

Breeding cheats

Understanding the social and psychological factors behind scientific misconduct will enable bad practice to be minimized, but never eliminated, says **Jim Giles**.

Take one prestigious laboratory. Add some pressing grant deadlines and a dash of apprehension about whether the applications will succeed. Throw in an overworked lab head, a gang of competitive postdocs and some shoddy record-keeping. Finally, insert a cynical scientist with a feeling that he or she is owed glory. It sounds hellish, but elements of this workplace will be familiar to many researchers. And that's worrying, as such an environment is, according to sociologists, the most fertile breeding ground for research misconduct.

Just a decade ago, such a statement would have been speculation. But sociologists are increasingly confident that they understand why scientists cheat. Studies of disgraced researchers, a series of high-profile misconduct cases, and a stream of government funding have created the discipline of research into research integrity. The results are a better understanding of those who betray science, and of the climate in which they do so. They also suggest how misconduct can be reduced, although there are good reasons to think it will never be eliminated.

To tease apart the factors behind acts such as fabricating data or unfairly appropriating ideas, sociologists say we must turn away from the media glare that surrounds extreme cases such as Woo Suk Hwang, the South Korean stem-cell scientist who faked high-profile papers on human cloning¹. Such cases are to research integrity what serial killers are to crime prevention, says Kenneth Pimple, an ethicist at Indiana University in Bloomington. Hwang and others grab the headlines, but minor acts of misconduct are much more common, and potentially more damaging to scientific progress.

That runs against the grain of traditional thinking on misconduct, at least among scientific societies, which have often argued that cheating is due mainly to a few bad apples. But that view now looks much less tenable. When scientists funded by the US National Institutes of Health were asked in 2002 about misconduct, a third said they had committed at least one of ten serious errant acts, such as falsifying data or ignoring important aspects of the regulations regard-

ing human subjects². Young physicists also returned disturbing results when questioned by the American Physical Society in 2003: more than 10% had observed others giving less than truthful descriptions of research techniques or analyses, for example.

To understand what is driving these figures, researchers would like to study confirmed cases of misconduct. Information here is sparse, as convicted scientists do not generally rush to tell their stories.

What data there are lie mainly in the files of the US Office of Research Integrity (ORI), which oversees biomedical misconduct investigations in the United States. Mark Davis, a criminologist at Kent State University in Ohio, trawled 92 ORI

cases from 2000 and earlier and revealed seven factors frequently associated with misconduct³. Some involve research climate, such as a lack of support from superiors or competition for promotion. Others, such as a tendency to blame the difficulty of a particular experimental task, point to ways in which individuals justify their own actions.

Habit-forming

To get a finer-grained image of these factors, sociologists turn to survey data. At the University of Oklahoma in Norman, for example, researchers asked doctoral students how they would react to specific ethical dilemmas, such as if a researcher takes an idea from a colleague

and, without letting that colleague know, uses it to apply for funding.

Many of the factors seen in Davis's survey cropped up again, but by asking students about their past and present experiences the Oklahoma team, which presented its work at the ORI conference in Tampa, Florida, last year, added new details. In particular, its work suggests that past experience, such as graduate training, can be more important than the current climate in

which people work. Day-to-day aspects matter — interpersonal conflict was associated with unethical decisions, for example — but former experiences, such as having worked in a lab where the head showed positive leadership, seem to be more important.

The need for support extends beyond the level of research groups. Brian Martinson from the HealthPartners Research Foundation in Minneapolis and his colleagues have studied misconduct using the theory of organizational justice, which states that employees are more likely to behave unethically if they believe their managers are treating them unfairly. Sure enough, Martinson's survey respondents were more likely to admit misconduct if they felt that governing structures, such as funding review bodies, had treated them badly⁴. In an as-yet unpublished role-playing exercise, Patricia Keith-Spiegel of Simmons College in Boston, Massachusetts, also found that researchers were more likely to act unethically if a negative decision by a review board was not properly explained.

With these results in place, misconduct experts can make tentative statements about how to limit problems. Robust and positive mentoring is top of the list. At the ORI, for example, director Chris Pascal says that a hands-on principal investigator (PI) who talks to junior scientists regularly and stresses the need to run experiments properly, rather than rushing out results, can make a big difference: "Get a PI like that and the risk of misconduct is much lower." Institutional policies that insist on good record-keeping are also essential, adds Pascal.

Both pieces of advice seem straightforward,

"Employees are more likely to behave unethically if they believe their managers are treating them unfairly."



Could identifying fraud risks create a *Minority Report*-style police state?



TEK IMAGE/SPL Pressure cooker: the competition between and within biomedical research labs can be intense.

but neither are followed as much as they should be. A 2003 ORI survey⁵ concluded, for example, that one in four lab heads did not take their supervisory roles seriously enough. Many institutions also fail to enforce data-management policies, says Pascal. That is worrying, as poor record-keeping was present in almost 40% of more than 550 misconduct cases studied in a survey published this month⁶.

Would these actions address all the causes of misconduct? Almost all scientists have felt pressure at some point in their careers, yet the surveys suggest that the majority do not commit even minor misdeeds. "It doesn't push everyone over the edge," says Nicholas Ste-neck, a historian at the University of Michigan in Ann Arbor who has worked on misconduct policies for the ORI and other organizations. "It comes down to individuals."

Here the research is more controversial. Alongside environmental factors, the Oklahoma group has looked for links between per-

sonality traits and ethical decisions. For each of the four areas looked at, from data management to experimental practice, the team found that subjects with high ratings for narcissism returned low scores. A sense of entitlement — 'I'm owed this result because of my hard work' — also predisposes researchers to misconduct. But so does having a trusting view of others.

Such results might improve understanding, but the potential for abuse worries some. Martinson says the situation reminds him of the science-fiction movie *Minority Report*, in which premonitions are used to apprehend individuals thought to be future criminals. Universities might, for example, choose to reduce misconduct risk by screening for traits such as narcissism in potential employees. "What you can do with this is frightening," says Martinson. "It doesn't lead to positive social control. At the extreme it leads to a police state."

That need not be case, argues Stephen Murphy, a PhD student who has worked on several



OPINION

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of the Oklahoma studies. Rather than weed out individuals, personality work can inform research-integrity courses. Asked about ethical decisions, for example, most researchers declare themselves more ethical than their colleagues. Illustrating this by giving scientists a questionnaire and then sharing the results with a group is a powerful way of showing researchers that they are more flawed than they think, says Murphy. Those with narcissistic tendencies would not be treated any differently, but they might benefit more from such an exercise.

Over the edge

Yet even when knowledge of individual and environmental factors has been plugged into integrity training, there remains a bigger question about the way science is run. Many scientists work under enormous pressure, even in an era of relatively generous funding. Career paths in science exacerbate the situation. Unlike many other professions, scientists must constantly prove themselves by publishing papers. Success also depends not just on the view of a few immediate colleagues, but on that of the whole field. "It's about building a reputation," says Martinson. "In science that's the coin of the realm."

The case of obesity expert Eric Poehlman shows how these factors can push people over the edge. During his trial last year, when he was sentenced to a year in jail after admitting falsifying data in papers and grant applications, he said: "The structure...created pressures which I should have, but was not able to, stand up to. I saw my job and my laboratory as expendable if I were not able to produce."

The similarities between Poehlman's testimony and that of many other fraudsters point to factors that institutions can tackle. The problem is that many of the risk factors for misconduct also seem to be what makes for good science. Most would agree that competition is needed to allocate over-subscribed research funds appropriately, as well as to push individuals to evaluate their ideas. So even with the best research environment and training, fraud is unlikely to disappear. "It's the dark side of competition," says Martinson. While the pressure remains, so will some level of misconduct. ■

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Ethics and fraud

The trajectory of the Hwang scandal highlights the shortness of the path between unethical behaviour and outright misconduct.

The fall of Woo Suk Hwang represents perhaps the highest-profile case in the sorry history of research misconduct. The sheer Shakespearian drama of the Korean cell biologist's eclipse, surrounded by fawning courtiers and plotting groups of acolytes and enemies and in full view of the television cameras, has left few researchers of any discipline, anywhere in the world, unaware of its circumstances.

But what really makes the Hwang case special is the importance of the impugned results (W. S. Hwang *et al. Science* **303**, 1669–1674; 2004 and **308**, 1777–1783; 2005). The claimed cloning of human embryos placed Hwang at the forefront of stem-cell research, perhaps the most acclaimed and contentious sphere of modern science. It is also the first major misconduct case to occur during the modern era of carefully patented biology, in which scientists may aspire not just to fame, but to fortune as well.

All of this raises some general questions about ethics and fraud that researchers had perhaps hoped were put to bed a long time ago. Many of these questions were last publicly addressed in the long and painful aftermath of the Baltimore case, in which a junior researcher, Thereza Imanishi-Kari, was accused of fraud in the laboratory of one of the United States' leading microbiologists.

David Baltimore was eventually vindicated and is today president of the California Institute of Technology. But when the allegations were made, the National Institutes of Health opened an Office of Scientific Integrity, which was later downgraded but continues to support fraud investigations at US universities while seeking to get academics to teach their students about ethics and misconduct.

"The US system for dealing with fraud, imperfect as it may be, is still more advanced than that of many other nations."

