

ONE YEAR AT THE HELM

Having taken on the biggest job in biomedicine — leading the US National Institutes of Health — Francis Collins must now help his agency over a funding cliff. **Meredith Wadman** looks at his record so far, and his plans to cushion the fall.

There were three scans of Francis Collins's genome, and all showed the same thing: the geneticist and physician has an increased risk of developing type 2 diabetes. After Collins received the results from the genetic-testing companies in the spring of 2009, shortly before he became director of the US National Institutes of Health (NIH), he hired a personal trainer and began working out three times a week. He jettisoned his favourite junk food — honey buns and oversized muffins — in exchange for yoghurt, granola bars and broccoli. The 60-year-old now dead lifts 48 kilograms, chest presses 43, and has lost more than 11 kilograms himself. "It has helped me a lot in terms of being able to take on the intensity of the job," he says.

That salubrious slimming is nothing compared with the crash diet that Collins's US\$31-billion-a-year agency is about to go on. Collins took control of the NIH — the world's largest biomedical-research funder — in the middle of a feast: a \$10.4-billion, two-year boon delivered in 2009 by the American Recovery and Reinvestment Act, as part of the US government's effort to revive a moribund economy. Next month, the last of that money will go out

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of the door, and its recipients will have spent the bulk of it by September 2011. "The Recovery Act provided an enormously timely and appropriate stimulus for the community after five years of flat funding," Collins said in an interview with *Nature* at the NIH's Bethesda, Maryland, campus last month. "But now we face this potential of falling off a cliff. That's the biggest challenge" of his job, he says.

Collins comes equipped for challenges, intellectually and temperamentally. From his co-discovery of the gene for cystic fibrosis 21 years ago, to his 15 years of leadership of the NIH's National Human Genome Research Institute — and, with it, the Human Genome Project — he has proved that he combines serious scientific know-how with a leader's vision (see go.nature.com/JbAf7H for a timeline of Collins's biography). With his boy-scout manners and folk-guitar habit, he is also a decided contrast to his immediate predecessor, the sharp-suited Elias Zerhouni, a radiologist whom many bench investigators viewed warily for not being a scientist's scientist.

Collins's exceptional self-discipline extends well beyond dieting. By the time he started the job, he had already formulated a 'pocket list' of

22 goals for his first year in office, from hosting a visit to the NIH by President Barack Obama to hiring a new cancer-institute director. Now, he proudly hands over the list (pictured opposite) of mostly ticked-off accomplishments: Obama visited the NIH last September, and Harold Varmus, a former NIH director, took the reins of the National Cancer Institute in July. "He's in a hurry," says Susan Shurin, the acting director of the NIH's National Heart, Lung and Blood Institute (NHLBI). "He moves fast and he likes to be surrounded by people who are going to make things happen."

Collins has detractors as well as fans. When he was appointed, some scientists voiced loud scepticism that he could separate his very public Christian faith from his policy decisions. There were also fears that his roots heading the Human Genome Project would lead him to favour NIH-initiated mega-projects over proposals by individual scientists. Others scolded him — and still do — for what they call his perennial overpromising on the fruits of the genomic revolution. "He is still leading people to believe that genetics is the key to everything," says Neil Greenspan, an immunologist at the Case Western Reserve University School of Medicine in Cleveland, Ohio. If, five or ten years from now, only a handful of therapies emerge as

