

# Beyond the origin

This issue of *Nature* anticipates next year's bicentenary of Charles Darwin's birth and the 150th anniversary of *On The Origin of Species*. We begin here with a look 50 years into the future.

"Creation is not an event that happened in 4004 BC," the geneticist Theodosius Dobzhansky wrote in 1973. "It is a process that began some 10 billion years ago and is still under way." The realization that the processes of biological creation are at once unspeakably old, and in continuous play around us, is one of the greatest discoveries of history. And yet this discovery — unlike that unceasing and ancient creation itself — can be assigned a well-defined and comparatively recent origin in the mid-nineteenth century.

Ideas on the transmutation of forms and the evolution of life have a long history; so, indeed, do Charles Darwin's personal views on the matter, which have provided historians with grist for many mills. (For *Nature's* Darwin coverage in this issue, see page 295, and online at [www.nature.com/darwin](http://www.nature.com/darwin).) But the way in which Darwin put together evidence and argument in *On the Origin of Species* marked a definitive break, and an undeniable beginning. The book, 149 years old this week, provided for the first time a way of reconciling life's past and present — a way to explain both the staggering diversity of life and its fundamental unity.

That view of life has been enriched and strengthened in the intervening century and a half, and will continue to be so. But the coming decades could also see Darwin's purview expanded in fundamental ways. The discovery of the universality of the genetic code in the 1960s — the same in elephants and *E. coli*, as the French molecular biologist Jacques Monod famously put it — magnificently bore out Darwin's view that life is united in a common descent. But that need not remain the case.

One distinct possibility is that evidence of life beyond Earth will be found by detecting tell-tale features in the spectra of planets orbiting other stars. Although astronomers are hardly likely to be able to observe variation and evolution of that life in the next 50 years, detection alone could provide insight into the frequency of life's origination. And that, in turn, could help illuminate how life came to be



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on Earth — a problem that classical Darwinism is hard put to answer.

An even more likely development is that life will be created *de novo* here on Earth. The first experiments in whole-organism synthetic biology, such as the synthetic mycoplasma being worked on at the J. Craig Venter Institute in Rockville, Maryland, will cleave quite closely to the designs already developed by natural selection. But there are already schemes for going further — for using different genetic codes, for example. Although the synthesis of complex organisms might remain the stuff of fantasy for some time (see page 310), new ways of building self-replicating, one-genome, one-cell organisms seem quite plausible. The development of creatures born from an idea, not an ancestor, will undoubtedly provide new insights into evolution, not least because the proclivities of such creatures to evolve will need to be kept in check.

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By the time the 200th birthday of *On the Origin of Species* is celebrated, the life under study by science may well no longer be united by common ancestry in the way that all life is today. In that sense, Darwin's view of the world will have been superseded. But whether that life exists around another star or in a bioreactor, it will still evolve, if given leave to, according to the simple and awe-inspiring algorithms of natural selection.

The essay of Dobzhansky's quoted earlier bears the now-famous title "Nothing in biology makes sense except in the light of evolution." That is so close to being an analytical truth — a necessary implication of what life itself is — that we can be certain it will continue to be true into the future. But that certainty in no way limits the diversity and sheer wonder of what we will find on the voyage that Darwin began. ■

## Call to action

European scientists who support neuroscience research on primates should tell their politicians why.

In 1996, Giacomo Rizzolatti and his colleagues at the University of Parma in Italy published a finding that many neuroscientists regard as a landmark. By means of electrodes inserted into the inferior frontal cortex of macaque monkeys, they discovered neurons that responded not only to the monkeys' own actions but also to similar actions the subjects observed in other monkeys. There is strong suggestive evidence of similar 'mirror neurons' in humans. Such neurons, now thought to have a role in understanding

others' behaviour and emotions, have stimulated a great deal of fundamental research, as well as hypotheses relating to several cognitive disorders, including autism.

No grants committee could have foreseen the relevance of these fundamental primate experiments to human pathologies. That is precisely why a new directive proposed by the European Commission earlier this month requires action by anyone who thinks such research to be desirable.

The directive's intent, laudable in principle, is to introduce a new baseline of regulation of the use of animals in research across the 27 member countries of the European Union (EU). Standards of care currently vary greatly across the member states. So the draft directive would enforce on every lab a level of regulation already implemented in the countries most protective of research animals' interests. Such

a reform is certainly needed. And indeed, although there is as yet no schedule for discussion and possible amendment by the European Parliament, it seems likely that a directive in some form will sooner or later be agreed by the parliament and the EU Council of Ministers.