This system, imperfect as it may be, is still more advanced than that of many other nations. Elsewhere in the world, cases of fraud have highlighted considerable shortcomings in the mechanisms for responding to misconduct.

Another celebrated fraud case involved Jan Hendrik Schön, a physicist at Bell Laboratories in Murray Hill, New Jersey, who was found guilty in 2002 of fabricating results in a massive and influential string of papers on superconductivity. However, the general view of the Schön case, outside the discipline directly involved at least, has been that no innocent civilians were hurt, and the fraud was unearthed and duly punished. There is almost a nagging sympathy for how such a smart young man could be so stupid.

The scope of the Hwang scandal tends to leave these and other recent misconduct cases in the shade, however. Although the full facts of the case remain unknown, its multidimensional outline is already clear. Barely a stone was left unturned in his lab's attempts to secure a positive result. Egg donors were energetically sought from

every conceivable source — including from junior researchers inside the laboratory itself, where allegations of coercion have been made. In the end, a result was claimed and the paper published in the complete absence of genuine scientific evidence to support it.

This will surely leave some people asking: if this single cell in the body of science was so malignant, how fares the rest? This is an awkward question and one that many in the community will seek to evade by referring to the fact that it happened in South Korea and couldn't happen here (wherever 'here' happens to be). And it is true that standards of oversight at many laboratories would, at least in theory, make this kind of scenario improbable. However, research — not least in the dynamic and fiercely competitive field of reproductive biology — is increasingly conducted through international collaborations. These often involve working with colleagues in countries, including China and South Korea, where mechanisms for supervising ethics and investigating misconduct are at relatively early stages of development.

"This will surely leave people asking: if this single cell in the body of science was so malignant, how fares the rest?"

It therefore falls to scientists who take research ethics seriously to confront the question head on, and to determine what steps should be taken to redouble our efforts to secure standards in both the ethics and conduct of research.

Hand in hand

A first step is to acknowledge that sound ethics and good research practice go hand in hand. The international stem-cell community showed some reluctance to distance itself from Hwang when serious questions were raised in this journal in May 2004 about the manner in which eggs had been obtained for his experiments (see *Nature* **429**, 3; 2004).

As soon as his main US collaborator, Gerald Schatten of the University of Pittsburgh, announced in November that he was bailing out of his collaboration with Hwang (see *Nature* **438**, 262–263; 2005), people began to speculate that Schatten must know there was a problem with the result of the seminal 2004 paper. After all, they inferred, no one would leave a wildly successful research group over ethical transgressions. Or would they?

The leadership of the scientific community has long argued for a solid line to be drawn between ethical transgressions — not informing patients of their rights, sexually harassing staff, coercing junior colleagues, that sort of thing — and actual research misconduct, which refers to the fabrication, falsification or plagiarism of scientific evidence.

In the wake of the Baltimore scandal, a congressionally mandated commission chaired by Kenneth Ryan called for a broader definition

of research misconduct that would embrace some forms of malfeasance beyond fabrication, falsification and plagiarism. His definition didn't cover bioethics, but it did class any breach of research regulations as misconduct.

Ryan's proposal was roundly condemned in the community, which fought a lengthy and successful battle to derail it. Researchers feared that the extension of misconduct investigations to embrace all kinds of professional laxity would lead to endless, fruitless investigation and, in particular, elicit groundless allegations from junior laboratory malcontents.

It is certainly true that there's a distinction between personal misbehaviour in the lab and outright scientific fraud, and it is perhaps

as well that special investigative procedures are retained exclusively for the investigation of the latter. Furthermore, the question of what constitutes an ethical transgression may vary between societies that elect to impose different rules, whereas scientific fraud knows no borders.

In view of the pattern of behaviour that led up to Hwang's disgrace, however, no one should argue ever again that despotism, abuse of junior colleagues, promiscuous authorship on scientific papers or undisclosed payment of research subjects can be tolerated on the grounds of eccentricity or genius. Research ethics matter immensely to the health of the scientific enterprise. Anyone who thinks differently should seek employment in another sphere. ■

Three cheers for peers

Thanks are due to researchers who act as referees, as editors resolve their often contradictory advice.

There is nothing like a high-profile fraud case to encourage journals to reflect on whether the standards and procedures they follow in selecting work for publication are thorough and appropriate. Misconduct creates a negative perception of journals' scientific peer-review processes, and the Hwang fraud saga has already fuelled some misconceptions about how the combination of referees and journal editors actually works.

Peer review remains by far the best available system for scientific quality control, however, and is an ultimately inspiring one at that. *Nature* is hugely grateful for the advice it receives from about 6,000 referees each year — typically two or three referees per paper. Most of their reports contain exactly what we need: a statement of what the referee considers the central message of the paper; an assessment of its significance; and a critique of technical or interpretational weaknesses, either in the work itself or in its presentation.

Between them, these elements add up to a verdict on the work's credibility and robustness. The system, it should be noted, is reliant on trust that what is written in the paper is actually true: it is not designed to detect the tiny minority of papers that are fraudulent.

The lives of editors and editorial boards of all journals are made interesting by the fact that, in many cases, the referees disagree on the verdict. And authors tend to be mightily upset if their papers are rejected when one or more reviewers are positive. Why, they demand to know, should the view of a negative reviewer be allowed to dominate the editors' selection decision?

To shed some light on how these decisions are reached, it is worth reflecting on some case studies of how and why referees differ in their view of papers submitted to *Nature* and the *Nature* research journals.

In one case, an exciting result relied on two techniques and a theoretical interpretation. The theoretical referee was very positive because the work validated an interesting idea. A specialist in one of the techniques was positive because he could find no flaw in its application. But the third referee uncovered a technical shortcoming in the second technique, and the paper was rejected after the editor assessed the significance of the shortcoming.

In another case, one of the referees recommended publication of

a paper, but also pointed out limitations in the value of the finding. The editor concluded that the paper lacked the significance that would justify inclusion in the journal.

On many other occasions, however, the editors' discretion in making a decision results in a paper's publication. In one such case, referees criticized a molecular-biology paper for a lack of mechanistic insight and expressed reservations about the appropriateness of some of the techniques the authors used. But the editors felt that the therapeutic implications of the paper merited publication and, after resolving the technical issues raised by the referees, pushed ahead with publication of what turned out to be a highly cited development.

Another paper concerned the innovative application of chemistry to an environmental problem. But before publication, the editor orchestrated considerable iteration between referees from quite disparate backgrounds to ensure that a common understanding of the paper and its reliability had been established.

In another case, efforts to obtain review of a paper in genetics led to seven refusals to review, one damning review and only one positive review. In this case, the editor identified an experiment that would improve the paper and suggested it, yielding interesting results that were then published and well received.

Only in a minority of cases does every referee agree on whether or not to publish a paper. The above examples illustrate just a few ways in which such differences arise and demonstrate why journals would lose the respect of their authors and readers if they were to act robotically on the referees' advice. Moreover, *Nature* often makes referees aware of what the others are recommending, which can sometimes provide useful feedback to the selection process.

"Only in a minority of cases does every referee agree on whether or not to publish a paper."

We would never claim that *Nature's* decision-making process is perfect. Its imperfections — along with those of every other journal — are among the multifarious reasons why over-reliance on journal publications as a measure of researchers' performance is dangerous. *Nature* has also dished out its fair share of historically embarrassing rejections (see *Nature* 425, 645; 2003). We can only work to ensure that what we publish will do justice to the diversity of expertise that is brought to bear on its selection, and, above all, stand the test of time. ■



PURDUE UNIV.

Misconduct? It's all academic...

The legal quagmire, strain and bad press of misconduct investigations leave many universities tempted to ignore misconduct allegations. But getting an investigation right can reduce the pain and boost an institution's reputation, says **Geoff Brumfiel**.

Rumours were flying at Purdue University nuclear engineering school in West Lafayette, Indiana, late in 2005. A recently hired physicist, Rusi Taleyarkhan, claimed to be pioneering a new form of energy called bubble fusion. But researchers both in and outside Purdue had concerns. Questions ranged from whether the neutron radiation in his experiment was from fusion or another source, to whether a supposedly independent confirmation of his findings was ghostwritten by Taleyarkhan.

Lefteri Tsoukalas, then dean of the school, asked the administration to launch a misconduct investigation. What happened next Tsoukalas describes as "a real eye-opener". For a month, he says, the administration ignored his request. An inquiry began only in March 2006, after *Nature* reported his and others' concerns (see *Nature* 440, 132; 2006).

But even since then, Tsoukalas says, little has been done. In October 2006, he resigned (see *Nature* 444, 664; 2006), saying that he has "little faith that Purdue is capable of running a research integrity investigation". Taleyarkhan has denied all wrongdoing. Purdue declines to comment.

The situation benefits no one, but is far from unique. Research ethicists and university misconduct officers say that academia's handling of scientific misconduct is often capricious and incomplete. Reasons are complex, but essentially come down to three issues: investigations

are laborious; they require legal and scientific expertise that administrators often don't have; and universities may fear that a guilty verdict will stain their reputation.

Countries vary in their approaches, but a look at US universities highlights the problem. Many ethicists told *Nature* the system is riddled with inconsistencies. "I wouldn't even go so far as to glorify the current arrangement as 'a system,'" says Arthur Caplan, a bioethicist at the University of Pennsylvania in Philadelphia.

