

MEDICINE

US government sets out Alzheimer's plan

Health-agency budget windfall includes funding for two promising clinical trials.

BY MEREDITH WADMAN

Of the top ten leading causes of death in the United States, Alzheimer's disease — which ranks sixth — is particularly devastating in that there is no cure, no way to prevent it and no proven way to slow its progression. And with at least 11 million Americans expected to have the disease by the middle of the century (see 'Degeneration generation') — boosting the annual costs of health care to more than US\$1 trillion — the US government is anxiously looking to researchers to improve the prognosis.

Last week, the government set out how it planned to spend a \$50-million top-up to this year's funding for the National Institutes of Health (NIH) in Bethesda, Maryland, announced in February as part of a bid to "prevent and effectively treat Alzheimer's disease by 2025".

The money adds to the \$448 million that the NIH was allocated to spend on the disease this year, and roughly half of it is already being used by scientists funded by the National Human Genome Research Institute and the National Institute on Aging. They are preparing to conduct whole-genome and whole-exome studies to discover mutations that may predispose someone to the disease or protect against it. The scientists are assembling a bank of thousands of DNA samples from patients and other people whose DNA could be informative — such as elderly individuals who carry predisposing mutations but show no sign of the disease. The first results from the effort are expected as early as the end of this year.

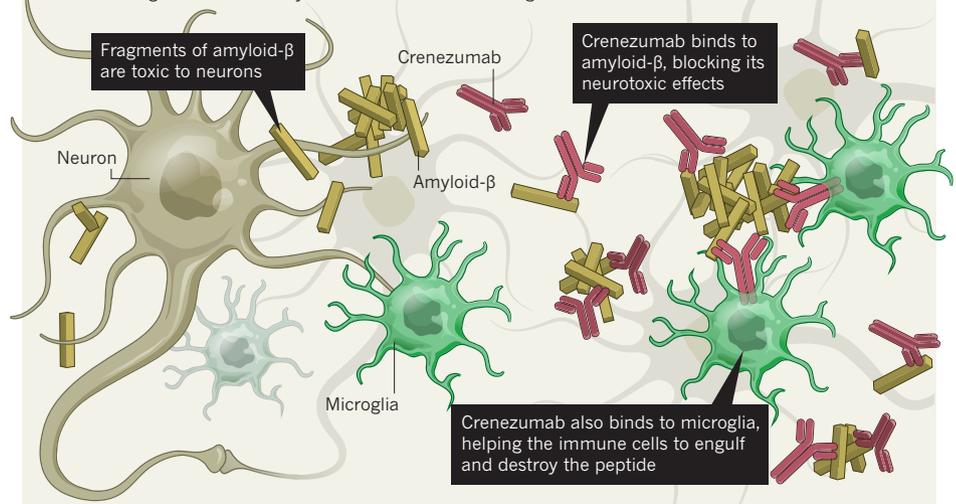
Of the remaining money, \$4 million will fund Alzheimer's-oriented grants to small businesses, and \$2 million will be used to help generate model human Alzheimer's cells from induced pluripotent stem cells. The rest will be devoted to two groundbreaking clinical trials, one of which builds on the fact that Alzheimer's begins to attack the brain 10–15 years before symptoms appear — a conclusion confirmed by new imaging tools that allow the disease to be monitored in living people.

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Nature Outlook on
Alzheimer's disease:
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This trial will receive \$16 million, and is the first attempt to avert the onset of Alzheimer's by treating people who have

NEURAL DEFENDERS

The drug crenezumab, an antibody, is thought to thwart Alzheimer's disease by binding to the peptide amyloid- β , blocking its toxic interactions with neurons and facilitating its destruction by immune cells called microglia.



not yet developed symptoms. It is a five-year study using an antibody called crenezumab, made by Genentech of South San Francisco, California. Already in phase II trials in patients with mild-to-moderate symptoms, the drug is thought to work by binding to fragments of amyloid- β — insoluble, neuron-damaging peptides that aggregate in the brains of those with Alzheimer's — both neutralizing it and making it easier for immune cells in the brain

to eliminate it (see 'Neural defenders'). The Banner Alzheimer's Institute (BAI) in Phoenix, Arizona, together with a team at the University of Antioquia in Medellín, Colombia, will test the drug against a placebo in 300 symptom-free people, two-thirds of whom carry a rare genetic mutation that makes them certain to get the disease. Mild cognitive impairment sets in at a median age of 44 in people carrying the mutation, and full-blown dementia at 49, decades earlier than is common with the more typical sporadic form of the disease.

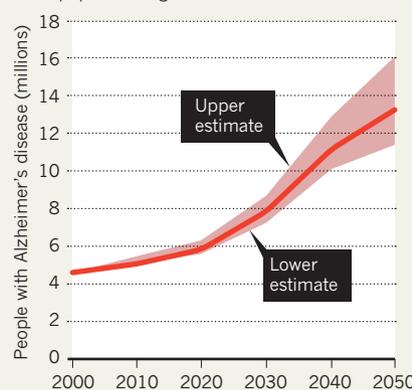
Most of the participants will come from a well-studied extended Colombian family living in Medellín and its surrounding rural areas that is estimated to have 5,000 members. They range from educated urbanites to humble farmers, all descendants of the same eighteenth-century founder. Although most do not know, and do not wish to know, their genetic status, about 1,500 are estimated to carry the mutation.

"You cannot meet these families and not be converted to their cause. It's heartbreaking," says Eric Reiman, one of the trial's three leaders and executive director of the BAI.

