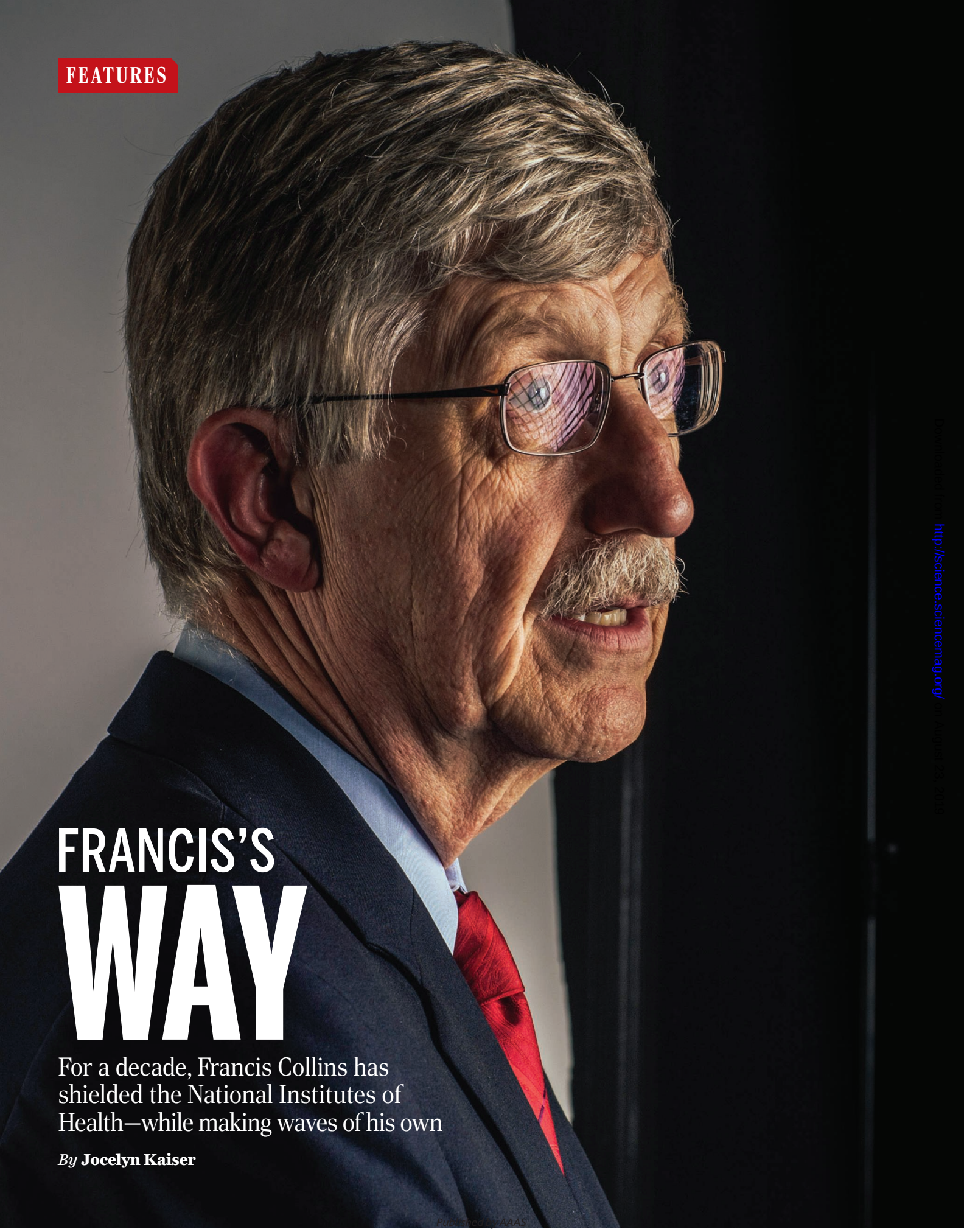


FRANCIS'S WAY

For a decade, Francis Collins has shielded the National Institutes of Health—while making waves of his own

By **Jocelyn Kaiser**

For months after President Donald Trump's inauguration in January 2017, biomedical scientists were on edge. The White House had asked geneticist Francis Collins to stay on as director of the National Institutes of Health (NIH) in Bethesda, Maryland, but nobody knew for how long. Some unconventional candidates for the NIH post, including a surgeon-turned-entrepreneur and a Tea Party member of Congress, provoked "major angst," recalls NIH observer Tony Mazzaschi, policy director for the Association of Schools and Programs of Public Health in Washington, D.C. Soon, Trump proposed slashing the agency's budget by 22%.