Little guidance

Most US misconduct proceedings follow a similar arc. If an accusation is received, administrators launch a preliminary inquiry. If that finds enough evidence, the university can open a full investigation. But beyond that, there's little guidance. Organizations such as the National Academies and the government's Office of Research Integrity (ORI) provide guidelines on research conduct, but no single document lays out investigative procedures.

Trouble can begin before the inquiry, says Kristina Gunsalus, a lawyer at the University of Illinois at Urbana-Champaign, who has led many proceedings. It's often unclear where whistleblowers should take their concerns, so young students end up discussing them with senior colleagues. The gossip that follows can damage the accused and prejudice an inquiry.

Whistleblowers can also be the target of

reprisals. Young people in particular are rarely protected, according to Barbara Redman, dean of nursing at Wayne State University in Detroit, Michigan, who has studied the issue. "Policies are incomplete," she says. Many lose their jobs, regardless of the outcome of their allegations.

Once an investigation starts, it can quickly enter legal limbo. Misconduct is not a legal charge, so in one sense it comes down to university policy. But if anyone is defamed, the university can find itself with a libel case. So it has a strong incentive to be secretive.

Then there's the pressure on investigators, generally scientists at the university, who are expected to serve as judge and jury to their colleagues. This can be awkward. Proceedings are often protracted and complex, with months of hearing testimony and evidence. "Every committee I have ever worked with comes back with these enormous circles under their eyes," says Gunsalus. "I cannot overstate the costs of these procedures for the people involved."

In part because the panels are made up of working scientists, they can deliver unexpected results. One recent example is the University of Pittsburgh's investigation into Gerald Schatten, an obstetrics professor. Schatten collaborated heavily with disgraced stem-cell scientist Woo Suk Hwang of Seoul National University (SNU) in South Korea. The SNU's investigation found that Hwang had faked many of his acclaimed cloning results, and a panel at Pittsburgh was

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charged with determining whether Schatten was also guilty of misconduct.

The panel concluded he was not, but found him guilty of 'research misbehaviour' — a term undefined by university policy and not included in the original charges. "What does it mean and what are the consequences?" asks Gunsalus. "I wish they had done better."

It's not surprising that the legal quagmire, strain and bad press leave many universities tempted to ignore allegations. "Universities have an incentive not to pursue them," says Redman. "They don't want to disgrace their faculty," adds Caplan. "It hurts morale."

Similar problems exist elsewhere. In Britain, for example, major funding bodies such as the research councils and the Wellcome Trust only award grants to universities that have established systems for dealing with misconduct allegations. But there is no body with the power to oversee investigations when they occur.

What can be done? One possible solution is to take investigations out of universities' hands and pass them to an independent body. But this can be controversial, as scientists don't take kindly to investigation by outsiders. The ORI briefly tried to take the lead in the late 1980s, but its heavy-handedness and lack of scientific expertise led to a backlash, according to Caplan: "The ORI blundered around like a brontosaurus in the research misconduct park."

Today, the ORI takes a lower-key role, providing guidelines and reviewing cases involving federal funds. Despite the failings of universities, most people now agree that in a country such as the United States, with a highly privatized university system, it's best to handle misconduct investigations on campus. "There are no better alternatives," says Gunsalus.

Scandinavian countries seem to fare better with independent supervision. In Denmark, whistleblowers can turn to a government body called the Danish Committees on Scientific Dishonesty (DCSD) if they think university boards have not investigated a claim properly. Finland and Norway have similar committees.

Although some of the DCSD's decisions have been controversial, such as when it criticized climate sceptic Bjørn Lomborg for cherry-picking data in his 2001 book *The Skeptical Environmentalist*, it is generally seen as a model for small countries in which it is hard to find independent investigators at the local level.

However, even DCSD member Vagn Lundsgaard Hansen, a mathematician at the Technical University of Denmark in Lyngby, believes claims should be dealt with by the university concerned where possible.

One way to help universities is to establish common systems and guidelines — although persuading them to comply isn't easy. After Germany's main funding agency, the DFG, asked universities to adopt guidelines in the late 1990s, it finally had to threaten to withdraw eligibility for funding if they didn't comply by mid-2002. The guidelines include establishment of university and DFG ombudsmen to whom whistleblowers can turn with concerns about a lab, and a committee that adjudicates on cases forwarded to it by the ombudsmen.

The universities reluctantly adopted the guidelines. But the ombudsmen expressed concern last October that universities are still not taking referred cases seriously. They complained that university presidents and rectors

play down cases, particularly concerns brought by young scientists against more senior colleagues. And when investigations do get started they drag on. The ombudsmen pledged to increase pressure on universities to improve — perhaps by requiring DFG grant application forms to refer to the university's guidelines, thus forcing department heads, who co-sign applications, to explicitly endorse them.

The key may be to convince universities that getting it right can bolster their reputation. The Massachusetts Institute of Technology (MIT)

"Asian universities are now showing the world how to conduct fast, fair and transparent investigations."

in Cambridge was widely praised for its investigation of immunologist Luk van Parijs, begun in August 2004. MIT moved fast to determine if an investigation was needed, handled complaints confidentially, found him guilty of fabricating results and fired him in October 2005.

Some Asian universities — once notorious for brushing misconduct claims under the carpet — are now showing the world how to conduct fast, fair and transparent investigations.

Quick justice

Last August members of a lab run by veteran biologist Akio Sugino at Osaka University claimed he had faked data in two papers. Two days later the biosciences school to which Sugino belonged formed an investigation committee, and released its conclusion that Sugino had fabricated data the next month. The 40-page report was published on the school's website and in December Sugino was dismissed.

That month the University of Tokyo concluded its investigation, begun in April 2005, into RNA researcher Kazunari Taira and his assistant. It reported that they were unable to provide notebooks to back up their results or to reproduce their experiments and, although it stopped short of finding fraud, fired both.

And in South Korea, the SNU completed its investigation into Hwang in four weeks, publishing its 50-page report on 10 January 2006.

Hisato Kondoh, dean of Osaka University's biosciences school, describes the secret of a successful investigation. "It's important to judge things based on facts, and make the results open as soon as possible, while protecting the rights of people who both reported allegations and are suspected," he says. "If the investigation takes time, everybody gets exhausted. Settling the case at the earliest possible opportunity and bringing the situation back to normal benefits all of us." ■

With additional reporting by Alison Abbott, David Cyranoski, Ichiko Fuyuno, Jim Giles and Lucy Odling-Smee.

See Editorial, page 229.



AHN YOUNG-JOON/AP

Different approaches: Purdue University (top left) is accused of dragging its feet, whereas the investigation of Woo Suk Hwang (above) in South Korea started promptly and took just four weeks.

Scientists behaving badly

To protect the integrity of science, we must look beyond falsification, fabrication and plagiarism, to a wider range of questionable research practices, argue **Brian C. Martinson, Melissa S. Anderson and Raymond de Vries.**

Serious misbehaviour in research is important for many reasons, not least because it damages the reputation of, and undermines public support for, science. Historically, professionals and the public have focused on headline-grabbing cases of scientific misconduct, but we believe that researchers can no longer afford to ignore a wider range of questionable behaviour that threatens the integrity of science.

We surveyed several thousand early- and mid-career scientists, who are based in the United States and funded by the National Institutes of Health (NIH), and asked them to report their own behaviours. Our findings reveal a range of questionable practices that are striking in their breadth and prevalence (Table 1). This is the first time such behaviours have been analysed quantitatively, so we cannot know whether the current situation has always been the case or whether the challenges of doing science today create new stresses. Nevertheless, our evidence suggests that mundane 'regular' misbehaviours present greater threats to the scientific enterprise than those caused by high-profile misconduct cases such as fraud.

As recently as December 2000, the US Office of Science and Technology Policy (OSTP) defined research misconduct as "fabrication, falsification, or plagiarism (FFP) in proposing, performing, or reviewing research, or in reporting research results"¹. In 2002, the Federation of American Societies for Experimental Biology and the Association of American Medical Colleges objected to a proposal by the US Office of Research Integrity (ORI) to conduct a survey that would collect empirical evidence of behaviours that can undermine research integrity, but which fall outside the OSTP's narrow definition of misconduct^{2,3}. We believe that a valuable opportunity was wasted as a result.

A proper understanding of misbehaviour requires that attention be given to the negative aspects of the research environment. The modern scientist faces intense competition, and is further burdened by difficult, sometimes unreasonable, regulatory, social, and managerial demands⁴. This mix of pressures creates many possibilities for

"Our findings suggest that US scientists engage in a range of behaviours extending far beyond falsification, fabrication and plagiarism."

