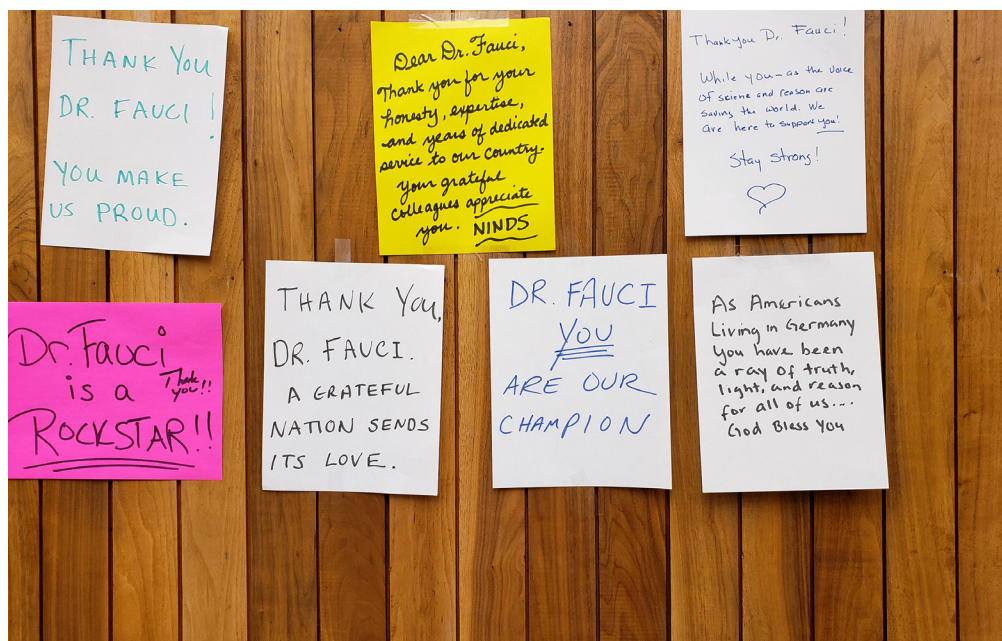
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## PHOTOGRAPHIC MOMENT



### Thank You, Dr. Fauci!



CREDIT: LAUREN HOCHMAN, NIH/BI

DECKING THE WALLS IN BUILDING 3I ARE HANDWRITTEN NOTES THANKING ANTHONY Fauci, director of the National Institute of Allergy and Infectious Diseases and member of the White House Coronavirus Task Force, for his role in keeping the public informed about the COVID-19 pandemic.

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