article-processing charges and Springer Nature (which publishes *Nature*) averaging $1,913 (see go.nature.com/2cn3zuy). The system as a whole risks charging multiple actors for the same product, and could price some places and people out of publishing.

Advocacy must be balanced with evidence in the open-access debate. Our research demonstrates that funders can clearly shape compliance through their mandates, and that this compliance needs to be monitored. Real barriers — such as infrastructure and funding — must be overcome to make mandates efficient. However, the rhetoric surrounding disciplinary barriers might be more a myth than a reality: when the proper structure and incentives are in place, researchers comply.

To move the conversation forward, we need a greater sense of the implications of open access on the scientific system's financial structure. We must study how certain publishing models will put pressure on some parts of the system while alleviating it from other areas, or even enriching them. We need to ensure that the mandates are sensitive to financial inequity across countries, disciplines, institutions and researchers.

Universities, industry and funding agencies should think collectively about robust and scalable models. Cooperation and foresight are the only ways to ensure that everyone has open access to research — both for readers who want to consume it, and for authors who wish to publish it. ■

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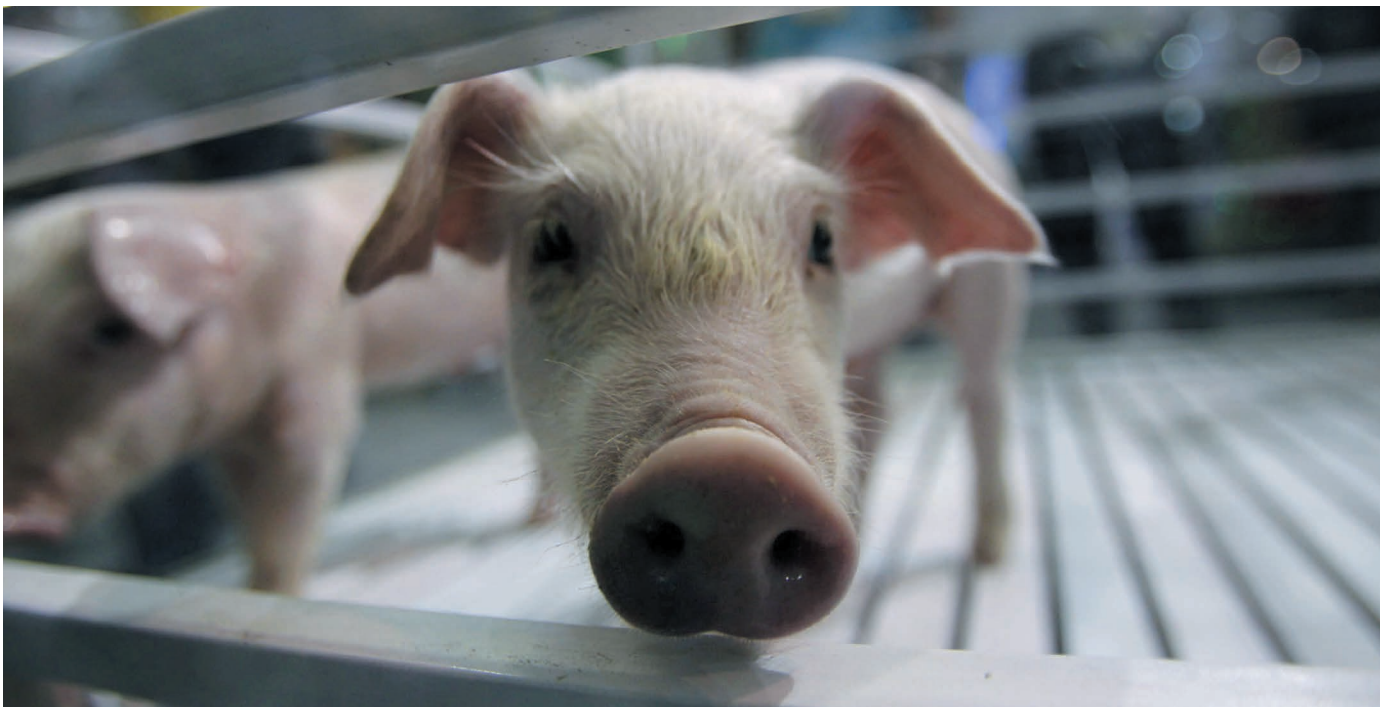
Supplementary Information accompanies this article: see go.nature.com/2yitfgn. C.R.S. did this work while at the US National Science Foundation, funded by an independent research programme.