Top ten behaviours	All	Mid-career	Early-career
1. Falsifying or 'cooking' research data	0.3	0.2	0.5
2. Ignoring major aspects of human-subject requirements	0.3	0.3	0.4
3. Not properly disclosing involvement in firms whose products are based on one's own research	0.3	0.4	0.3
4. Relationships with students, research subjects or clients that may be interpreted as questionable	1.4	1.3	1.4
5. Using another's ideas without obtaining permission or giving due credit	1.4	1.7	1.0
6. Unauthorized use of confidential information in connection with one's own research	1.7	2.4	0.8 ***
7. Failing to present data that contradict one's own previous research	6.0	6.5	5.3
8. Circumventing certain minor aspects of human-subject requirements	7.6	9.0	6.0 **
9. Overlooking others' use of flawed data or questionable interpretation of data	12.5	12.2	12.8
10. Changing the design, methodology or results of a study in response to pressure from a funding source	15.5	20.6	9.5 ***
Other behaviours			
11. Publishing the same data or results in two or more publications	4.7	5.9	3.4 **
12. Inappropriately assigning authorship credit	10.0	12.3	7.4 ***
13. Withholding details of methodology or results in papers or proposals	10.8	12.4	8.9 **
14. Using inadequate or inappropriate research designs	13.5	14.6	12.2
15. Dropping observations or data points from analyses based on a gut feeling that they were inaccurate	15.3	14.3	16.5
16. Inadequate record keeping related to research projects	27.5	27.7	27.3

Note: significance of χ^2 tests of differences between mid- and early-career scientists are noted by ** ($P < 0.01$) and *** ($P < 0.001$).

the compromise of scientific integrity that extend well beyond FFP.

We are not the first to call attention to these issues — debates have been ongoing since questionable research practices and scientific integrity were linked in 1992 report by the National Academy of Sciences⁵. But we are the first to provide empirical evidence based on self reports from large and representative samples of US scientists that document the occurrence of a broad range of misbehaviours.

The few empirical studies that have explored misbehaviour among scientists rely on confirmed cases of misconduct⁶ or on scientists' perceptions of colleagues' behaviour⁷⁻⁹, or have used small, non-representative samples of respondents^{8,9}. Although inconclusive, previous estimates of the prevalence of FFP range from 1% to 2%. Our 2002 survey was based on large, random samples of scientists drawn from two databases that are maintained by the NIH Office of

Extramural Research. The mid-career sample of 3,600 scientists received their first research-project (R01) grant between 1999 and 2001. The early-career sample of 4,160 NIH-supported postdoctoral trainees received either individual (F32) or institutional (T32) postdoctoral training during 2000 or 2001.

Getting data

To assure anonymity, the survey responses were never linked to respondents' identities. Of the 3,600 surveys mailed to mid-career scientists, 3,409 were deliverable and 1,768 yielded usable data, giving a 52% response rate. Of the 4,160 surveys sent to early-career scientists, 3,475 were deliverable, yielding 1,479 usable responses, a response rate of 43%.

Our response rates are comparable to those of other mail-based surveys of professional populations (such as a 54% mean response rate from physicians¹⁰). But our approach certainly leaves room for potential non-response bias; misbehaving scientists may have been less likely than others to respond to our survey, perhaps for fear of discovery and potential sanction. This, combined with the fact that there is

probably some under-reporting of misbehaviours among respondents, would suggest that our estimates of misbehaviour are conservative.

Our survey was carried out independently of, but at around the same time as, the ORI proposal. The specific behaviours we chose to examine arose from six focus-group discussions held with 51 scientists from several top-tier research universities, who told us which misbehaviours were of greatest concern to them. The scientists expressed concern about a broad range of specific, sanctionable conducts that may affect the integrity of research.

To affirm the serious nature of the behaviours included in the survey, and to separate potentially sanctionable offences from less serious behaviours, we consulted six compliance officers at five major research universities and one independent research organization in the United States. We asked these compliance officers to assess the likelihood that each behaviour, if discovered, would get a scientist into trouble at the institutional or federal level. The first ten behaviours listed in Table 1 were seen as the most serious: all the officers judged them as likely to be sanctionable, and at least four of the six officers judged them as very likely to be sanctionable. Among the other behaviours are several that may best be classified as carelessness (behaviours 14 to 16).

Admitting to misconduct

Survey respondents were asked to report in each case whether or not ('yes' or 'no') they themselves had engaged in the specified behaviour during the past three years. Table 1 reports the percentages of respondents who said they had engaged in each behaviour. For six of the behaviours, reported frequencies are under 2%, including falsification (behaviour 1) and plagiarism (behaviour 5). This finding is consistent with previous estimates derived from less robust evidence about misconduct. However, the frequencies for the remaining behaviours are 5% or above; most exceed 10%. Overall, 33% of the respondents said they had engaged in at least one of the top ten behaviours during the previous three years.

Among mid-career respondents, this proportion was 38%; in the early-career group, it was 28%. This is a significant difference ($\chi^2 = 36.34$, d.f. = 1, $P < 0.001$). For each behaviour where mid- and early-career scientists' percentages differ significantly, the former are higher than the latter.

Although we can only speculate about the observed sub-group differences, several explanations are plausible. For example, opportunities to misbehave, and perceptions of the likelihood or consequences of being caught, may change during a scientist's career. Or it may be that these groups

received their education, training, and work experience in eras that had different behavioural standards. The mid-career respondents are, on average, nine years older than their early-career counterparts (44 compared with 35 years) and have held doctoral degrees for nine years longer.

Another possible explanation for sub-group differences is the under-reporting of misbehaviours by those in relatively tenuous, early-career positions. Over half (51%) of the mid-career respondents have positions at the associate-professor level or above, whereas 58% of our early-career sample are post-doctoral fellows.

Addressing the problem

Our findings suggest that US scientists engage in a range of behaviours extending far beyond FFP that can damage the integrity of science. Attempts to foster integrity that focus only on FFP therefore miss a great deal. We assume that our reliance on self reports of behaviour is likely to lead to under-reporting and therefore to conservative estimates, despite assurances of anonymity. With as many as 33% of our survey respondents admitting to one or more of the top-ten behaviours, the scientific community can no longer remain complacent about such misbehaviour.

Early approaches to scientific misconduct focused on 'bad apples'. Consequently, analyses of misbehaviour were limited to discussions of individual traits and local (laboratory and departmental) contexts as the most likely determinants. The 1992 academy report⁵ helped shift attention from individuals with 'bad traits' towards general scientific integrity and the 'responsible conduct of research.'

Over the past decade, government agencies and professional associations interested in promoting integrity have focused on responsible conduct in research^{5,11,12}. However, these efforts still prioritize the immediate laboratory and departmental contexts of scientists' work, and are typically confined to 'fixing' the behaviour of individuals.

Missing from current analyses of scientific integrity is a consideration of the wider research environment, including institutional and systemic structures. A 2002 report from the Institute of Medicine directed attention to the environments in which scientists work, and recommended an institutional (primarily university-level) approach to promoting responsible research¹³. The institute's report also noted the potential importance of the broader scientific environment, including regulatory and funding agencies, and the peer-review system, in fostering or hindering integrity, but remained mostly silent on this issue owing to a dearth of evidence.

In our view, certain features of the research working environment may have unexpected

and potentially detrimental effects on the ethical dimensions of scientists' work. In particular, we are concerned about scientists' perceptions of the functioning of resource distribution processes. These processes are embodied in professional societies, through peer-review systems and other features of the funding and publishing environment, and through markets for research positions, graduate students, journal pages and grants. In ongoing analyses, not yet published, we find significant associations between scientific misbehaviour and perceptions of inequities in the resource distribution processes in science. We believe that acknowledging the existence of such perceptions and recognizing that they may negatively affect scientists' behaviours will help in the search for new ways to promote integrity in science.

Little attention has so far been paid to the role of the broader research environment in compromising scientific integrity. It is now time for the scientific community to consider what aspects of this environment are most salient to research integrity, which aspects are most amenable to change, and what changes are likely to be the most fruitful in ensuring integrity in science. ■

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SMALL SPARKS PACK A BIG PUNCH
Sparks made in the lab offer clues to how lightning works
www.nature.com/news

Universities scramble to assess scope of falsified results

Biologists are rushing to quantify the fallout from a case of scientific misconduct unmasked last week. The Massachusetts Institute of Technology (MIT) confirmed on 27 October that it had fired immunologist Luk Van Parijs for fabricating and falsifying data.

The institute said that Van Parijs, an associate professor of biology, had acknowledged to its officials that he altered data in one published article, in unpublished manuscripts and in grant applications. The California Institute of Technology (Caltech) and Harvard University have both now opened inquiries into some of Van Parijs's other published work.

Authorities at all three universities say they have found no evidence that anyone else was involved in the misconduct. Van Parijs previously worked in the labs of Caltech's president, David Baltimore, and physician Abul Abbas, head of pathology at the University of California, San Francisco.

Van Parijs, a 35-year-old native of Belgium who lives in Falmouth, Massachusetts, did not respond to interview requests. His primary studies involved using short pieces of RNA to silence genes that have gone awry in autoimmune diseases. Early indications suggest that his misconduct will not affect his field as dramatically as semiconductor research was affected by Bell Laboratories physicist Jan Hendrik Schön¹. Colleagues spent years following Schön's line of research until in 2002 it was discovered that he had falsified some of his data.

Van Parijs co-authored a heavily cited paper for *Nature Genetics* in 2003 describing how to use a stripped-down virus, called a lentivirus, as a delivery system for genes that can silence other genes². The paper has not been called into question, and other researchers have shown that the approach works, at least in animal models and cell cultures. Clinical trials in human patients are now being planned.

infects cells in a different way from the one that causes AIDS.

John Moore from Cornell University in New York and his colleagues tried a different approach (see page 99). They combined three compounds that each uses a different mechanism to block the virus's entry into cells. Merck's compound CMPD167 competes with the virus for cell

receptors inside the vagina. Bristol-Myers Squibb's BMS-378806 interacts with the virus itself, stopping it binding to cells. And a peptide developed by Moore's team inhibits the process used by the virus to enter a cell.

