

# THIS WEEK

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## Close the deal

*Science-based evidence and enlightened diplomacy have brought within reach a historic opportunity for nuclear détente with Iran. It must be seized.*

In a diplomatic tour de force, negotiators from six world powers and Iran reached — against the odds — a tentative agreement on 2 April to ensure that Iran's nuclear programme is for peaceful purposes only. It is science-informed diplomacy and foreign policy at its best. Even the most optimistic of seasoned nuclear-weapons and non-proliferation experts were surprised by the comprehensiveness of the interim accord, its level of detail, and the substantial concessions made on both sides. Few had expected this degree of progress given the decades of hostility and intransigence on both sides.

In a perhaps unprecedented flurry of published opinion pieces and statements, experts have overwhelmingly lent their support to the accord. They have also subjected it to robust online peer review, highlighting the positive outcomes, but also pointing out the technical loopholes and details that they feel must still be negotiated or clarified before the 30 June deadline for a final agreement.

The emphasis on getting the scientific and technical assessments that underpin the issues right, to offer political leaders confidence in the projected outcomes, has played a central part in getting to this crucial juncture. Two physicists, both at the Massachusetts Institute of Technology in Cambridge in the 1970s, had key roles: Ali Akbar Salehi, head of Iran's Atomic Energy Organization, and Ernest Moniz, the US energy secretary. In long face-to-face discussions, the men thrashed out the complex nuclear science to come up with acceptable compromises that did not cross the red lines of either side. Importantly, the lead negotiators, US secretary of state John Kerry and Iranian foreign minister Mohammad Javad Zarif, have taken on board their scientific advice.

Scientists share a language, culture and values that can help to transcend politics and enmity. Researchers involved in past nuclear-weapons treaties say that scientific collaboration between adversaries is crucial to building trust and confidence, but they emphasize that it takes time. Iran has been ostracized by many governments for almost four decades, and rebuilding trust on both sides will take years. That this rapprochement is now under way can only be commended — especially at this time of exceptional political instability in the Middle East, which has unexpectedly aligned some of Iran's and the West's strategic interests. Any easing of the sanctions on Iran and its political isolation will also benefit the country's isolated scientific community.

Experts are unanimous that the framework of the deal shows that it could essentially put Iran's nuclear programme on ice for well over a decade — and so buy the time needed to build greater trust and to develop further measures to ensure that any eventual larger Iranian nuclear programme remains peaceful. The accord would, for example, block Iran's potential route to a plutonium bomb, by redesigning the country's Arak heavy-water reactor to make it much less capable of producing weapons-grade plutonium. Moreover, all plutonium-containing spent fuel would be shipped out of the country.

Iran's potential to make a bomb using enriched uranium would also be curtailed to the extent judged necessary by scientists to ensure

that, for the foreseeable future, it would take the country more than a year to 'break out' and develop a nuclear weapon, leaving enough time for international intervention (see page 274). The Vienna-based International Atomic Energy Agency would also be given unprecedented powers to inspect Iran's entire nuclear programme for 25 years to ensure that, were Iran to violate the agreement either overtly or covertly, this would be detected quickly.

**“Scientists share a language, culture and values that can help to transcend politics.”**

Iranian and other scientists emphasize the interplay of science and politics. The breakthrough was made possible, they say, only by the election of the relative reformer Hassan Rouhani to the Iranian presidency in 2013

and of Barack Obama to the US presidency in 2008. Both leaders have been more open to pragmatic and constructive dialogue between the two nations than their predecessors. Critics of the deal have yet to put forward any credible alternatives, or any substantive challenges to its technical underpinnings, relying rather on political rhetoric and stoking fear to justify inaction. The late US president Ronald Reagan famously adopted the Russian proverb “Trust, but verify” with respect to the monitoring of nuclear-disarmament treaties with the Soviet Union. It is time once again for progressive policies to prevail over dangerous inaction. ■

## Numbers matter

*Researchers need help in making the statistical power of animal experiments clear.*

Albert Einstein is said to have noted that theories should be as simple as possible, but no simpler. By the same token, biomedical researchers doing *in vivo* experiments should use as few animals as possible, but no fewer. On page 271, *Nature* reports a move by UK government funding agencies to require grant applicants to show how they calculated the number of animals needed to make the results of an experiment statistically robust. In recent years there have been concerns that sample sizes in individual experiments can be too low, especially in preclinical research that attempts to determine whether a drug is worth pursuing in human studies.

Too-small sample sizes can lead to promising drugs being discarded when their effectiveness is missed, or to false positives, as well as to ethical issues if animals are being used in studies that are too small to provide reliable results.

The UK research councils' move is to be applauded. And Britain is

not alone in pursuing such improvements: the US National Institutes of Health has been testing the use of a grant-review checklist that includes features such as experimental design, to improve the reproducibility of preclinical research in animals.

The burden for this should not fall on funding bodies alone. Institutions must also increase the amount of support offered to researchers in designing the statistical aspects of an experiment. Such support is too often limited or ad hoc: study design is complex and needs careful consideration by people who truly understand the issues (see *Nature* 506, 131–132; 2014).