But in early June 2017, relief came when the White House announced that Collins would remain NIH director. Two years later, biomedical scientists are counting themselves lucky. Collins has helped shield NIH from threatened budget cuts as well as the upheaval that has shaken many other federal agencies under the Trump administration. As he completes a decade as NIH director this month, Collins, 69, has been a survivor—he's one of a few top-level holdovers from former President Barack Obama's administration and has served longer than any other NIH head in 50 years. Observers say Collins has also been one of the most influential directors ever to shape NIH, which with a budget of $39 billion this year is the world's largest biomedical research agency.

The plainspoken, guitar-playing, motorcycle-riding scientist—who took the helm of NIH after 15 years as director of NIH's genome institute—has used charm to rally Congress to restore growth to NIH's budget after more than a decade of stagnation. He has launched ambitious research initiatives in cancer, neuroscience, and precision medicine. He has tackled, with mixed results, vexing community problems, such as a lack of minorities in science, the struggles of young scientists to gain funding, and sexual harassment. With two key exceptions—the recent curtailment of fetal tissue research by Trump officials and pressure to scrutinize foreign scientists' ties to their home countries—NIH has largely escaped political interference during his tenure.

"He's had multifaceted successes. … He's always probing to do bigger and better things," says Anthony Fauci, director of NIH's National Institute of Allergy and Infectious Diseases since 1984. "He likes large initiatives that challenge the status quo, which is exactly what you want in an NIH director," says Elias Zerhouni, Collins's predecessor.

Yet Collins has detractors on NIH's campus and among the 300,000 researchers supported with NIH grants. Beneath a relaxed, affable public persona and a knack for conveying excitement about biomedical research in simple terms to the public and lawmakers, he is driven to achieve his priorities, whether pushing basic discoveries toward treatments or crafting policies to promote diversity in science. That drive has sometimes meant charging ahead without buy-in from those around him.

Early in his tenure, he ruffled feathers by shuttering a workhorse NIH research center and creating a new one to speed drug development. Some academic researchers have complained that his centrally managed projects aimed at generating large amounts of data drain resources from curiosity-driven individual grants. Still, even some former critics have come around. University of California (UC), Berkeley, evolutionary biologist and *eLife* Editor-in-Chief Michael Eisen, who had decried Collins's "big science" initiatives and called for him to be replaced soon after Trump was elected, has changed his mind. "He is trying to do the right thing for the institution. You also appreciate that he's probably a bulwark against worse things for science," Eisen says.

> **"He's always probing to do bigger and better things."**
> **Anthony Fauci**, National Institute of Allergy and Infectious Diseases

Collins's intense focus on what he believes in can come across as arrogance, says biochemist Mark Lively of Wake Forest University's School of Medicine in Winston-Salem, North Carolina. But overall the biomedical research community has benefited from his leadership, Lively says: "I'm glad he's still there."

And Collins is, too. "I didn't expect to [still] be here," he says. But, he adds, "It is a privilege, indeed, to be able to stay at the helm of this remarkable institution with such an incredible mission. So I'm happy to be here. I hope I'm still doing a good job."

ON A WARM JULY DAY as Collins prepares to hand out employee awards in an NIH auditorium, he reaches for his guitar, decorated with silver strands representing DNA. He has just told the story of a young man pictured on a giant screen behind him, who died this spring at NIH after 4 years of treatment for a rare kidney cancer. Collins says the patient's death shows that "our solutions don't always work." He then sings an Andy Grammer song that the patient liked: "I'm not givin' up, I'm not givin' up, givin' up." After applause, he tells his staff: "You don't give up. … You figure out how to move science forward."