When the researchers tested combinations of the compounds in macaques, they found that they offered at least partial protection

against a virus closely resembling HIV. But three animals that received the three compounds together were all protected against infection. These results were enough to persuade the drug firms to give away rights to the compounds, says Moore. "This is the first time there has been a joint announcement like this," adds Mark Mitchnick, chief scientific officer of the International Partnership for

Microbicides, the non-profit group that will develop the gel.

Partners including the Bill and Melinda Gates Foundation and the US National Institutes of Health are helping to fund a clinical trial, set to start in 2007. This is estimated to cost between US\$150 million and \$200 million and will involve about 10,000 women in Africa. ■
Narelle Towie

IMAGE
UNAVAILABLE
FOR COPYRIGHT
REASONS

Sacked: Luk Van Parijs, seen as a rising star in biology, was found to have falsified data.

Because of such work, Van Parijs was considered a rising star. "He had incredible potential," says Abbas, who worked with him in 1997 and 1998 at Brigham and Women's Hospital in Boston. "He was a superstar in the making."

But in August 2004, MIT put Van Parijs on administrative leave after some of his lab colleagues made allegations of misconduct to the institute's authorities. After the lab was closed, his students and postdocs scrambled to get jobs elsewhere, and MIT began the inquiry that culminated in his sacking.

Abbas says that Van Parijs has e-mailed him

and denied falsifying data in more than one paper. "He apologized for the disappointment he has caused," Abbas says.

MIT officials say that they will submit the results of their investigation to the Office of Research Integrity, the federal agency that monitors research conduct for the US National Institutes of Health. It has been at least a decade since the institute has uncovered a case of misconduct, the officials say.

MIT has not publicly identified the paper that contains the falsified results. But in May, *Current Opinion in Molecular Therapeutics* published a correction to a 2004 review^{3,4} on which Van Parijs was the lead author. The note said that unpublished experiments cited in the paper — involving genetically controlling tumour growth in mice — could not be documented.

Investigators are now probing several of Van Parijs's older publications. Caltech is looking at two articles published in *Immunity*, including one co-authored by Baltimore^{5,6}. And Harvard is looking into a 1997 paper in the *Journal of Experimental Medicine*⁷.

The *Immunity* work dealt with a cell signalling pathway that governs the processes by which cells in the immune system live and die. An expert in the field, who asked not to be named, said that Van Parijs's experiments had never directly been replicated. "We really would like to know if the work is reproducible, so the field can move forward," the immunologist said, "or whether we have to do an about-face." ■

Rex Dalton

Additional reporting by Erika Check

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Where are they now?

Nature catches up with some past fraud investigations — and finds that, whether researchers are found to be guilty or innocent, the wounds are slow to heal.

JON SUDBØ



NORWEGIAN RADIUM HOSP.

Jon Sudbø, a doctor and researcher at the Norwegian Radium Hospital in Oslo, confessed in January 2006 to fraud on an extraordinary scale (see *Nature* 439, 248–249; 2006). He admitted creating some 900 fictitious patients in a 2005 *Lancet* paper on the effect of certain painkillers on oral cancer risk in smokers, since retracted. An independent commission of inquiry was set up to discern the details of the fraud; last June it reported that the bulk of Sudbø's 30-plus publications were invalid because of the fabrication and manipulation of data.

Sudbø resigned the day after the commission released its report and was stripped of his medical and discipline degrees late last year. He is reportedly still in Oslo with his family but not working. Richard Horton, editor of *The Lancet*, co-hosted a meeting in Norway last month to establish what could be learnt from the case. He thinks that because Sudbø used public funds to pay for fraudulent work, he will probably face criminal proceedings. **L.O.-S.**

THEREZA IMANISHI-KARI



A 1986 paper in *Cell* on immunity in transgenic mice acquired international fame — not because of what it reported, but because of the

slew of investigations it spurred. Among the paper's authors were Thereza Imanishi-Kari and Nobel laureate David Baltimore, then both at the Massachusetts Institute of Technology. A postdoc in Imanishi-Kari's lab accused her of falsifying data in the *Cell* paper. The decade-long saga that followed involved a series of investigations, including one by the Energy and Commerce Congressional committee. Imanishi-Kari was cleared of all charges in 1996.

After doing no research for ten years, Imanishi-Kari reorganized a research programme at Tufts University in Medford, Massachusetts. Although pleased with the response of colleagues to her publications, she feels the case still overshadows her grant applications. "Being a woman in science is one kind of handicap; being wrongly accused is another," she says.

Henry Wortis, one of Imanishi-Kari's collaborators at Tufts, says people should judge her by her current work, published in leading journals such as *Immunity*. "That's the quality of work she's been unable to do for ten years," he says. "It's been a considerable loss to research." **L.O.-S.**

JAN HENDRIK SCHÖN



The fraud that came to light in the spring of 2002 is by far the most serious to strike physics in recent years. Jan Hendrik Schön was a rising star at Lucent Technologies' prestigious Bell Laboratories in Murray Hill, New Jersey, and author of a string of papers in *Nature* and *Science*. His reputation collapsed following a Bell Labs report that found Schön guilty of falsifying data in at least 16 papers on the electronic properties of new materials, such as organic films that might one day replace silicon-based electronics.

Schön's whereabouts are now unknown, and

he has declined to comment on his research while investigations are continuing (the University of Konstanz in Germany is still assessing the work he did to earn his PhD there in the mid-1990s). But shock waves from the case have hit physicists, mainly in the shape of new research guidelines. Some of Schön's co-authors were criticized for not spotting their colleague's misconduct, prompting the American Physical Society to issue new rules stating that co-authors should be accountable for important data in papers they sign off. **J.G.**

ANDERS PAPE MØLLER



T. A. MOUSSEAU

In late 2003, the Danish Committees on Scientific Dishonesty concluded that Anders Pape Møller, one of the world's leading experts in behavioural ecology, was guilty of 'scientific dishonesty'. A former colleague, Jørgen Rabøl, had accused Møller of using flawed data in a paper published in the journal *Oikos*. The paper has since been retracted.

Unconvinced, the National Council for Scientific Research in Paris, where Møller was and is still based, appointed an independent 'committee of wise men' to examine the case. In late 2004, the committee concluded that Møller was innocent: although it found that good lab practices hadn't been followed, it could not prove intent to commit scientific fraud. Møller did not respond to invitations for interview.

An impressive publication list in the past two years suggests that Møller's output has not been dimmed. But a collaborator, Timothy Mousseau at the University of South Carolina in Columbia, says that the consequences of the case rumble on. "Even though a complete investigation found no evidence, people get emotionally caught up in these kinds of interactions. There is no easy way to clear your name." **L.O.-S.**

BELL LABS

**WOO SUK HWANG**

Follow the story of the infamous South Korean stem-cell researcher online. www.nature.com/news/specials/hwang

BAE JAE-MAN/YONHAP/AP

WOO SUK HWANG

South Korea's stem-cell researcher Woo Suk Hwang is arguably the highest-profile scientific fraudster ever. In two hugely cited papers in *Science* in 2004 and 2005, Hwang claimed to have derived stem cells from cloned human embryos. But on 10 January 2006, Seoul National University announced after a four-week investigation that all of his claims were fabricated.

The legal issues have been harder to clear up than the scientific ones. Prosecutors started an investigation the day that the university report was released, and delivered their own report on 12 May 2006. They charged Hwang with fraud, embezzlement, and violation of the country's bioethics law. But more than half-a-dozen hearings later, the court has still not reached a conclusion. The proceedings have not prevented Hwang from doing research: he is now carrying out animal cloning experiments at his new laboratory in Yongjin, 50 kilometres south of Seoul. **D.C.**

SHINICHI FUJIMURA

In the 1980s and 1990s, amateur archaeologist Shinichi Fujimura was known throughout Japan for his 'divine hands', thanks to his

discovering a string of stone artefacts that dated back to 700,000 years ago. Then in 2000, Japanese newspaper *Mainichi Shimbun* published photos of Fujimura digging holes to bury tools that he later announced as major finds, and he confessed to fraud.

The Japanese Archaeological Association released the results of its final investigation in 2004. It concluded that all of the 168 sites dug by Fujimura had been faked — forcing Japanese history textbooks to rewrite their descriptions of the Palaeolithic period. The Tohoku Paleolithic Institute, where Fujimura held the post of deputy director, was also dissolved in 2004.

Fujimura, aged 56 years, was hospitalized for mental illness, and then reportedly remarried, changed his name and is now living quietly in a small town near the Pacific coast. **I.F.**

LUK VAN PARIJS

Once considered an exciting prospect in immunology and RNA interference, Luk Van Parijs was sacked from the Massachusetts Institute of Technology (MIT) in Cambridge in October 2005 after admitting that he had altered data in a published paper, unpublished manuscripts and grant applications. The

institute inquiry that prompted the confession was sparked by allegations from some of his lab members.

