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Standards for papers on cloning

In the wake of the Hwang scandal, journals have been reviewing their refereeing procedures. Following a survey of experts, here are *Nature*'s thoughts on papers about cloning, with an invitation to comment.

Cloning cells or organisms by nuclear transfer is laborious, time-consuming and expensive. The timescale for replication of published results may be on the order of years. But conversely, a successful cloning experiment has the advantage, rare in science, that it can usually be evaluated relatively easily, by DNA testing of tissues collected during the procedure.

Peer review aims to assess credibility but is by and large incapable of detecting dishonesty (although *Nature* is currently reviewing its procedures with respect to image manipulation). With the caveat that peer review will continue to be based largely on trust, what data can be regarded as sufficient proof of cloning? Before the Hwang scandal, the gold standard for proving that an animal had been cloned from nuclear transfer was to test for identical nuclear DNA fingerprints of the clone and nuclear donor. On the other hand, mitochondrial DNA from the cloned animal should differ from that of the nuclear donor, providing a straightforward way of ruling out sample mishandling or outright fraud.

In the light of all that has happened, we think it sensible from now on to ask authors to provide not only nuclear but also mitochondrial DNA fingerprints for all cloning papers submitted to *Nature*. It should be noted, however, that there may be confounding factors in interpreting such data. For instance, the mitochondrial contribution of the nuclear donor may vary depending on the species, on whether it is an interspecies hybrid, and on the nuclear-transfer technique used. In the case of papers reporting new embryonic stem-cell lines, nuclear DNA fingerprints of the lines should be presented for comparison with existing lines, to help rule out sample mishandling (intentional or accidental) or contamination with other cell lines.

How much data should be provided when papers are submitted? Authors of cloning papers should always present enough data to document the logical flow and efficiency of a cloning procedure. But we may in addition require authors to provide raw data on request, for inspection by reviewers or editors. This allows an additional level of verification should questions arise during the review process, by ensuring that the data presented in the paper are an accurate interpretation of the raw data.

Independent tests

In the light of the extraordinary circumstances surrounding the Hwang case, *Nature* commissioned an independent scientist to verify that the dog Snuppy (B. C. Lee *et al.* *Nature* **436**, 641; 2005) is indeed a clone, by DNA fingerprinting analysis of blood samples from Snuppy and the nuclear donor. The indications are positive and the results are being peer-reviewed as we go to press. However, a few scientists have suggested that *Nature* should make such independent tests a condition of publishing cloning papers.

After weighing this suggestion carefully, we concluded that imposing such a standard on the cloning field as a condition of publication would be an overreaction, and one with myriad inherent logistical problems. For example, who will pay for testing, how will mishandling of samples be prevented, and how will the scientists running the verification tests be acknowledged for what could be significant additional work? Moreover, because the cloning field is not unique in its susceptibility to fraud, it would follow that we should require independent verification of all our papers, which is untenable in the current system. The gains of detecting the rare cases of fraud would be negated by the impediments to publication this would bring.

However, in the best interests of science, we encourage researchers embarking on landmark cloning studies to seek independent verification themselves, and to include a report of these findings in their initial submission. And keeping in mind the principle that extraordinary claims require extraordinary proof, *Nature* may in rare cases demand it.

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Nature and most other journals require as a condition of publication that authors make relevant reagents available to the scientific community, and encourage the deposition of cell lines and mutants in established repositories. But it has now been suggested that journals take this a step further, and require the deposition of critical samples in repositories such as the American Type Culture Collection, where they can be cheaply and rapidly made available to other researchers following publication. We are currently weighing up the practicalities of implementing such a requirement, and we would welcome feedback on whether we should and, if so, how to best do it.

Regardless of what repository is used, we urge scientists embarking on what are likely to be landmark cloning studies to ensure that critical samples are properly stored for later verification. As part of this procedure, an independent scientist not involved in the study should obtain and store cells from the nuclear donor, oocyte donor and the resulting animal or stem-cell line (or oversee their deposition in a repository). This precaution is especially important in the case of human donors, where it may not be possible to go back to the subjects to obtain additional tissues for later verification. Funding agencies should make granting dependent on procedures to ensure later verification of samples, and institutions should demand this for approval by the institutional review board.

The Hwang debacle reminds us that science is largely a self-correcting process in which scientists, editors, reviewers, journalists, funding agencies and institutions all play crucial corrective roles. In the aftermath of this deception, we should all undertake close scrutiny of our procedures and standards, with an eye towards preventing it from ever happening again. We should be vigilant against knee-jerk reactions and witch hunts. *Nature* welcomes feedback on its approach (e-mails may be sent to authors@nature.com). ■

A new ERA?

