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ON THE RECORD

"That's one small step for *a* man, one giant leap for mankind."

Computer analysis shows that Neil Armstrong, the first man on the Moon, didn't fluff his lines after all.

"If you had told me I would have death threats in a case like this, I would have said you were crazy. But I did."

Judge John Jones is stunned by what happened when he struck down the decision of a school board in Dover, Pennsylvania, to teach intelligent design in schools.

OVERHYPED

Allergy-free kittens

Allerca of San Diego, purveyor of "the world's first scientifically proven hypoallergenic cats", is making much of the fact that its kitties were bred naturally rather than using transgenic methods, all in a mere 18 months. How did the firm avoid years of selective breeding? It stumbled across three cats with mutated allergen proteins during pre-testing for the gene-silencing method it was preparing to use, neatly sidestepping most of the hard work. And how did Allerca obtain "independent confirmation" that the $4,000 cats are for real? Ten blindfolded volunteers, stroking experimental or control cats. The research has yet to find a publisher.

J. BURTON/NATUREPL.COM

SCORECARD

Endurance

Mars rover Opportunity caused joy and panic as it reached 1,000 days of exploring — it was built to last just 90 days, so the onboard software could only accommodate dates with 3 digits.

Astronomy

Iceland's capital Reykjavik was plunged into darkness last week as lights were switched off to give locals an unprecedented view of the night sky, despite a few clouds.

Sources: Kansas.com, Reuters

SIDELINES

Youthful duo snags a swift Nobel for RNA control of genes

The call from Stockholm was received by two unusually young scientists, an impressively short time after they demonstrated a fundamental control of gene expression.

The 2006 Nobel Prize in Physiology or Medicine has gone to Andrew Fire, now at Stanford University, California, and Craig Mello, now at the University of Massachusetts Medical Center in Worcester. Both are in their forties. It honours a discovery that has transformed biological research and may, in the future, prove useful in treating human disease.

STANFORD UNIV.; UNIV. OF MASSACHUSETTS

Silence is golden: Craig Mello (left) and Andrew Fire.

The discovery is called RNA interference, or RNAi. When a gene is to be expressed, it sends instructions to the cell's protein synthesis machinery. The intermediary is messenger RNA (mRNA), which has a structure complementary to that of the gene. In their breakthrough paper, published in *Nature* in 1998, Fire and Mello, and colleagues, demonstrated that these mRNAs can be targeted for destruction by specific double-stranded forms of RNA (A. Fire *et al. Nature* **391,** 806–811; 1998).

Researchers already knew that 'antisense' RNA — an artificial molecule whose sequence complements the mRNA — could silence specific genes when taken up by a cell. But the effect was modest and inconsistent. And, confusingly, the same effect was seen with 'sense' RNA.

In a series of simple and elegant experiments on a muscle gene in the nematode worm *Caenorhabditis elegans*, Fire and Mello showed that a powerful and consistent effect required the sense and antisense RNAs to be stuck together, as double-stranded RNA. When injected with the double-stranded RNA, the worms twitched awkwardly, just like mutant worms lacking the muscle gene. The researchers also showed that mRNA was destroyed by the treatment, rather than being masked as others had believed. And they showed that the double-stranded RNA can cause more copies of itself to be made, can spread between cells and can even be inherited by progeny.

In the *Nature* paper the researchers speculated that organisms might use this mechanism to control expression of their genes — a fact soon shown to be true. RNAi turned out to be an important way of controlling 'jumping genes', which can insert themselves throughout the genome and disrupt gene function. It is also thought to help protect against viral infections, at least in simple organisms.

Fire and Mello's subsequent research, and that of the many researchers who flooded the field after them, have since filled in the details. The RNAi pathway has been fully worked out and shown to apply to all genes — not just in worms but in nearly all other species.

"There is hardly a lab not using the tools of RNAi to turn off the genes that they are studying," says Tom Tuschl of Rockerfeller University, New York, who joined the RNAi élite soon after the Fire and Mello discovery. RNAi reagents have been used to find genes involved in everything from ageing to cancer. Clinical hopes are pinned on finding ways to use RNAi to reduce the activity of genes that cause disease.

Most Nobel prizes are given many years after the relevant discovery. The Fire and Mello award, given just eight years after publication of their paper, is reminiscent of Kary Mullis's 1993 chemistry Nobel. That prize was awarded for his 1985 invention of the polymerase chain reaction — a method of gene amplification that invaded research labs just as fast and comprehensively as the RNAi technique has.

Ronald Plasterk of the University of Utrecht in the Netherlands, who worked with Fire when they were young researchers at the Laboratory of Molecular Biology in Cambridge, UK, says he felt that a Nobel was around the corner. But he didn't think it would be so soon. For a laugh, on the morning of the announcement Plasterk asked his postdoc to call Fire in a pronounced Swedish accent. "But then we heard he had really won, so the joke had to be dropped."

Mello seemed stunned when interviewed on the Nobel webcast, not long after he had heard the news. "I seem too young," he said. "And isn't the gap unusually short?" ■

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