Surprisingly, Van Parijs has co-authored a publication since the scandal, on a paper published in *The Prostate* in February 2006. The study's first author — urologist Qiang Zhang of Northwestern University in Chicago, Illinois — says that he and his co-authors included Van Parijs as an author because he had provided helpful ideas when giving a seminar in Zhang's department a few years earlier. He and other collaborators contacted by *Nature* have not communicated with Van Parijs since he left MIT. **L.O.-S.**

BENGÜ SEZEN

In March 2006, Dalibor Sames, a chemist at Columbia University in New York, withdrew two papers and part of a third from the *Journal of the American Chemical Society* (JACS). Work done by graduate student Bengü Sezen, he said, couldn't be reproduced. The work was in the field of carbon-hydrogen bond functionalization, which aims to selectively break bonds within a molecule.

The case got a lot of coverage on the ever-lively chemistry blogs, and a few press outlets mentioned the issue, including *Nature* (**440**, 390–391; 2006).

Sames is not commenting further until an inquiry is completed, and Columbia University says that it is against its policy to "comment on the existence or non-existence of any internal investigation into allegations of research misconduct". But Sezen has vigorously defended herself in e-mails to the editor of *JACS* and the press. **E.M.**

Lucy Odling-Smee, Jim Giles, Ichiko Fuyuno, David Cyranoski, Emma Marris

E. QUINN/CORBIS

How much fraud?

Statistics relating to the prevalence of scientific fraud and misconduct are sparse. But here are a few.

UNITED STATES

Of 3,247 researchers funded by the National Institutes of Health who responded to a survey, 1.4% admitted to plagiarism and 0.3% admitted to falsification of data. 15.5% of responders said that they had changed the design, methodology or results of a study in response to pressure from a funding source (B. C. Martinson *et al. Nature* **435**, 737–738; 2005).

In 2005, the Office of Research Integrity received 265 allegations of misconduct. Of 22 cases that it closed in that year, research misconduct was found in eight. Of these eight cases, three were for falsification; two involved falsification and fabrication; two involved fabrication; and one involved plagiarism.

UNITED KINGDOM

Of 13 cases of suspected fraud brought to the Committee on Publication Ethics (COPE) between 1998 and 2003, seven

were given up because of lack of documentation or lack of a response from the author or institution.

JAPAN

Of 1,323 research institutes that responded to a Science Council of Japan survey in 2006, only 13.4% had guidelines on what behaviours are defined as misconduct and how to act if misconduct is reported. Just 12.4% of institutes had discussed dishonest behaviour with their researchers in the past ten years.

GERMANY

The ombudsmen of the German Research Foundation (DFG) were called in 45 cases of misconduct in 2004, and took up 36 of them. Of these 36 cases, misconduct was found in one investigation.

DENMARK

Of 25 investigations that were concluded by the Danish Committees on Scientific Dishonesty between 2003 and 2005, dishonest behaviour was found in two of them.



A dolphin's demise

1860



Indians wary of nuclear pact

1863

SCIENTIFIC PUBLISHING

A Scientist's Nightmare: Software Problem Leads to Five Retractions

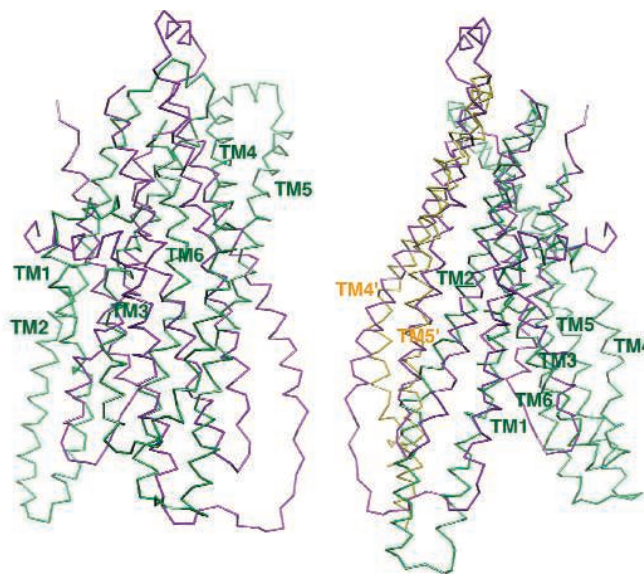
Until recently, Geoffrey Chang's career was on a trajectory most young scientists only dream about. In 1999, at the age of 28, the protein crystallographer landed a faculty position at the prestigious Scripps Research Institute in San Diego, California. The next year, in a ceremony at the White House, Chang received a Presidential Early Career Award for Scientists and Engineers, the country's highest honor for young researchers. His lab generated a stream of high-profile papers detailing the molecular structures of important proteins embedded in cell membranes.

Then the dream turned into a nightmare. In September, Swiss researchers published a paper in *Nature* that cast serious doubt on a protein structure Chang's group had described in a 2001 *Science* paper. When he investigated, Chang was horrified to discover that a homemade data-analysis program had flipped two columns of data, inverting the electron-density map from which his team had derived the final protein structure. Unfortunately, his group had used the program to analyze data for other proteins. As a result, on page 1875, Chang and his colleagues retract three *Science* papers and report that two papers in other journals also contain erroneous structures.

"I've been devastated," Chang says. "I hope people will understand that it was a mistake, and I'm very sorry for it." Other researchers don't doubt that the error was unintentional, and although some say it has cost them time and effort, many praise Chang for setting the record straight promptly and forthrightly. "I'm very pleased he's done this because there has been some confusion" about the original structures, says Christopher Higgins, a biochemist at Imperial College London. "Now the field can really move forward."

The most influential of Chang's retracted publications, other researchers say, was the

2001 *Science* paper, which described the structure of a protein called MsbA, isolated from the bacterium *Escherichia coli*. MsbA belongs to a huge and ancient family of molecules that use energy from adenosine triphosphate to transport molecules across cell membranes. These so-called ABC transporters perform many



Flipping fiasco. The structures of MsbA (purple) and Sav1866 (green) overlap little (left) until MsbA is inverted (right).

essential biological duties and are of great clinical interest because of their roles in drug resistance. Some pump antibiotics out of bacterial cells, for example; others clear chemotherapy drugs from cancer cells. Chang's MsbA structure was the first molecular portrait of an entire ABC transporter, and many researchers saw it as a major contribution toward figuring out how these crucial proteins do their jobs. That paper alone has been cited by 364 publications, according to Google Scholar.

Two subsequent papers, both now being retracted, describe the structure of MsbA from other bacteria, *Vibrio cholera* (published in *Molecular Biology* in 2003) and *Salmonella typhimurium* (published in *Science* in 2005). The other retractions, a 2004 paper in the *Proceedings of the National Academy of*

Sciences and a 2005 *Science* paper, described EmrE, a different type of transporter protein.

Crystallizing and obtaining structures of five membrane proteins in just over 5 years was an incredible feat, says Chang's former postdoc adviser Douglas Rees of the California Institute of Technology in Pasadena. Such proteins are a challenge for crystallographers because they are large, unwieldy, and notoriously difficult to coax into the crystals needed for x-ray crystallography. Rees says determination was at the root of Chang's success: "He has an incredible drive and work ethic. He really pushed the field in the sense of getting things to crystallize that no one else had been able to do." Chang's data are good, Rees says, but the faulty software threw everything off.

Ironically, another former postdoc in Rees's lab, Kaspar Locher, exposed the mistake. In the 14 September issue of *Nature*, Locher, now at the Swiss Federal Institute of Technology in Zurich, described the structure of an ABC transporter called Sav1866 from *Staphylococcus aureus*. The structure was dramatically—and unexpectedly—different from that of MsbA. After pulling up Sav1866 and Chang's MsbA from *S. typhimurium* on a computer screen, Locher says he realized in minutes that the MsbA structure was inverted. Interpreting the "hand" of a molecule is always a challenge for crystallographers,

Locher notes, and many mistakes can lead to an incorrect mirror-image structure. Getting the wrong hand is "in the category of monumental blunders," Locher says.

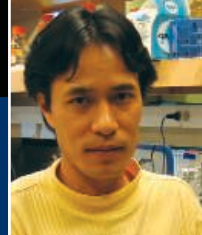
On reading the *Nature* paper, Chang quickly traced the mix-up back to the analysis program, which he says he inherited from another lab. Locher suspects that Chang would have caught the mistake if he'd taken more time to obtain a higher resolution structure. "I think he was under immense pressure to get the first structure, and that's what made him push the limits of his data," he says. Others suggest that Chang might have caught the problem if he'd paid closer attention to biochemical findings that didn't jibe well with the MsbA structure. "When the first structure came out, we and others said, 'We really ▶



1866



1868



1871

don't quite believe this is right," says Higgins. "It was inconsistent with a lot of things."

The ramifications of the software snafu extend beyond Chang's lab. Marwan Al-Shawi, a biochemist at the University of Virginia in Charlottesville, says he's now holding on to several manuscripts he was about to submit. Al-Shawi has been using Chang's MsbA structure to build computer models of an ABC transporter involved in human cancer drug resistance. David Clarke of the University of

Toronto in Canada says his team had a hard time persuading journals to accept their biochemical studies that contradicted Chang's MsbA structure. Clarke also served on grant panels on which he says Chang's work was influential. "Those applications providing preliminary results that were not in agreement with the retracted papers were given a rough time," he says.

At Scripps, colleagues are standing behind the young researcher. "He's doing some really

beautiful work, and this is just an absolute disaster that befell him," says Chang's department chair, Peter Wright. "I'm quite convinced he'll come out of it, and he'll go on to do great things." Chang meanwhile has been reanalyzing his original data and expects to submit papers on the corrected structures soon. The new structures "make a ton of sense" biologically, he says. "A lot of things we couldn't figure out before are very clear."