Journals are also responsible for ensuring that the research they publish is reported in sufficient detail for readers to fully appreciate key details of experimental and analytical design. Many publications — including *Nature* — have endorsed the ARRIVE guidelines for reporting animal research (C. Kilkenny *et al.* *PLoS Biol.* 8, e1000412; 2010). These are, however, hugely detailed, and compliance at this level is difficult for early, exploratory research.

Journals published by Nature Publishing Group nevertheless encourage the use of ARRIVE. In 2013, we implemented a reporting checklist that demands that authors supply key details of study design. For animal studies, these include the methods of sample-size determination, randomization and study blinding, as well as exclusion criteria (see *Nature* 496, 398; 2013). An impact analysis on the effectiveness of the changes introduced in 2013 is currently under way.

Sample size is just one of a suite of issues that need to be addressed if poor reproducibility is to be tackled. Journals have a key part to play in dealing with this problem, but so do others. Credit to

those academies that take a lead. This month, for example, the UK Academy of Medical Sciences held a meeting in London at which researchers, funders and representatives from research institutions and universities attempted to provide recommendations for improving reproducibility by examining case studies in disciplines from epidemiology to particle physics, and by exploring the role of culture

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and incentives. There are no magic bullets — all parts of the research community need to chip away at the problem.

Undoubtedly, part of the challenge is the culture that pushes investigators in many parts of the world to produce more and more with the same resources. The drive to maximize the number of papers and the impact of findings is pervasive.

In a commentary published in *Nature Biotechnology* last year, experimental psychologist Marcus Munafò and his colleagues compared modern biomedical research with the 1970s automobile industry (M. Munafò *et al.* *Nature Biotechnol.* 32, 871–873; 2014). The fast-moving but error-prone car production lines of the United States found themselves losing ground to Japanese manufacturers that stressed the importance of quality-control at every step in their factories.

The moral of the story: quality assurance adds a burden, but it is worth the effort for a longer-term gain in public confidence. Making sure that the power of an animal experiment suits its purpose is an important way for funders and researchers to contribute. ■

## ANNOUNCEMENT

## Time to tackle cells' mistaken identity

The differences between a cow and a monkey are clear. It is easy to tell a moth from a mosquito. So why are there still scientific studies that mix them up? The answer is simple: hundreds of cell lines stored and used by modern laboratories have been wrongly identified. Some pig cells are labelled as coming from a chicken; cell lines advertised as human have been shown to contain material from hamsters, rats, mice and monkeys.

Which is worse: that such crude mix-ups exist, or that, every day, researchers use cell lines that somebody, somewhere has already found to be mislabelled, misidentified or contaminated? To solve the first problem is a huge challenge. To address the second is a more manageable task, and one that researchers, journals, universities and funders must take seriously.

*Nature* and the Nature research journals are strengthening their policies to improve the situation. From next month, we will ask authors to check that they are not working on cells known to have been misidentified or cross-contaminated, and will ask them to provide more details about the source and testing of their cell lines.

This may sound like an obvious way to deal with a problem that has been known about for decades. But tests to check the contents of cell lines are complex and time-consuming, and until recently were expensive. What makes the time ripe for action is a combination of a rising awareness of the problem among scientists in certain communities (cancer research in particular), the availability of proper tests and resources (see J. R. Masters *Nature* 492, 186 (2012), and page 307), and the willingness of some funders to tackle the matter — including the US National Institutes of Health and the Prostate Cancer Foundation in Santa Monica, California.

Problems have already been found with more than 400 cell lines. In the long term, the goal must be to change testing routines worldwide to ensure that new mix-ups are not propagated. The least that scientists should already be doing is checking whether the cell line they are using is one of those already marked with a red flag.

In 2013, Nature journals started to ask authors to report the source of their cell line and whether the cell line had been authenticated. Most have not done so. Out of a sample of around 60 cell-line-based papers published across several Nature journals in the past two years, almost one-quarter did not report the source. Only 10% of authors said that they had authenticated the cell line. This is especially problematic given that almost one-third said that they had obtained the cell lines as a gift from another laboratory.

From 1 May, all authors of papers involving cell lines that are submitted to Nature journals will be asked whether they have checked their cell lines against publicly available lists of those known to be problematic. We will in particular monitor compliance in cancer research. The focus on cancer is a first step, chosen because the cell-line problem has been best documented in this field, and because the cancer community is already reacting to the issue. Some specialist journals, such as the *International Journal of Cancer*, are now systematically asking for authentication. This is important not only for its effects on basic research, but also because of the potential for translational research to founder if cell lines are contaminated.

Other fields are not immune to cell-line problems, and we hope to extend the systematic checks to them in future. More details of the new policy, whom it affects and where the cell lines should be checked are available at [go.nature.com/zqjubh](http://go.nature.com/zqjubh).

That a cell line used in a research project appears on a watch-list need not make the research invalid, or mean that the paper will automatically be rejected. Authors will be asked to explain why the misidentification does not undermine the conclusions. But we reserve the right to ask for data to be removed if the justification is judged insufficient by editors and referees. ■