It's "vintage Francis Collins," says veteran NIH cancer researcher Stephen Chanock at a reception after the ceremony. "He's wonderful, an old-fashioned kind of person," Chanock says. Collins grew up home-schooled in rural Virginia in a family that sang and staged plays. After earning a Ph.D. in chemistry and then a medical degree, he headed a lab at the University of Michigan, where he and collaborators used a gene-hunting technique he'd developed to identify the cystic fibrosis gene. At NIH, he led the Human Genome Project to its completion in 2003. But Collins drew criticism then—and still occasionally does—for hyping the payoff from genomic medicine. When Obama named him NIH director, some researchers worried Collins would favor data-intensive, big biology projects; another concern was that his outspoken Christian faith would influence his leadership.

His religion never became an issue—he followed Obama's order to loosen rules for stem cell research, which some Christians oppose, and has defended fetal tissue research despite criticism from antiabortion groups. But he has run NIH with the same firm hand with which he led the genome institute's sequencing projects. ("It's Francis's way or no way," says an NIH senior scientist who asked not to be named.) In 2010, with almost no discussion, he proposed dismantling the National Center for Research Resources, a cherished NIH center that helped pay for expensive resources such as primate centers and electron microscopes. In its place, he launched a new center that would "reengineer" drug development. The creation of the National Center for Advancing Translational Sciences (NCATS) rankled investigators, lawmakers, and some NIH institute directors. Drug company executives scoffed at the idea that NIH could improve on the success rate of industry, which spends billions of dollars on drug development.

"I'm a physician [and] also a basic scientist. I'm impatient about figuring out how basic science discoveries can find their way into clinical benefits," Collins says now. He maintains that 7 years after its launch, NCATS "has a pretty strong track record."

Former Eli Lilly scientist Bernard Munos agrees. NCATS is hampered by having to spend most of its budget on a program it inherited that funds large translational

Francis Collins has led the National Institutes of Health with a firm hand.

PHOTO: (OPPOSITE PAGE) STEPHEN VOSS

Francis Collins's good relationships with key congressional leaders have led to a string of healthy budget increases for the National Institutes of Health since 2016, reversing a 12-year erosion.

grants at academic health centers. Even so, he says, it has produced tools, such as tissue chips, 3D bioprinting, and stem cell technologies, that will help industry. NCATS is "still a work in progress," but "much of the early opposition has waned," says Munos, now a consultant in Indianapolis.

Even scientists who spoke out against abolishing the National Center for Research Resources say its programs, now managed by other institutes, are running smoothly. The reorganization "wasn't necessary, but it worked out," Lively says.

COLLINS'S LEGACY also includes three big biology projects announced by Obama, starting in 2013 with the 10-year Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. Neuroscientists conceived of the project, which develops tools to probe how neural circuits control thoughts and movement. So far, its fruits include a brain cell census and a device that converts brain activity into speech.

"BRAIN seized the moment extremely well" by bringing together scientists from various disciplines to harness new approaches, says neuroscientist Karl Deisseroth at Stanford University in Palo Alto, California. "The field has become even more complex and exciting."

The Cancer Moonshot, launched in 2016 at the behest of then–Vice President Joe Biden after his son Beau died from brain cancer, also emphasizes large collaborations and big data. Collins's signature project, however, is the 2015 Precision Medicine Initiative that led to All of Us, an effort to amass a trove of data on the genomic basis of disease by collecting health records and DNA sequences from 1 million volunteers.

"I am totally over-the-moon excited about All of Us and the transformation that it's going to create as a platform for figuring out how do people stay healthy and how do you manage chronic illness when it happens," says Collins, who first proposed the project in 2004 as head of the genome institute. Zerhouni, who vetoed that proposal because of costs, says it's unclear whether All of Us, which is pooling disparate health records and could see a high dropout rate, will measure up to similar projects run by U.S. health providers and the United Kingdom's national health system. All of Us has so far enrolled more than 180,000 participants, and NIH says it is on schedule.