IMAGINECHINA/REX/SHUTTERSTOCK

A gene-edited 'micropig' was developed in 2015 by the BGI genomics institute in Shenzhen, China.

Use the patent system to regulate gene editing

Governments should use patents to shape the deployment of CRISPR–Cas9 as they have done for past technologies, argues **Shobita Parthasarathy**.

Next month, researchers, policymakers, ethicists and social scientists will meet in Hong Kong for the second International Summit on Human Gene Editing.

Since the first summit, held in Washington DC nearly three years ago, researchers have continued to apply the versatile gene-editing technology CRISPR–Cas9 to diverse domains — from crop enhancement and pest eradication to human disease. Many have flagged the ethical, economic and environmental concerns raised by manipulating plant and animal genomes, including our own. But, so far, governments have struggled to develop viable approaches to regulation.

A crucial part of the arsenal for shaping

the future of gene editing is hiding in plain sight: the patent system.

In the past, patents have played an important part in regulating new technologies and research, from the atom bomb to work involving human embryonic stem cells. Some organizations and individual researchers using CRISPR–Cas9 are already creating licensing agreements that reflect their own moral codes. In my view, government-driven efforts centred on national patent systems should be deployed to help regulate gene editing.

NEW LAWS NEEDED

Last year, the US National Academies of Science, Engineering, and Medicine recommended that clinical trials involving gene editing in human eggs, sperm or embryos should be permitted only for the treatment and prevention of serious disease or disability. They also urged that a "stringent oversight" system be developed to limit the use of the technology in this context[1]. In July, the Nuffield Council on Bioethics, a highly respected bioethics body in the United Kingdom, similarly stated that the use of heritable genome editing "could be ethically acceptable" only after appropriate governance measures are put in place[2].

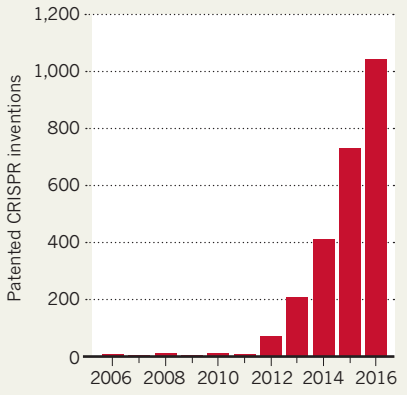
These recommendations haven't yet translated into legal frameworks or formal governance structures. And the history of regulating emerging biotechnologies suggests that such laws could be a long time coming, if they end up being formed at all[3]. For now, when it comes to editing genes in humans and other organisms, the United States and the United Kingdom — along with many other countries — rely on laws and policies that cover existing genetic-engineering technologies. Or, as in the case of human germline editing in the United States, the government simply bans the use of federal funds for such research.

Such policies have been criticized for decades as being inadequate[4]. Their insufficiencies are considerably more problematic in the context of gene editing, which, largely thanks to the development and uptake of CRISPR–Cas9 (see 'Invention protection'), promises to have much greater societal impact than previous technologies for modifying genomes.

In the United States, for instance, the oversight provided by the 'coordinated framework' (developed in the 1980s to deal with genetically engineered organisms) handles only immediate risks. The framework covers the management of altered plants and animals that have already been created, and does not consider the socio-economic, ecological or ethical consequences of creating organisms not found in nature. Likewise, since 2016, a condition in the budget for the US Food and Drug Administration has prohibited the agency from authorizing clinical trials in which a "human embryo is intentionally created or modified to include a heritable genetic modification". But there is nothing to stop US researchers using private funds to edit the genes of human embryos in the lab.

INVENTION PROTECTION

The number of patents for inventions involving CRISPR–Cas9 has soared in just a few years.



Data for 2017 and 2018 are not yet complete; patent applications are generally published 18 months after filing at a patent office.

SOURCES: IPSTUDIES, SWITZERLAND; FAMPAT-QUESTEL

HISTORICAL PRECEDENTS

How could patents help? These legal instruments — which give inventors the right to prevent others from commercializing their technologies — are usually seen solely as contracts that incentivize innovation. In fact, they can do much more, directly and indirectly.