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Some potential initial goals for the NIH Director
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- Scientific plans**
- 1) Assure that ARRA funds are being used in the most effective way possible, and that there will be measurable outcomes
 - 2) Develop a comprehensive plan for the use of the Common Fund
 - 3) Develop a plan to revitalize the Intramural program
 - 4) Make an effective plan for the future of the National Children's Study
 - 5) Make certain that the process for approval of human embryonic stem cell lines is conducted in the most scientifically and ethically rigorous fashion
- Outreach to scientific community**
- 6) Conduct listening sessions with big thinkers in the scientific community on the five themes
 - 7) Based on those sessions, make plans about how to encourage innovative and risk-taking research in each of those critical areas (intersects with Common Fund)
 - 8) Use all means available to ensure that conflict of interest issues for NIH extramural grantees are addressed in a rigorous fashion
- Outreach to Congress/administration**
- 9) Make a compelling case to the administration and the Congress for the NIH FY11 budget
 - 10) Build a strong relationship with Secretary Sebelius and her DHS team, including a visit by the Secretary to NIH
 - 11) Host a visit by the President to NIH
 - 12) Build effective high level partnerships with FDA, CDC, CMS, and AHRQ
- Outreach to public**
- 13) Revitalize COPR, emphasize trust and transparency in all things
 - 14) Review current communication systems, and begin implementation of new media
- Organization and staffing**
- 15) Hire a Chief of Staff and organize the Director's senior leadership team
 - 16) Hire a new leader of the Office of Legislative Policy and Analysis (OLPA)
 - 17) Organize a rigorous review of the Office of the Director and its many components – does structure match function?
 - 18) Hire a Director for DPCPSI
 - 19) Hire a new Director for NCI
 - 20) Hire a new Director for NHGRI
 - 21) Develop an effective working relationship with the SMRB, and lay out a clear agenda for their work
 - 22) Eliminate certain bureaucratic rules that make no sense, such as the limitation on the number of DHHS employees that can attend a scientific meeting

Collins's to-do list: first-year aims are mostly done.

a direct result of the genome project, “you could end up with a lot of people [in Congress] getting upset and cutting the NIH because they are not producing what they claimed”.

Such concerns do not worry a lean, list-checking Collins. “My job it seems to me is not to spend my time apologizing for being optimistic. But rather to try to take that optimism and turn it into reality,” he says.

Morning to night

On a sultry morning in mid-July, Collins straps on his black motorcycle helmet and rides his Harley-Davidson the 15 minutes from his suburban Maryland home to the NIH campus. Collins had grabbed his usual, abbreviated night of sleep, after recording an interview for the *Charlie Rose Show*, marking the tenth anniversary of the draft sequencing of the human genome, and then staying up until nearly midnight to watch the popular talk-show air. In between, he had participated in a conference call with senior government officials, discussing how to enrol 20,000 subjects in a long-term study of the health effects on workers cleaning up the Gulf of Mexico oil spill. Having risen at his usual time of 5:00 a.m. — “that is a protected time, before all hell breaks loose, when I can actually try to think and plan,” he says — he is now on his way to a 7:45 a.m. interview with a candidate to head the NHLBI.

Collins wasted no time on his first day as NIH director either, when he announced five ‘themes’ — areas of what he calls “exceptional opportunity” — that would receive special

priority during his tenure (see *Nature* 460, 939; 2009). Collins targeted translational medicine, health-care reform, global health and “empowering and energizing the research community”. And he said he wanted to apply high-throughput technologies including genomics and proteomics to answer, as he puts it, questions with ‘all’ in them, such as “what are all of the major pathways for signal transduction in the cell?”

He also had to deal with some of the issues left over from Zerhouni’s watch. He was faced with the delicate job of making new human embryonic stem-cell lines available for federal funding fast enough to suit a community that was hankering for them after eight years of drought — without any missteps that would provide ammunition to opponents of the research. Between December and June, the agency approved 75

new stem-cell lines. (Collins points to the approvals as evidence that he “will not allow my own personal spiritual beliefs to interfere with decision-making or priority setting”.) But the agency has also drawn criticism for rejecting scores of disease-specific cell lines because of the broad legal language used in patient-consent forms (see *Nature* 465, 852; 2010).

Collins also faced the aftermath of several scandals in which NIH-supported academics had flouted reporting rules by failing to disclose five- and six-figure sums that they had collected from drug companies. In May, the NIH published proposed changes that would tighten the rules governing financial-interest reporting by its grantees.