—GREG MILLER

U.S. OCEAN POLICY

Fisheries Bill Gives Bigger Role to Science—But No Money

New rules governing the U.S. fishing industry offer scientists much greater power to keep marine populations from collapsing. But although advocates for marine conservation are celebrating the changes in a 30-year-old law that Congress adopted earlier this month, they are disappointed that the focus remains on managing individual species rather than ecosystems. And they worry that the responsible agency—the National Oceanic and Atmospheric Administration (NOAA)—may not have enough money to implement many of the provisions in the revised law.

The bill, a reauthorization of the 1976 Magnuson-Stevens Fishery Conservation and Management Act, requires the eight regional fishery councils to follow the advice of their scientific committees, prevents continued overfishing, and calls for more research by NOAA on deep-sea corals. "We're very excited," says Steven Murawski, chief science adviser for NOAA Fisheries. The bill awaits the president's signature after legislators gave their approval in the final hours of the 109th Congress. Yet that same Congress failed to complete work on the 2007 budgets of most agencies, including NOAA's (*Science*, 15 December, p. 1666), raising doubts about how the agency will manage existing operations, let alone take on new ones. "Where is the money for all this?" wonders John Ogden, director of the Florida Institute of Oceanography in Tampa.

The new version is the first update in a decade. Environmentalists and researchers had feared that the revision might weaken the current law, because the House Resources Committee had proposed abolishing a rule requir-

ing depleted stocks to be rebuilt within 10 years. But the deadline remains in place. "I'm very gratified," says Carl Safina of Stony Brook University in New York.

The bill breaks new ground by telling councils to end overfishing within 2 years after a species is deemed overfished. The current law was vague, and some councils allowed continued overfishing on the way to a rebuilding target, a practice that has made recovery harder for some species. "It's a significant improvement," says Gerald Leape of the National Environmental Trust in Washington, D.C.



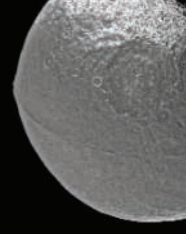
Catch phrases. New fishery legislation is intended to stop overfishing of species whose populations have crashed, such as these cod in Gloucester, Massachusetts.

In addition, councils will now be required to set catch limits and to follow scientific advice, two practices that are voluntary under the current law. But a Senate provision for penalties when fishers end up exceeding an annual limit was removed before final passage, and even setting all the catch limits is in question. The six NOAA fishery science centers that crank out most of the limits will require more resources, as well as more data from observers and NOAA survey vessels. This workload "is certainly a challenge," admits Murawski, referring to a pending 2007 spending plan that could shrink NOAA Fisheries' budget from \$667 million to \$541 million.

The same budget uncertainties imperil several other directives. A registry for recreational marine fishing and grant licenses would allow the agency to better estimate the impact of non-commercial catches (*Science*, 24 September 2004, p. 1958). But Murawski warns that "it's not going to be a cheap program." Another mandate would create a research program to map and monitor deep-sea corals.

Many scientists are deeply disappointed that the bill does not require an ecosystem-based approach to managing fisheries, as was recommended by several recent commissions. Instead, the bill continues the current species-by-species approach, while requesting a 180-day NOAA study of the state of the science of ecosystem management. It also authorizes the agency to begin funding pilot programs based on the study but doesn't set a level. "It's a major missed opportunity," says Ellen Pikitch of the University of Miami's Pew Institute for Ocean Science in Florida.

—ERIK STOKSTAD



STEM CELLS

How Young Korean Researchers Helped Unearth a Scandal ...

SEOUL AND TOKYO—The announcement delivered a devastating blow to stem cell researchers around the world: On 29 December, a Seoul National University (SNU) investigative team said there was no evidence Woo Suk Hwang and his team had produced any of the patient-specific stem cells they described in a June 2005 *Science* paper. Many Koreans lamented that the revelations dashed the country's hopes for worldwide scientific respect. But the report also vindicated dozens of anonymous young Korean scientists who, without knowing one another, worked together and with the media to unravel a huge scientific fraud.

Two papers published in *Science* by Hwang and colleagues at several institutions in Korea and the United States were hailed as seminal breakthroughs in stem cell research. A March 2004 paper reported the first stem cell line produced from a cloned human embryo. The second paper, published in May 2005, reported the creation of 11 stem cell lines that genetically matched nine patients with spinal cord injury, diabetes, and an immune system disorder. Scientists hope such stem cells could someday lead to insights into many hereditary conditions as well as the creation of replacement tissues genetically matched to patients.

Those hopes, however, began to unravel shortly after midnight on 1 June 2005, when someone sent a message to the "tip off" mailbox on the Web site of a long-running investigative TV news program called *PD Notebook* aired by the Seoul-based Munhwa Broadcasting Corp. (MBC). According to one of the program's producers, Bo Seul Kim, the writer said his conscience had been bothering him over problems he knew of with Hwang's research. Asking *PD Notebook* to contact him, he closed his message by writing: "I hope you don't refuse this offer to get at the truth."

They didn't. When *PD Notebook* execu-

tive producer Seung Ho Choi read the message several days later, he asked producer Hak Soo Han to meet the tipster that night. According to Han's recollection of the meeting, the tipster said he had been involved in the research leading to Hwang's 2004 paper in *Science*. He agreed to an interview on tape as long as his identity was concealed, during which he said he had left the team because of ethical and technical concerns. He claimed that despite Hwang's statements to the contrary, some of the eggs used for that research



Clear misconduct. Jung Hye Roe, SNU's dean of research affairs, announced that the investigative committee found no evidence of cloned stem cells in Hwang's lab.

came from junior researchers in Hwang's lab. Producer Kim says the scientist provided names, donation records, and an e-mail message he had received from one of the researchers saying she had donated eggs under pressure from Hwang. The tipster also claimed that based on his knowledge of the team's work, Hwang couldn't have produced the patient-specific stem cells reported in the 2005 paper, although he admitted having no hard evidence of fabrication.

"It was very difficult for me to believe what this person was suggesting," Han told *Science*. But the tipster's documentation of problems surrounding egg donations seemed trustworthy. So Han decided to look into the 2005 paper as well. The producers persuaded two others with inside knowledge of Hwang's lab to help. Han also recruited three scientists from outside the Hwang team as consultants.

Han says the *PD Notebook* team and its advisers began to identify potential problems with the paper, using tactics that they later conceded were journalistically unethical. Claiming they were working on a documentary about Korean biotechnology, *PD Notebook* reporters interviewed co-authors of the 2005 paper and found that the majority had never actually seen the cloned embryonic stem cells. The TV crew also learned from their

advisers that teratomas, benign tumors that embryonic stem cells form when injected under the skin of experimental mice, had been produced only for stem cell lines 2 and 3; careful scientists would have produced teratomas from all 11 lines.

Kim says that because one of the informers suggested that the stem cell lines in the 2005 paper could have come from MizMedi Hospital in Seoul, the producers requested and received the DNA fingerprinting data for 15 lines derived at the hospital from embryos created through in vitro fertilization. Through one of their sources, the producers got a sample of stem cell line number 2 and passed it to an independent testing laboratory. The lab found that line number 2 genetically matched a MizMedi line. "Did we actually have evidence that Hwang faked his research?" Han recalls wondering. (SNU would come to the same

conclusion months later, announcing on 29 December that stem cell lines 2 and 3 from Hwang's lab came from MizMedi's stem cells.)

Han says he got the news of the lab test results on 19 October while he was in the United States preparing to interview Sun Jong Kim, another co-author of the 2005 paper who had left MizMedi to join the University of Pittsburgh research team led by Gerald Schatten, a Hwang collaborator and co-author of the 2005 paper. In an attempt to



Speak no evil. MBC's initial broadcast on irregularities in egg donation for Hwang's research set off a wave of protests.

get an admission of wrongdoing from Kim, Han says, the TV team resorted to some misrepresentation of its own. When the producers met him on 20 October, Han and his partner filmed Kim with a hidden camera; they didn't reply when he asked if they were recording him. In the interview, Han told Kim they had information that could prove Hwang's work was falsified. He also tricked Kim into believing that Korean prosecutors had begun an investigation and told Kim he didn't want to see him get hurt.

On hidden camera, Kim then told Han he followed directions from Hwang to make photographs of two cell lines appear to represent 11 cell lines. The falsified photos appear in the supplementary online material accompanying the 2005 *Science* paper. Han says he now "really repents" their unethical reporting ruses. And those lapses nearly led to their work being dismissed entirely.

But on 11 November, before *PD Notebook* broadcast any of its findings, Schatten announced he was terminating his relationship with Hwang because of concerns about "ethical breaches" in oocyte collection. Schatten emphasized that he was still confident of the research results. On 22 November, MBC broadcast the *PD Notebook* program containing allegations that donors were paid for eggs used in the research leading to the 2004 paper, that junior lab members were among the donors, and that Hwang had lied about the oocyte sources in the *Science* paper. Two days later, Hwang admitted in a press conference that he knew about junior members donating eggs but lied to protect their privacy. He resigned as director of the newly announced Stem Cell Hub but vowed to continue his research (*Science*, 2 December 2005, p. 1402).