They can lead to higher prices for products, for instance, and reduce people's access to important technologies if inventors use them to establish and maintain monopolies. Perhaps most importantly, they can shape innovation trajectories. Patent laws were a major factor in the 'war of the currents' in the 1880s, driving people to favour engineer George Westinghouse's alternating current (AC) over the direct-current system invented by Thomas Edison. (Westinghouse licensed the US patents for AC from inventor Nikola Tesla.) The decisions that governments make about whether to grant patents implicitly demonstrate their moral approval of an invention and indicate what types of technology are likely to generate exclusive markets[5].

"Patents can shape innovation trajectories."

The idea that governments could use patent systems to shape both the development of a technology and its impact on society is not new. In the 1940s, the US Congress used the patent system to control the development and commercialization of atomic weaponry.

To try to reduce the possibility of private actors developing atomic bombs, or of US intelligence leaking, Congress created a three-tier system of non-patentable, government patentable and privately patentable technologies in the Atomic Energy Act of 1954 (ref. 6). The US Patent and Trademark Office offered standard patents for technologies that fell into the 'privately patentable' category. But inventions that would be useful only in the production of fissionable material, or when using such material or atomic energy in a military weapon, were non-patentable. The government (specifically, the Atomic Energy Commission) could also step in and require 'compulsory licenses' for technologies deemed to be in the public interest.

Even further back, in the nineteenth century, the governments of several European countries, including France, Switzerland and Italy, limited or even banned patents on foods and pharmaceuticals to ensure that people had sufficient access to these products[7].

EXISTING FRAMEWORKS

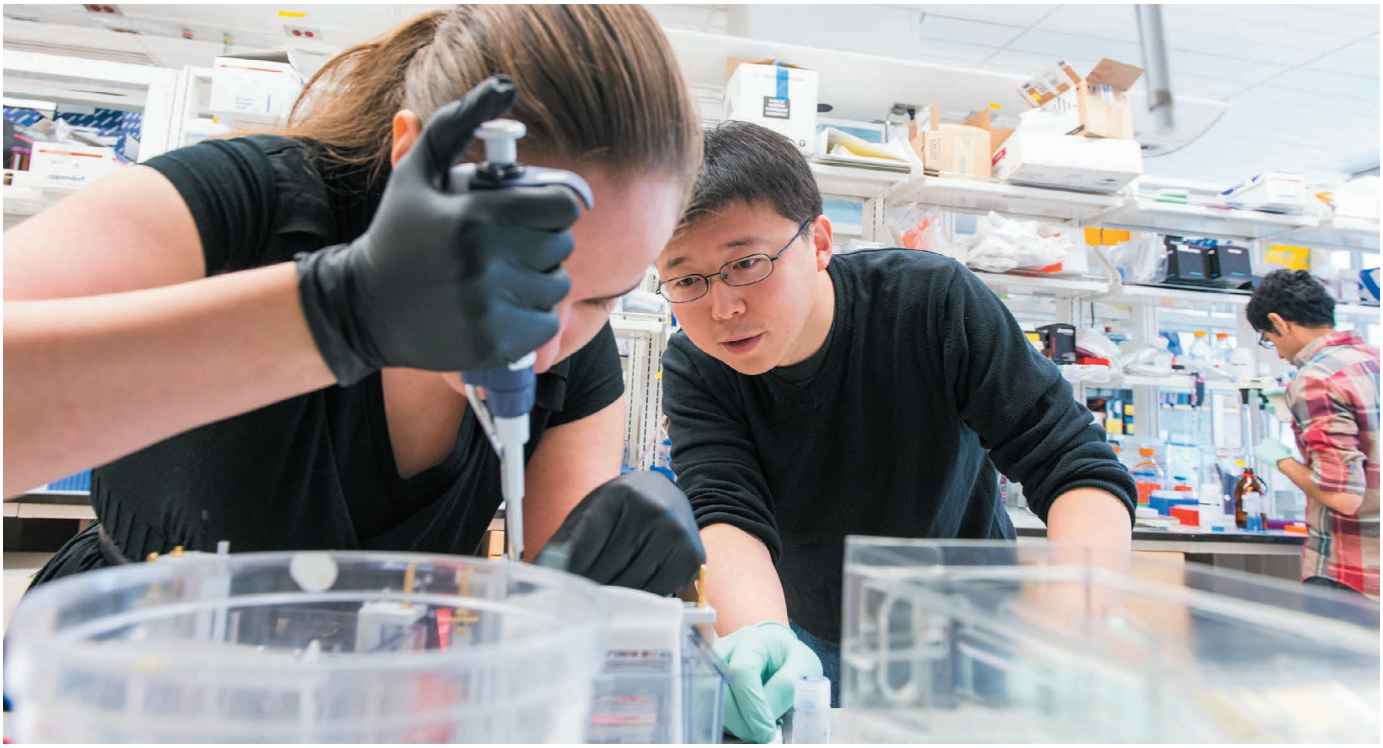
Biotechnology, including gene editing, is already regulated to some degree through patents.