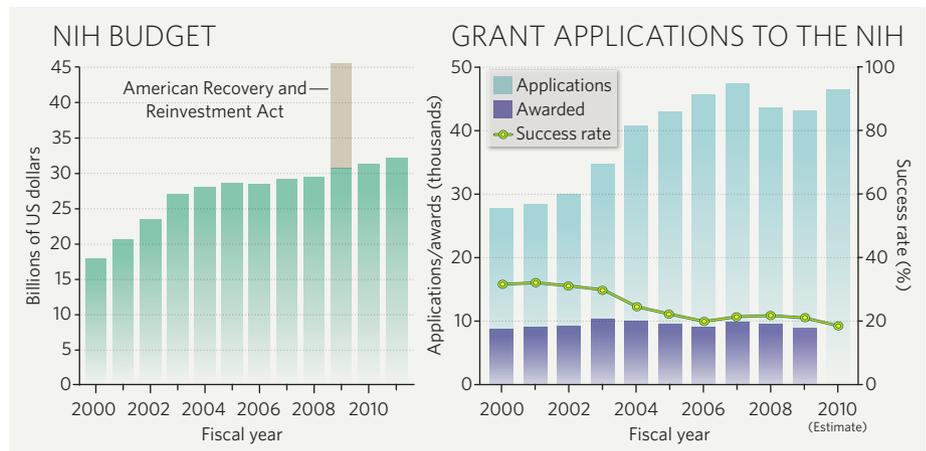
Still, nothing Collins has faced so far comes close to the budget straits that the agency now confronts as the government struggles

to control ballooning deficits, fight two wars and deal with the detritus of a major economic crisis. As NIH director, “what happens to you is going to depend on things beyond your control”, says Anthony Fauci, director of the National Institute of Allergy and Infectious Disease since 1984. “I hope that circumstances beyond his control start leaning towards helping him rather than hindering him.”

Slim chances

Already, this year, success rates for scientists applying for the agency’s research-project grants have dipped to an estimated 19%, down from 21% in 2009 and far lower than the comfortable 32% of a decade earlier (see ‘Grant applications to the NIH’). The worsened odds partly reflect an increase of about 10% in the number of applications, many of which are recycled from failed stimulus grant proposals. In 2011 and 2012, the grant success rates are expected to fall further as stimulus funding runs out and its recipients attempt to extend support for their projects.

The NIH’s baseline budget is also approaching dangerous waters. Although agency supporters were heartened last month when key subcommittees of the Senate and House of Representatives approved Obama’s request for a 3.2%, \$1-billion boost that would bring the budget to \$32 billion in 2011, the increase is not guaranteed to survive final congressional wrangling this autumn or winter. And it does no more than match the government’s predicted biomedical inflation rate. Things could be even bleaker in 2012: this June, Collins, like every other federal agency director, was asked by the White House’s Office of Management and Budget, as part of its planning process for the 2012 US budget, to identify cuttable programmes amounting to 5% of the agency’s budget. This is hardly a calamity compared with the deep research cuts occurring in some European countries, but still a shock to the NIH, which has faced only one absolute



funding cut since 1970, and that only a 0.1% shave (see 'NIH budget'). Late last month, Collins collected from the directors of the NIH's 27 institutes and centres a list of targeted programmes, constituting 7% of their budgets — the 7% giving him some flexibility to cut less here and more there. The final list is due to the White House in mid-September.

The initial response of the institute directors to his request was "full of angst", says Collins. "But there has also been a sense of 'We need to look hard at everything we are doing at a time like this.'" He remains hopeful that given Obama's emphasis on science, "when the dust all settles and they [the White House] decide exactly what to do, we will be at some level a bit protected, but we don't know that".

All or none

All this has been a growing cloud on the horizon even as Collins has been fleshing out his five themes. He has emphasized translational research, throwing his weight behind a programme aimed at speeding treatments for rare and neglected diseases towards human trials. He has embraced health reforms by overseeing the spending of \$400 million in Recovery Act money earmarked for research into the 'comparative effectiveness' of medical treatments. And he has promoted his global health priority with initiatives such as a collaboration involving Britain's Wellcome Trust medical charity, in which the NIH will contribute \$25 million over five years to study the genetic and environmental underpinnings of chronic diseases in sub-Saharan Africa.