For now, however, the urgent question facing the research community concerns the exact form that the directive will eventually take. As currently worded, it poses an immediate and substantial threat to neuroscience research and to the very benefits to human and animal health that the document says it wishes to support. In particular, it imposes major new restrictions on invasive research using primates. For any primate-research proposal to be approved, it would have to be shown that no alternative species might serve, and that there is relevance to serious diseases or conditions, or to species preservation.

Applied research is mostly carried out in species such as rats or mice for nearly all diseases, including neurological or psychiatric disease. Primates are instead important for more basic research — finding out how the brain works. Most of the labs carrying out invasive research on monkeys in Europe, by recording directly from single neurons, for example, study neurobiological aspects of

consciousness such as attention, or decision-making, or how signals are coded in the brain.

Primates such as macaque monkeys are essential for such work given the similarity of their brains to our own. If we don't understand how brains function in health we will not come close to finding out how to fix brains in disease. It is hard to imagine how brain prosthetics and brain-machine interfaces, which are tantalizingly close to realization, could be properly developed without the support of fundamental primate studies.

The current wording of the directive's text could allow a broad permissive interpretation if an ethics committee decided that very basic research was indeed a prerequisite to finding cures to disease. But in the prevailing climate that seems all too unlikely. It is essential, therefore, that any directive clearly and explicitly permits fundamental research on non-human primates other than great apes. It is also essential that Europe's researchers contact their European Parliament members (MEPs) to tell them as much. They can be found here: <http://tinyurl.com/5k32uf>. MEPs will certainly be hearing from opponents to such research. In politics, the number of voices raised does matter. ■

## Stem-cell futures

In the changed political climate, US agencies can provide a new kind of leadership.

Given his campaign promises, it seems likely that US President-elect Barack Obama will move quickly after his inauguration on 20 January to lift the Bush administration's restrictions on federal funding for human embryonic stem (ES) cell research. That will be good news for American scientists, if only because they will no longer have to decide between the human ES cell lines best able to answer their questions and the lines for which they can receive federal funds. But perhaps the biggest advantage is that their most important funding agency, the US\$29-billion National Institutes of Health (NIH), can now start to lead from the front.

The agency has a lot of catching up to do. Since 9 August 2001, when President George W. Bush declared that federal funding could only support work with human ES cell lines already in existence, the NIH has largely had to sit on the sidelines while others stepped in to fill the gap. Several US states launched their own initiatives for funding stem-cell research, complete with peer-review panels and regulatory policies. Meanwhile, in a miracle of organization and diplomacy, the International Stem Cell Forum, a working group chaired by the UK Medical Research Council, coordinated scientists across 11 countries to thoroughly compare and characterize some five dozen ES cell lines, only a few of which could be studied using NIH funds.

Indeed, many of the state, private and international organizations operating during the agency's (relative) absence from the field now have experience and expertise that the NIH lacks — not to mention the capacity and willingness to perform tasks that once might have gone to the NIH by default.

Given this reality, the post-20 January NIH should not expect

to take on the kind of primary leadership role for stem cells that it took for projects such as the Human Genome Initiative. But the agency can take the lead in coordinating and facilitating the many stem-cell programmes that are already under way.

As an example, consider the legal complications that can sometimes bedevil research collaborations trying to work across international borders — or even across state lines. Researchers joke that some collaborations require as many lawyers as scientists. The NIH could do much to simplify matters, particularly in helping states to ensure that human stem-cell lines are derived and used under ethical guidelines, including informed consent.

The NIH could also take responsibility for pushing forward the often tedious work needed to address essential questions. How many ES cells would it take to cause a tumour? How can animals be used to predict the behaviour of transplanted cells? When is a cell pluripotent, and to what extent does the pluripotent state vary?

Before the NIH can pitch in, however, it needs to stand back. The agency should review the portfolio of research it already funds to learn where particular effort is needed to push through translational barriers; it should look for fundamental biological questions where progress might have been slowed by researchers shying away from ES cell research. To get this insight, the NIH must reach out to other governmental and private programmes promoting stem-cell research to discover which strategies have been most successful. Those entities, some of which tirelessly tout their successes in public, must also be willing to reveal their mistakes and limitations. With this knowledge in hand, the NIH can then decide how to foster existing efforts, what new projects to establish, and how it can guide scientists in its own labs to fill in the gaps. ■

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