

► fatal conditions such as muscular dystrophy or heart disorders.

Before giving a green light to clinics wishing to offer the treatment, the HFEA will probably want further evidence that the procedure is safe, and will vet applications on a case-by-case basis.

The United Kingdom was one of the few countries that explicitly banned mitochondrial replacement by law. In many countries, including China and Japan, the techniques are prevented by regulations that should be simpler to overturn, without legislative intervention, says Tetsuya Ishii, a bioethicist at Hokkaido University in Japan.

The same applies to the United States.

Since 2001, the FDA has enforced a moratorium on mitochondrial replacement, after a New Jersey fertility clinic conducted a related procedure to improve conception rates. Mitalipov's push to launch a clinical trial of mitochondrial replacement set off a series of scientific, ethical and policy reviews that are still under way.

In February 2014, an FDA advisory panel held a two-day meeting to consider the science of mitochondrial replacement. The panel identified areas in which it wanted to see more data, such as the long-term health of monkeys conceived through the procedures, before it could move to allow mitochondrial replacement.

It will probably take two to five years to fill in these gaps, says Evan Snyder, a stem-cell biologist at Sanford-Burnham Medical Research Institute in La Jolla, California, who is chair of the FDA panel.

Australia is also pondering three-person IVF. Although the country's lawmakers opted against relaxing the rules after a 2011 review of human-cloning legislation, the UK vote will "provide enormous ammunition" for those seeking changes, says David Thorburn, a geneticist at the University of Melbourne, Australia. Still, he adds, "my gut feeling is that it's unlikely to succeed until this has been done in practice in the UK". ■

## POLICY

# NIH ponders 'emeritus grants'

*A proposal to pay senior biomedical researchers to wind down their labs draws scepticism.*

BY BOER DENG

For years, biomedical researchers in the United States have warned of a worrisome trend: as competition for grants increases, younger scientists are finding it harder to keep up. In 1980, the average age at which researchers received their first major award from the US National Institutes of Health (NIH) was 38; by 2013, this had risen to more than 45 (ref. 1). And the overall share of grant funding won by scientists younger than 36 withered from 5.6% in 1980 to just 1.2% in 2012.

Like ageing Crown princes, junior biomedical researchers in the United States face long years as leaders-in-waiting. Now, in a 3 February posting, the NIH has asked researchers whether the agency would be wise to give 'emeritus grants' to senior scientists to induce them to wrap up their research. The funding would "help to ensure the orderly transition of an experienced researcher's work when they wish to go on to something else, and also to recognize their legacy", says Sally Rockey, the NIH's deputy director for extramural research. If entrenched grant recipients leave the lab, the NIH hopes, more money will be available for early-career scientists.

Those who support the idea say that it could ease the pressure on senior researchers to continue working in order to bolster their retirement accounts, which in the United States largely depend on employee contributions. The evidence for this is anecdotal, however, and proponents of emeritus grants admit that few senior researchers complain that they lack money to close their labs.

But judging from more than 100 comments left on Rockey's widely read blog, many

researchers are highly sceptical of the plan, and are incensed by what they perceive as a retirement bonus for the already better-resourced. "The idea of allocating precious limited federal research dollars to a special 'emeritus' award appears, at best, tone deaf, and at worst, suggests underlying biases within the NIH that favour established researchers," says neuroscientist Benjamin Saunders, a postdoctoral researcher at Johns Hopkins University in Baltimore, Maryland.

Economic research suggests that paying older scientists to abandon their labs is unlikely to be the most effective way for the NIH to achieve its ultimate goal. Policies for adjusting markets work better when they are direct, says labour economist Richard Freeman of the National Bureau of Economic Research in Cambridge, Massachusetts. "If your goal is to have more young researchers have independent awards and positions, it would be more

efficient just to give them that," he says. "Any time you try indirect methods, there is much more uncertainty as to what will happen."

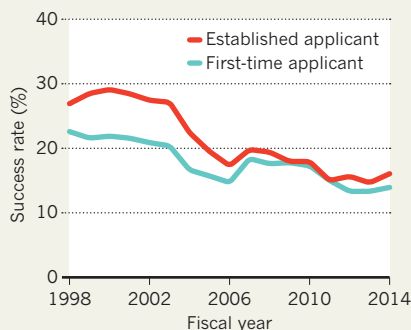
But the NIH has had mixed success with policies designed to give more money to new investigators. Since 2007, the percentage of grants won by new applicants has approached the share reaped by experienced scientists (see 'Age gap'), but critics say that funded proposals from younger researchers are of lower quality than those from older scientists. And despite the NIH's efforts, the average age at which a researcher wins his or her first award has not declined.

This may be partly because of broader demographic changes in the biomedical workforce. About 1 in 3 working scientists was over 50 in 2010, compared with 1 in 5 in 1993. This helps to explain why the average age of NIH principal investigators has risen. The age of first innovation itself might be increasing, too, according to analyses of patent filings and the age at which Nobel laureates win their prizes. Benjamin Jones, an economist at Northwestern University in Evanston, Illinois, has found that over the past century there has been a shift towards productive science at older ages, perhaps because innovation now requires more knowledge<sup>2</sup>.