Collins has also been launching high-tech assaults on the 'all' questions, committing \$175 million in Recovery Act money to accelerate The Cancer Genome Atlas — a five-year-old effort to develop a detailed catalogue of all of the mutations associated with 20 common cancers. Collins's emphasis on these types of ambitious projects has led some to question his commitment to the individual investigator and the mainstay, multi-year 'R01' grants that fund many such scientists. But his defenders say there is no evidence that Collins is advancing the first at the expense of the second. "Francis fully gets the importance of funding some of the larger efforts that can be so transforming. But I think he's also paying very close attention to maintaining a vigorous pipeline of R01-funded research," says Levi Garraway, a cancer biologist at Harvard Medical School and Dana-Farber Cancer Institute in Boston, Massachusetts, who holds investigator-initiated NIH grants and also participates in The



From home to office in 15 minutes on Collins's red Harley.

Cancer Genome Atlas project.

Collins says that big-team science is the only way to produce some tools that greatly benefit individual investigators. But he says that the individual lab "is where almost all of the discoveries of the present and the future are going to come from". And these labs are at the centre of his push to "energize and empower" the research community by addressing peer review, training and other workforce issues. Anaemic success rates for research-project grant applicants have created "a terribly stressful circumstance, particularly for early-stage investigators", says Collins, noting that the average age for winning a first R01 award has now crept above 42 years old. As a partial response to this, he has been planning the launch in 2011 of an award that will allow promising young investigators to skip postdoc positions entirely, giving them five-year funding to launch independent labs.

As for the immediate concerns of thousands of NIH grantees edging towards the funding cliff, Collins says that the agency will be "sympathetic" in allowing Recovery Act-funded grantees to spend their money over more than two years, "making it more of a ramp instead of a cliff". "We will be doing other things which may assist the ability to give new grants, but hurt the people who already have them," he adds. Those will include cutting individual grant budgets

"as we have to, in order to keep as many researchers going as possible".

These measures bring cold comfort for many in postdoc purgatory with little prospect of securing independent funding. "I didn't think it would be some Glory Hallelujah moment when Collins was appointed," says one 35-year-old scientist in his second postdoc, who asked to remain anonymous. He would like Collins to make it possible for those more than five years beyond their PhDs to secure transition funding such as a coveted 'K99' award, which supports postdocs in the shift to independent positions. "To be brutally honest, I haven't noticed any difference in his tenure after the first year compared to Zerhouni," he says.

But if Collins hasn't impressed some struggling bench scientists, his skill as a public communicator may nonetheless help to improve the NIH's prospects — or at least lessen its immediate peril. William Talman, president of the Federation of American Societies for Experimental Biology, attributes the White House's request for a \$1-billion boost for the NIH — even in a stark funding climate — to Collins's persuasive powers. "He has been a superb advocate for the NIH with the administration and with Congress."

Collins has the rare gift of being able to translate complex concepts into simple language, leaving his audiences — including all-important congressional audiences — feeling brilliant about their grasp of his material. (In one typical analogy he describes a haplotype, a group of genetic markers that are inherited together, as being like a neighbourhood of houses that moves together — with a causative mutation residing at one street address.)

"The most important thing he has done really is his public outreach," says Shurin, who recalls as typical Collins's May guitar performance for patient advocacy groups affiliated with her institute. Set to the tune of Del Shannon's hit *Runaway*, his lyrics described the anxieties raised by confronting a readout of one's own genome — "I'm a walking through the genes/ Don't know what all this means/ Oh what can the meaning be?/ Behind that G and T?/ And I wonder..." He received a standing ovation.

Collins is going to need all of that support and more to help those funded by the agency over the cliff — or down the ramp — ahead. "I don't have any magic here," says Collins. "I wish I did."

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Collins's biographical timeline accompanies this article online at go.nature.com/JbAf7H