Although some scientists grumble that Collins prioritizes such projects over investigator-initiated grants, the criticism has subsided as the NIH budget has improved. The numbers were bleak in the first years of Collins's leadership. In 2011, after years of flat budgets, NIH was funding less than one in five of the grant applications it received, a record low. Two years later, as part of a government-wide retrenchment, the agency's budget fell by 5%. But in 2016, Congress began to ease tight overall spending caps. The 21st Century Cures Act, passed by Congress that year, created a $4.8 billion fund over 10 years for Obama's three science initiatives. And since Trump's election, Collins has helped persuade Congress to reverse repeated presidential proposals to slash NIH's budget. In June, the House of Representatives voted to give NIH its fifth consecutive $2 billion raise, which would bring its budget to $41 billion in 2020.

Collins has been "able to gain and maintain the support of Congress," says biologist Keith Yamamoto of UC San Francisco. Adds Kathy Hudson, a consultant in Washington, D.C., who was Collins's policy chief until late 2016: "He has managed to cultivate a huge number of very important friends on [Capitol] Hill, and I think that has to do with personal interactions."

COLLINS HAS ALSO SHAPED the agency's leadership and policies. "One of his legacies will be that he will have appointed a huge number of institute directors," says Story Landis, a former director of NIH's National Institute of Neurological Disorders and Stroke. Mazzaschi says Collins has "had just a stellar record of recruiting noted scientific minds." Of the current 27 institute and center directors, Collins has appointed 16, six of them women.

Addressing a lack of diversity among NIH investigators became a Collins priority in 2011, when a study reported that from 2000 to 2006, black investigators, who submitted only 1.3% of all grant proposals, were 13 percentage points less likely than whites to win NIH's standard R01 awards. NIH responded by pouring $250 million over 5 years into a new investigator mentoring network and an undergraduate program for minorities. Collins also created a Scientific Workforce Diversity office headed by Hannah Valantine, a black cardiologist and researcher who had led diversity efforts at Stanford. At a meeting of Collins's board in June, Valantine reported modest improvements: The difference in grant success rates between black applicants and whites dropped to seven points in the years 2013 to 2018, and the annual number of awards to black investigators more than doubled over that period to 113.

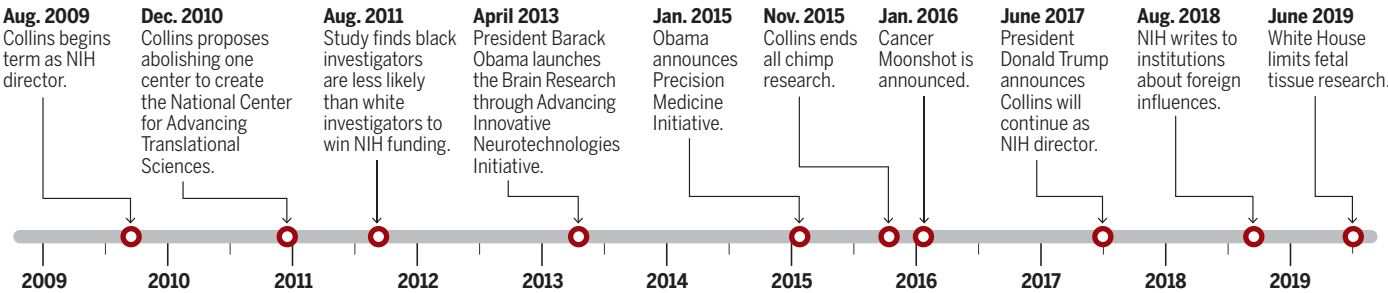
"There is progress being made, but … there's still way, way, way more to do," said Roy Wilson at the board meeting. Wilson chairs NIH's diversity working group and is president of Wayne State University in Detroit, Michigan. But Collins is encouraged: "For the first time, it made me feel like we may be on the right track," he says.

Another stubborn problem is that the average age of first-time Ph.D. investigators has hovered at 42 years for 2 decades, up from 36 in 1980. Collins's remedy starting in 2017 was to set aside money each year

PHOTO: CHIP SOMODEVILLA/GETTY IMAGES

A decade at the top

Francis Collins has led the National Institutes of Health (NIH) through lean times and plenty, always following a personal compass toward big biology and translational research.



to fund 200 additional young investigators' first research grants. For each of the past 2 years, the number of early-stage investigators supported by the agency has risen, reaching 1287 awards last year.