A novel component of the European Research Area will require national funders' cooperation.

Anyone who knows what COST, EURYI, ESF, ELSO, ESOF, EUROHORCS and FENS are probably spends their days deciphering European research policy. These bodies — and there are many more — represent independent Europe-wide initiatives aimed at encouraging scientists and research funding agencies to think European rather than national.

When former European research commissioner Philippe Busquin coined the term European Research Area (ERA) in 2000, he was endorsing such efforts and committing the European Commission to the common aim. But he was also thinking bigger. The vast majority of research money in Europe is in the hands of national funding agencies, which mostly do not allow it to be spent in other countries. In an ideal ERA, national agencies would see the value of sharing much more of their funds in activities for which a larger European scientific community makes sense.

The persistent resistance of many countries in the European Union to this ideal is unsurprising. Nevertheless, the commission has just launched another step towards it: Eurobiofund. This is a new forum that will bring together public and private research funding bodies to listen to pitches from European bioscientists.

The scientists will present hot areas of basic research that they believe need trans-national support if Europe is to remain competitive with the United States and Asia. Funding bodies could sign up to a specific theme, such as lipidomics, and put out a joint call for proposals to be handled by a common evaluation system. They will not necessarily create a shared pot of money, but each could fund their own scientists who win the open competitions. As an incentive for national agencies to flout their own traditions in this way, the commission will top up any joint project with money from its Seventh Framework Programme of Research, which is to be launched at the end of this year.

Funding organizations have signed up to the principle of the Eurobiofund, with the first forum to take place this November in Finland. The commission has given the European Science Foundation (ESF) €1 million (US$1.2 million) to set up and run the initiative.

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The success of this experiment depends on many factors — in particular, whether its budget is confirmed within the Framework programme, whose detailed contents will be defined later this year.

But it also depends on whether agencies are genuinely ready to support joint evaluation procedures. The experience with EURYI — the European Young Investigator Awards, which are also administered by the ESF and established by EUROHORCS (the European Heads of Research Councils) — provides grounds for only cautious optimism. Against historical odds, Germany's research council, the DFG, managed to persuade its government to pay into a common financial pot, but then found that other agencies had failed to get similar agreements. As a result, EURYI winners must be funded by their own national agencies. And to make matters worse, British funding agencies have already pulled out of the scheme.

Despite this, Eurobiofund is a positive sign of the commission's willingness to generate ideas for the European Research Area and serve as a catalyst. It may end up being just a small step towards the ideal, but it is the biggest single step that we have seen for some time. European scientists should give it their full support. ■

Circulation challenge

The lack of monitoring of ocean currents must be addressed quickly.

The idea of a 'mini ice age' triggered by a shutdown of the oceans' thermohaline circulation (THC) has been rich fodder for dramatic scenes from Hollywood to the Pentagon. The currents of the THC take cold surface water from high latitudes southwards at depth, driving low-latitude warm surface waters north. This powerful heat conveyor belt is driven by differences in salt-water density. According to models, if sufficient fresh water is added to the ocean, which could happen as a result of global warming, the THC may cease. Indeed, palaeoclimate studies suggest that the THC has shut down a number of times during colder climates in the past 100,000 years.

But most climate researchers have long abandoned the notion of isolated cold regions amidst a globally warming world. It now seems less likely that even a full collapse of the THC — which, although improbable, might still occur towards the end of the century — would significantly cool Britain or Scandinavia (see page 256).

The matter is not yet closed, however. A weakening of the THC — and recent observations published in *Nature* have suggested that the currents have begun to change — may lead to perturbations in global climate systems, with unknown side effects. There are many uncertainties, but it is clear that people in Western Europe and eastern North America are less threatened by a consequent rapid climate change (and are more capable of adapting to it) than many people in poorer societies.

More measurements are clearly needed if we are to fill the enormous gaps in our knowledge of ocean behaviour. Autonomous observation tools, such as drifting floats and moored buoys, are now allowing scientists for the first time to monitor the state of the ocean currents almost in real time. This is an important advance, but observations must be sustained for much longer periods than foreseen in the six-year RAPID programme (see www.noc.soton.ac.uk/rapid/rapid.php). Furthermore, they should be augmented globally if we are to anticipate possible changes in ocean behaviour with any confidence. ■

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