The other trial will receive \$7.9 million and is being led by Suzanne Craft, a neuropsychologist at the University of Washington and associate director of geriatric research at the VA Puget Sound Health Care System,

DEGENERATION GENERATION

The prevalence of Alzheimer's disease is expected to rise sharply in the United States as its population ages.



both in Seattle. It will test an intranasal insulin spray against placebo in people with mild cognitive impairment or early Alzheimer's. Insulin receptors are abundant in synapses in brain regions that are important for memory and cognition, and in Alzheimer's, amyloid- β can knock out the receptors and disrupt memory formation. Flooding rat brain cells with insulin has been found to block the fragments and protect the receptors (F. G. De Felice *et al. Proc. Natl Acad. Sci. USA* **106**, 1971–1976; 2009). When Craft tried the strategy in humans by giving intranasal insulin to people with mild cognitive impairment or early Alzheimer's, the results were impressive: about three-quarters remained stable or improved cognitively over the four months of treatment, Craft says.

PLAN FOR THE FUTURE

Craft says that she was “thrilled” to be funded for a larger, follow-on trial. But like many in the field, she worries that the national Alzheimer's plan is under-funded in the long term. “We all would like to believe that this is an important moment,” she says, “but we need to see follow-up in order to be truly convinced that this will provide an ongoing, coherent effort to address Alzheimer's disease.”

On 15 May, an advisory council to the US Department of Health and Human Services recommended that the government quickly ramp up research spending to \$2 billion per year if it wants to meet its goal of developing effective treatments and preventive measures by 2025. That would mean a quadrupling of the NIH's current spending on Alzheimer's research.

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“We really have all the pieces we need to move forward in the development of effective therapeutics,” says Paul Aisen, a neuroscientist at the University of California, San Diego, and director of the Alzheimer's Disease Cooperative Study — a 21-year-old programme of government-funded clinical studies aimed at developing Alzheimer's treatments. “The missing piece right now is the money.”

The first test of a follow-up will come later this year as Congress wrestles over the administration's 2013 budget request for the NIH. Included in the request is an additional \$80 million for Alzheimer's research. Proponents say that a failure to adequately fund research today will only lead to higher costs later.

“We're in trouble now,” says Aisen, “but in another 20 years, if things don't change, we're going to be in a dreadful situation.” ■

POLICY

Global council aims to coordinate science

Research-agency heads from around the world agree to formulate shared principles to aid collaborations.

BY RICHARD VAN NOORDEN

International research collaborations are multiplying fast, with one-quarter of the world's science and engineering publications now featuring authors from more than one country. But not all national funding agencies manage their science in the same way — researchers in China win grant funding through very different processes from their European peers, for example — which can hamper projects that span borders.

To tackle the problem, a voluntary forum, the Global Research Council (GRC), has been formed to share best practice and encourage common principles. Last week, the leaders of about 50 national research-funding agencies met at the headquarters of the US National Science Foundation (NSF) in Arlington, Virginia, to discuss the GRC's agenda: issues such as peer review, data sharing, research integrity, open access, career development and ethical conduct in research on humans. As the largest-ever gathering of research agencies, it was a “historic moment,” says Suzanne Fortier, president of Canada's Natural Sciences and Engineering Research Council.

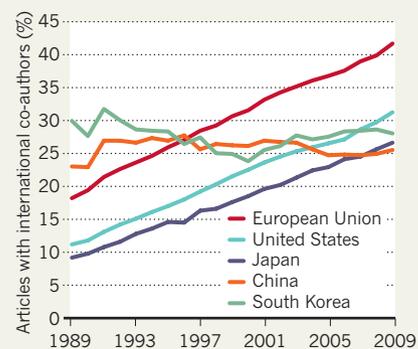
NSF director Subra Suresh, who coordinated the meeting, hopes that the GRC will broker international collaborations and co-funding arrangements to boost the globalization of science (see ‘Global science’). From now on, says Glaucius Oliva, president of Brazil's National Council for Scientific and Technological Development, agencies will get together much more frequently — with at least one meeting in each of five world regions before each annual global meeting of the GRC — and will send more staff members on exchange visits abroad.

Organizing the forum was certainly an impressive feat, but it isn't yet clear how the GRC might develop. “The key thing is that this shouldn't become a big, expensive, international science talking shop,” says Kieron Flanagan, who studies science and technology policy at the University of Manchester, UK.

The GRC's first meeting produced a set of short, uncontroversial statements on common principles for peer review to assess the merit of proposed scientific projects. The principles include transparency, integrity, impartiality and confidentiality, but are not legally binding,

GLOBAL SCIENCE

The proportion of research papers from international collaborations is increasing in many regions.



SOURCE: NSF SCIENCE AND ENGINEERING INDICATORS 2012

serving only as common aspirations. “If the statements stay at this general level they're not going to be Earth-shattering,” says Flanagan.

But behind the scenes, agency heads were sharing tips and experience. Oliva, for example, says that his agency is coming under government pressure to focus on practical problems, and is rethinking its evaluation systems to include indicators that value innovation. “It's nice to see how other countries are dealing with these indicators,” he says.

Before the next major GRC meeting — in Berlin in 2013, by which time the council is expected to have almost 100 members — the group will discuss research integrity and open access to scientific data and published research. The basic principles of research integrity have already been laid down in international guidelines such as the Singapore Statement, agreed by researchers and funders in 2010. But Matthias Kleiner, who heads the DFG, Germany's main research-funding agency, says that the GRC could discuss practical questions such as how to tackle the problem of researchers being sanctioned for misconduct in one country, but continuing their research freely elsewhere.

Agreeing on principles for open access will be much tougher, says Kleiner. But it is such an important issue, he adds, that “only in a global collaboration could we come to really reliable, practical, sustainable solutions”. ■

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