In 1998, the European Parliament and Council passed a directive on the legal protection of biotechnological inventions. This harmonized Europe's approach to patents in the emerging field; it covers all European Union countries and the 38 member countries of the European Patent Office. It also addressed people's concerns about the moral and socio-economic implications of individuals being able to obtain patents on living entities, such as human embryos or genetically engineered plants and animals.

The directive states that governments can grant patents on animals that have been modified only if the resulting benefit to humankind outweighs the animal's suffering. It even includes prohibitions on patenting processes that could be used to modify human sperm, eggs or embryos.

Moreover, some scientific organizations and researchers who use CRISPR–Cas9 have themselves recognized the power of patents to govern gene editing, and are writing their own licensing agreements.

For example, the Broad Institute of MIT and Harvard, in Cambridge, Massachusetts, is a non-profit research institution that holds expansive patents on CRISPR–Cas9 technology. It prohibits its licensees from using CRISPR–Cas9 to modify human embryos, alter ecosystems or modify tobacco plants[8]. Similarly, Kevin Esvelt at the Massachusetts Institute of Technology (MIT), also in Cambridge, holds a patent on a 'gene drive' that could be used to spread a particular genomic alteration throughout an animal population. He requires those who wish to license this patent to disclose their proposed use, and has suggested that other scientists working on gene drives do the



JUSTIN KNIGHT/MCGOVERN INST.

Silvana Konermann (left) and Feng Zhang helped to develop CRISPR–Cas9 at the Broad Institute in Massachusetts, which holds many CRISPR patents.

same. He argues that this will enable public discussion[9].

What I'm calling for, however, is different: more-formal, comprehensive, government-driven regulation using the patent system.

This would cover all domains of gene editing, not just certain areas of research. It would have more transparency and political legitimacy than individual efforts ever could, by involving government institutions that are explicitly charged with representing the public interest. And it would enable governments to exploit the unique vantage point that patent offices have on the early stages of scientific fields and industries. (Inventors usually file patent applications before they try to get regulatory approval for new technologies.)

In the United States, Congress could authorize a working group to convene an advisory committee for gene-editing patents. The working group could include: individuals from the Environmental Protection Agency, who are trained in assessing ecosystem impacts; staff from the Department of Commerce, which oversees the US Patent and Trademark Office; personnel from the Department of Health and Human Services, who have deep understanding of biomedical research, health-care costs and research ethics; and staff from the Government Accountability Office, which in the past few years has developed expertise in technology assessment. The advisory committee should also comprise scientists, physicians, ethicists, social scientists, historians, lawyers and representatives from the private sector.

Building on existing laws such as the 1954 Atomic Energy Act, the committee could put together a regulatory framework for reviewing and awarding patents related to gene editing. It would need to incorporate the perspectives of citizens at every step[10], and might place inventions into distinct categories. Perhaps the use of CRISPR–Cas9 for editing human embryos would not receive patent protection, for instance, whereas the use of the technology to correct a common mutation that causes heart failure would.

Under such a framework, the committee could identify inventions that are likely to be so important to the public interest that the government should monitor closely how associated patents are used and licensed, and step in to force broad licensing if a patent holder charges too high a price for access to their invention. (Currently, the 1980 Bayh–Dole Act gives the US government 'march-in' rights in the case of taxpayer-funded research, although it has never been used in this way[11].)

The EU directive on the legal protection of biotechnological inventions already provides Europe with some guidance on which gene-editing processes and products to exclude from patentability[5]. But 20 years on, additional oversight is needed. To develop a more detailed governance framework, the European Patent Office should convene an advisory committee to develop a framework, similar to the one proposed for the United States. This could then by adopted by the European Patent Office and EU member countries.

Ultimately, patent law will need to be just one of many regulatory schemes. Some developers might still create and use ethically problematic technology, even if they are unable to patent it. But existing approaches, and the entities that are conventionally tasked with overseeing areas of scientific research, seem ill-equipped to address complex societal and value-based concerns in an increasingly privatized world. Patents, which affect the thousands of investigators now using CRISPR–Cas9 in both the private and public sector, should be part of the mix. ■

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