CREDIT: KIM JAE-HWAN/AP/GETTY IMAGES

Despite Hwang's admissions, *PD Notebook* producers bore the brunt of public anger over the revelations. The backlash intensified after Han and another top producer held a 2 December press conference announcing that a report questioning the authenticity of Hwang's work was yet to come. After Sun Jong Kim and another colleague in Pittsburgh, Jong Hyuk Park, told another television program that the interview with *PD Notebook* had been coerced, all 12 of the *PD Notebook* sponsors canceled their ads, and on 4 December, MBC apologized for the producers' use of unethical tactics.

Producer Kim says that 20,000 angry postings filled up MBC's online bulletin boards, and that the network received so many threatening calls that reporters had a hard time using the phones for work. On 7 December, MBC

suspended *PD Notebook* and decided not to air the segment covering questions about the 2005 paper and the interview with Sun Jong Kim.

Given Hwang's popularity among the Korean public and the trust he enjoyed among researchers worldwide, the matter might well have ended there. But, according to an official of the Biological Research Information Center (BRIC), which provides online news on scientific trends and careers primarily for young researchers, at 5:28 a.m. on 5 December, a contributor to a BRIC Internet message board placed a cryptic post with the English header, "The show must go on ..." The anonymous poster suggested that readers look for duplicated pictures among the supporting online material accompanying the 2005 *Science* paper. The poster ended his message with the tease: "I found two! There are rumors that there are more ..."

More than 200 posts followed, identifying apparently duplicated photographs. There was also an online discussion about whether someone

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STEM CELLS

... And How the Problems Eluded Peer Reviewers and Editors

The paper landed in *Science*'s online database on 15 March 2005, a Tuesday. Immediately, the journal's editors recognized a submission of potentially explosive importance. A group in South Korea was describing 11 embryonic stem (ES) cell lines created from the DNA of ailing patients. The advance, eagerly anticipated in the stem cell world, would be a first, and critical to using stem cells to combat disease.

Little did *Science*'s editors, or the nine outside researchers who would examine the paper with varying degrees of scrutiny, realize just how explosive the paper would be. Today, its lead author Woo Suk Hwang stands accused of one of the boldest scientific frauds in memory. Investigators at Seoul National University (SNU), where most of the work was done, announced on 29 December that they could find no evidence of any of the 11 stem cell lines claimed in the paper. On the 10th floor of *Science*'s offices in Washington, D.C., meanwhile, members of the editorial department are spotting problems in Hwang's 2005 paper, as well as another landmark paper from his group published in 2004.

Could *Science* have detected the fraud? *Science*'s editors and many stem cell researchers

believe not: The 2005 paper was positively received by its peer reviewers, upon whom *Science* relied heavily to determine whether the paper was worth publishing. "Peer review cannot detect [fraud] if it is artfully done," says Donald Kennedy, *Science*'s editor-in-chief. And the reported falsifications in the Hwang paper—image manipulation and fake DNA data—were not the sort that reviewers can easily spot.

Martin Blume, editor-in-chief of the American Physical Society and its nine physics journals, says that peer review overlooks honest errors as well as deliberate fraud. "Peer review doesn't necessarily say that a paper is right," he notes. "It says it's worth publishing."

That said, *Science*, like other high-profile journals, aggressively seeks firsts: papers that generate publicity and awe in the scientific community and beyond. The practice comes with some risks, critics say, because by definition firsts haven't been replicated. "Is the reviewing looser" on a potentially high-impact paper? asks Denis Duboule, a geneticist at the University of Geneva, Switzerland, who sits on *Science*'s Board of Reviewing Editors. "Frankly, I don't ▶

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should inform *Science*. Someone did e-mail *Science* editors pointing out the duplicated photos. By that time, however, Hwang had already notified the journal of what he termed an accidental duplication of some of the photos. *Science* editors and scientists around the world were still willing to give Hwang the benefit of the doubt, believing that photos had been mixed up sometime between paper acceptance and publication online.

But the BRIC posts continued. On 6 December, another anonymous BRIC poster wrote that there appeared to be duplications in the DNA fingerprinting traces and posted evidence to support that claim the following day. At about this time, the BRIC postings were reported in the general Korean media and then picked up worldwide. On 12 December, SNU said it would launch an investigation. With public opinion starting to turn, on 15 December, MBC broadcast the *PD Notebook* segment showing Kim—with his face blurred—admitting that he doctored photographs at Hwang's direction. The next day, Hwang and Schatten told *Science* they wanted to withdraw the 2005 paper.

Like most scientists in Korea, Hong Gil Nam, a chemist at Pohang University of Science and

Technology and BRIC's first director, has mixed feelings about how the drama has played out. He's sorry to see the scandal unfold but hopeful that the postings on BRIC indicate that "young scientists have a good attitude toward research integrity."

The SNU committee is continuing its work, investigating the legitimacy of Hwang's 2004 paper in *Science* and the group's more recent paper in *Nature* claiming to have produced the first cloned dog. A host of questions remain about whether and when other people at the lab learned about the fraud. Korea's Supreme Public Prosecutors' Office says it is considering a probe of possible criminal activity, pending the outcome of the SNU investigation. The BRIC message board is as lively as ever. And MBC resumed broadcasting *PD Notebook* on 3 January, this time with more people from within Hwang's lab who were willing to talk about what their disgraced boss had done. Among the revelations, *PD Notebook* alleges that Hwang's team collected more than 1600 oocytes from egg donors—not the 427 originally reported—for cloning research for the 2004 and 2005 papers.

—SEI CHONG AND DENNIS NORMILE

With reporting by Gretchen Vogel.

TERRORISM

Indian Scientist Slain in Surprise Attack

HYDERABAD, INDIA—A retired mathematics professor was shot and killed, and four colleagues were wounded, at the Indian Institute of Science (IISc), one of India's premier research outfits, on 29 December. Police have branded the incident in Bangalore a terrorist attack, although as *Science* went to press, no group had claimed responsibility.

The slain scientist, M. C. Puri of the Indian Institute of Technology in New Delhi, was a specialist in operations research, or the use of mathematics to aid in decision-making. Among the injured is IISc's Vijay Chandru, co-inventor of Simputer, a hand-held computing device. The injuries of Chandru and the other victims were not life-threatening.

The attack came without warning on the last day of an international meeting on operations research. "There were no security alerts issued to us," says IISc Director Padmanabhan Balaram. According to eyewitness accounts, at about 7:30 p.m., a single gunman wielding an automatic rifle began spraying bullets into a crowd of scientists filing out of an auditorium after the day's last talk. "A few of us were walking to the next building when we heard sounds like the heavy use of firecrackers," says S. Sadagopan, direc-

tor of the Indian Institute of Information Technology in Bangalore. On 3 January, police announced the arrest of a suspect: a 35-year-old man who claimed to be a member of Lashkar-e-Taiba, a Pakistan-based militant organization.



Victim. M. C. Puri.

The incident has sent jitters through India's vast R&D establishment. At the annual Indian Science Congress here in Hyderabad this week, police assigned 5000 officers to protect the 5000 participants, including 75 foreigners. And aftershocks are being felt in Bangalore. In addition to IISc, the region, India's Silicon Valley, is home to more than 150 information technology firms, the Indian Space Research Organization, and several high-profile defense labs. The space and defense labs say they have enhanced

already tight security. But IISc, with more than 400 researchers and 2000 students, is an academic campus largely open to the public. Balaram says he does not want IISc to become a high-security zone as a consequence of the attack: "The ambience of the university will be lost if you convert it into an armed fortress."

—PALLAVA BAGLA

Some Things on the Horizon for 2006:

European Thumbs Green for GM

BERLIN—The new year is looking brighter for European researchers and farmers who want to plant genetically modified (GM) crops. On 14 December, the German government approved the first three varieties of GM maize to be allowed in the country, and a few days later, new agricultural minister Horst Seehofer said he would encourage the planting of GM crops. That's a stark contrast from Seehofer's predecessor, Renate Kunast, who as a member of the Green Party pushed through restrictions on GM planting that researchers said made field trials impossible (*Science*, 25 June 2004, p. 1887).

In late December, the European Commission proposed new rules that would allow organic foods to be labeled as such with up to 0.9% accidental contamination with GM products or seeds from neighboring farms or during processing. Several consumer groups have vowed to fight the proposal to protect what Friends of the Earth Europe says are consumers who want food free of "genetic contamination."

—GRETCHEN VOGEL

Lobbyists Tout Funding Poll

Science boosters believe that the results of a November poll offer one more reason for lawmakers to jump onto the bandwagon this year and increase federal support for academic research—especially if nobody thinks too much about what the answers might mean.

Commissioned by a coalition of business leaders, educators, and professional societies (futureofinnovation.org), the survey reports that 78% of 800 adults, all registered voters, favor spending tax dollars on academic science. Some 70% say they like a key component of one plan being peddled to Congress (*Science*, 21 October 2005, p. 423) that would increase federal funding for the physical sciences by 10% annually for the next 7 years. Support tops 80% among Democrats and those with postgraduate training.

Still, answers to an open-ended question about the value of "university research" revealed some fuzziness about what that phrase actually signifies. One respondent, for example, wrote that "it is very important that young kids get an opportunity [to learn math and science]"; another noted that "education is one of the most important issues we face today."

—JEFFREY MERVIS