An even bigger challenge is an imbalance between the healthy supply of young scientists and the number of senior-level jobs, says Michael Teitelbaum, a demographer at Harvard Law School in Cambridge, Massachusetts. The problem has been exacerbated by erratic NIH funding. From 1998 to 2003, the agency's budget doubled, to US\$27.2 billion. Flush with grant money, academic research centres expanded, making jobs for biomedical-

## AGE GAP

The US National Institutes of Health has sought to increase funding for new investigators, with mixed results.



SOURCE: NIH

science graduates plentiful and attracting more students to the field.

Fortunes subsequently reversed. Since 2003, the NIH's budget has contracted by around 25% in real terms, increasing competition for dwindling grant money among the surplus of early-career scientists created during the boom.

Without steady growth in the NIH budget, some have suggested that the solution is to train fewer graduates for careers in biomedical research. But the pipeline of new investigators shows no signs of drying up. In 2013, US universities conferred 8,471 biomedical PhDs. These joined thousands of other researchers eligible

that year for the NIH's Early Stage Investigator awards — 785 grants aimed at researchers who had graduated in the past decade. Too many heirs are awaiting too few crowns. ■

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2. Jones, B. F. *Rev. Econ. Stat.* **92**, 1–14 (2010).

MARK MOFFETT/MINDEN/GETTY; RALPH LEE HOPKINS/GETTY



Ground finches (left) tend to have large beaks for cracking seeds, whereas warbler finches spear insects.

#### EVOLUTIONARY BIOLOGY

# Darwin's finches join genome club

Scientists pinpoint genes behind famed beak variations.

BY GEOFF MARSH

Researchers have sequenced the genomes of all 15 species of Darwin's finches, revealing a key gene responsible for the diversity in the birds' beaks. The study, published online in *Nature* this week<sup>1</sup>, also redraws the family tree of these iconic birds, whose facial variations helped Charles Darwin to formulate his theory of natural selection.

The finches are endemic to Ecuador's Galapagos archipelago and Costa Rica's Cocos Island. Their beaks are adapted to their preferred food: warbler finches, for example, spear insects with thin, sharp beaks, whereas ground finches crack open seeds with strong, blunter beaks. The birds are a textbook example of adaptive radiation, in which a single ancestor responds to a selective pressure — in this case, food availability — by diversifying into several species.

Darwin was the first to note this, during his

groundbreaking 1831–36 voyage aboard the HMS *Beagle*. “One might really fancy,” he wrote in his diary, “that from an original paucity of birds in this archipelago, one species had been taken and modified for different ends.” Almost two centuries later, his early suspicions have been widely confirmed.

Initially, the finches were classified on the basis of their physical characteristics. More recently, it has incorporated variations in key DNA sequences. But nobody had compared whole-genome data from all 15 species until a team led by Leif Andersson, a geneticist at Uppsala University in Sweden, analysed samples from 120 individual birds. “When we did the whole DNA sequence of all the species, we could redraw that tree,” he says.

Overall, the researchers found good agreement with current taxonomy, but also some interesting deviations. For example, they conclude that the ground finch *Geospiza difficilis*,

which is spread across six islands, actually comprises three species.

Andersson's team also discovered extensive mixing of genes between species. This is in line with field observations of hybrid birds made by study co-authors Peter and Rosemary Grant, evolutionary biologists at Princeton University in New Jersey who have worked in the Galapagos for decades. The genomic data reveal that the birds have been crossbreeding throughout their evolutionary history.

Darwin famously sketched his initial idea of phylogeny as a branching tree, above which he wrote “I think”. Now, says Peter Grant, “he might wish to redraw that tree by making connections between some of the branches, representing the hybridization and gene exchange”.

By looking at closely related finches that have different beak shapes, the researchers were able to pinpoint the genes responsible for beak morphology. One of those genes, *ALX1*, is involved in the facial development of vertebrates, including fish and mammals. In humans, for example, loss of *ALX1* leads to severe facial deformities<sup>2</sup>.

In the finches, the gene displayed two distinct variants that matched up neatly with beak shape. Individuals from a species with a highly variable beak shape — the medium ground finch (*Geospiza fortis*) — had a mixture of the blunt and pointed gene variants. The finding dovetails nicely with work by the Grants that documents the species' rapid evolution as recently as the 1980s, when a drought affected the bird's food supply and its beak started to become more pointed to accommodate a new diet<sup>3</sup>.

Andersson suspects that *ALX1* drove that adaptation, but others say the picture is more complicated. Beaks “differ in many parameters, not just being blunt or pointed”, says Ricardo Mallarino, an evolutionary biologist at Harvard University in Cambridge, Massachusetts. Functional studies of *ALX1* should help to reveal exactly what the gene controls, he says. His colleague, evolutionary biologist Arkhat Abzhanov, says that *ALX1* may be especially important for finches with very specialized beaks.

What would Darwin make of the findings? “We would have to give him a crash course in genetics,” Grant says. “But then he would be delighted. The results are entirely consistent with his ideas.” ■

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2. Uz, E. *et al. Am. J. Hum. Genet.* **86**, 789–796 (2010).
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