But that approach is a "Band-Aid," says Gary McDowell, who recently stepped down as executive director of Future of Research, a nonprofit in Abington, Massachusetts, that represents young scientists. The grants do nothing to address what McDowell says is the deeper problem: an oversupply of young scientists with little hope of winning tenure track jobs, who often serve as cheap labor in labs. "What I really would have liked Collins to do is pivot away from this constant expansion and address how to make things sustainable" by limiting the number of trainees NIH supports, McDowell says. "There is no long-term view."

THE #METOOSTEM movement criticized Collins last year for failing to beef up NIH's policies after news reports of several alleged incidents of sexual harassment by NIH-funded investigators. After months of criticism, Collins announced tougher measures in June, saying he hopes to follow a working group's recommendation that institutions and grant applicants be required to report sexual harassment findings to NIH. "I am regretful that we did not take firmer action sooner," he says, for which he partly blames legal advice that such cases be left to investigators' institutions. "I think people who look at it now ought to be feeling somewhat reassured that we get it," he says.

Collins recently won praise for vowing not to serve on all-male panels at scientific meetings. Diversity in science is "associated with greater productivity," he says. His dismissal of "manels," he says, is not "just a nice thing to do. … It's driven by a desire to see science flourish."

Collins's strategy for protecting NIH in the Trump era has been to keep a low profile—and it has largely succeeded, agency observers say. But Collins suffered a rare loss in June, when the Trump administration clamped down on research that uses fetal tissue donated after elective abortions. In December 2018, Collins had defended the research as ethical when done properly and called it a mainstay. Instead, the Department of Health and Human Services, NIH's parent agency, announced it was ending intramural studies using fetal tissue and would require lengthy special ethics reviews for new extramural grants and renewals.

Francis Collins (left) works with Idowu Aimola, a postdoctoral fellow from Nigeria participating in a new training program for African researchers.

Reports that the White House overruled him and Secretary of Health and Human Services Alex Azar are "basically accurate," Collins says. He adds that even applications for a new $20 million NIH program to find alternatives to fetal tissue in research, which "the pro-life community very much wanted us to do," will need to go through the ethics review because the studies will use fetal tissue as a comparator. Although he opposed the policy, he adds, "I understand the sincerity and the passion of those who felt that fetal tissue research crosses an ethical line."

Collins has also faced pressure from Congress and the Trump administration to crack down on foreign scientists believed to be stealing the fruits of federally funded research, with China portrayed as a major threat. After NIH called out more than 60 grantee institutions for possible violations of NIH rules, at least two universities dismissed faculty members, all of Asian descent, for allegedly failing to report foreign funding or sharing confidential grant proposals. "This has been a painful experience," he says. "Foreign nationals who are wonderful contributors to our medical workforce … are feeling as if they are being targeted or even profiled." But, he adds, "I don't think people are getting fired for trivial reasons."

Many researchers, however, fear that the campaign—perceived to target foreign-born scientists—will damage U.S. science in the long run. One former NIH official suggests that instead of pushing back against the White House, Collins "caved" to keep his job.

After 10 years, Collins has plenty on his to-do list. He wants to expand NIH's support of artificial intelligence and machine learning and is looking to hire a data czar, probably from Silicon Valley. He's also excited about gene therapy, which is finally reaching the clinic for some inherited childhood diseases. Collins has used NIH's Common Fund, a pot of money that Zerhouni created for initiatives that cut across institutes, to support industry and academic scientists who are devising better ways to get gene-editing tools such as CRISPR into patients' tissues.

Investigators may not be inclined to propose such applied research, but Collins says it's "something we should pull out all the stops to do." It's an example of why he still works 100-hour weeks. "You do have the ability to steer science in pretty powerful ways, by identifying things that just aren't going to happen without a push." ■

PHOTO: NATIONAL INSTITUTES OF HEALTH

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Science **365** (6454), 632-635.
DOI: 10.1126/science.365.6454.632