different purposes: some to test gene-editing technologies; others to edit various disease-related genes; and some to unravel the mechanisms behind early embryonic development. Huang's team led the first report, published in April 2015, in which the researchers used the CRISPR–Cas9 enzyme complex to snip chromosomes at specific locations, excise DNA and replace it with other genetic material[3].

In the latest study[1], Huang's team used 'base editing', a modification of CRISPR–Cas9. It guides an enzyme to specific gene sequences, but does not cut the DNA. Instead, the Cas9 enzyme is disabled and tethered to another enzyme that can swap individual DNA base pairs. For now, this technique can convert guanine (G) to adenine (A), and cytosine (C) to thymine (T). Hundreds of genetic diseases are caused by single-base changes, or 'point mutations', and so such editing at the embryonic stage could potentially stave off such conditions.

Huang's team chose one mutation common in the Chinese population: a switch from an A to a G at a certain spot in the *HBB* gene, which can lead to β-thalassaemia, a recessive blood disorder associated with severe or fatal anaemia. Researchers generally source embryos from *in vitro* fertilization (IVF) clinics, but it's rare for these facilities to have embryos with two copies of the same rare mutation. So Huang's team found a person with the blood disorder, extracted their skin cells and used cloning techniques to develop embryos with the same genetic make-up.

The team reported that in 8 of 20 cloned embryos, they were able to convert the errant G back into an A in one or both copies of the gene. (Repairing only one copy might be enough to cure a recessive disease.) That rate is too low for the technique to be considered for clinical use, but is high relative to that achieved in other gene-editing studies. "The repair rate is pretty good, and certainly promising," says Gaetan Burgio, a geneticist at the Australian National University in Canberra. "Our study opens new avenues for therapy of β-thalassaemia and other inherited diseases," says Huang.

"The repair rate is pretty good, and certainly promising."

But scientists caution that not all cells in the eight embryos were fixed. Such embryos are 'mosaic', meaning that they have a patchwork of cells with different genetic make-ups, which is potentially dangerous. "It looks like solid work, but highlights that the problem of mosaicism remains a challenge for any form of gene editing in the human embryo," says Dieter Egli, a stem-cell biologist at Columbia University in New York City.

Some scientists also question whether Huang's team looked thoroughly enough for unintended genetic changes, called off-target effects, that might have been caused by the base-editing procedure, although the authors reported that none was found.

Huang says that future experiments will be more comprehensive, but that this first study was a successful proof of principle that the base-editing technique can be used to correct a disease mutation in a human embryo. It may be that conventional CRISPR–Cas9 cannot fix embryos when both copies of a gene are faulty, although this isn't yet clear. In August, for instance, Mitalipov's team reported[4] using CRISPR–Cas9 to repair a mutation in a gene that can cause a potentially deadly heart disorder, by using the other, healthy copy of the gene as a template.

In the future, Huang says, he plans to ask for oocytes and sperm from donors who have one mutated copy of the gene — and so are unaffected by the condition, but are carriers of the disease — and use these to produce embryos. Some of those embryos would have two mutated copies, and some one, but Huang wants to edit both types. That raises the contentious idea that gene editing might be used not only to prevent severe disease, but also to eliminate the chance of people becoming carriers of the disorder. "Base editing can repair the mutant site and block it from being passed on to the next generation," he says. ■

1. Liang, P. *et al. Protein Cell* http://dx.doi.org/10.1007/s13238-017-0475-6 (2017).
2. Komor, A. C., Kim, Y. B., Packer, M. S., Zuris, J. A. & Liu, D. R. *Nature* **533,** 420–424 (2016).
3. Liang, P. *et al. Protein Cell* **6,** 363–372 (2015).
4. Ma, H. *et al. Nature* **548,** 513–519 (2017).

DATA SCIENCE

Internet research triggers scrutiny

Concern over the use of public data spurs guideline update.

BY ELIZABETH GIBNEY

British graffiti artist Banksy is renowned for his anonymity. But that status was dented last year when researchers published a paper that cross-referenced the locations of Banksy's street art with public information about people's addresses and likely movements (M. V. Hauge *et al. J. Spatial Sci.* **61,** 185–190; 2016). The team, led by academics at Queen Mary University of London, concluded that someone previously suspected to be Banksy probably was the secretive artist.

Because the study used public data, a university ethics committee said that the work was exempt from formal review — and informally advised academics that it would do no harm because a UK national newspaper had already identified the person in question as Banksy. But for some ethicists, the paper highlights growing concerns about the potential hazards of research that uses public data. "I think this study should never have been done," says Jake Metcalf, a technology ethicist at the think tank Data & Society in New York City.

Metcalf is one of several academics calling for new guidelines to steer scientists through ethical quandaries in Internet research. The unprecedented availability of online data — together with tools to draw patterns from it, such as machine learning — is opening up research possibilities that outpace existing ethics frameworks around privacy, consent and harm, says Charles Ess, a research ethicist at the University of Oslo and a member of the Association of Internet Researchers. The association will discuss how to update its guidelines at its annual meeting on 19 October in Tartu, Estonia.

A flurry of similar initiatives is under way. Earlier this year, the SATORI project, funded by the European Commission, published recommendations on Internet research as part of an effort to standardize and update research-ethics guidelines. In September, the US National Science Foundation funded a US$3-million, 4-year study called PERVADE — of which Metcalf is a part — that aims to chart attitudes to data-research ethics, produce best-practice guidelines and create tools to assess the potential harms of such work. And some British universities are preparing their first guidelines on the ethics of Internet research, after the UK Research Integrity Office, a national advisory body, published non-binding recommendations about it last December.

Common themes among these efforts include rethinking what counts as 'public' data, the ethical use of social media and the need to consider a study's potential harm to wider society, as well as to individuals. Many countries have long-standing ethical checks for research that intervenes in human lives. But those principles, set up for medical and psychological studies, apply to research on human subjects,

A Banksy artwork in Cheltenham, UK. Scientists tried to find the artist's true identity using public data.

MATT CARDY/GETTY

the definition of which often excludes Internet research, says Metcalf.

In the United States, for instance, studies using public data (which includes that purchased from a third party) generally do not count as human-subjects research because they don't access private, identifiable information about people. They don't need to be checked by an institutional review board (IRB) or require informed consent. Guidelines issued in 2013 add that researchers should sometimes consider seeking review — if a person incorrectly assumed that access to his or her public information was restricted, for example. But IRBs have no obligation to adopt these proposals, and different committees may come to different verdicts, says Metcalf.

Peter Hedges, head of the research-operations office at the University of Cambridge, UK, argues that even researchers who use information that is undeniably public, such as Twitter data, should review the ethics of their work.

When ethics committees do assess data studies, their viewpoint might be too narrow, says Ansgar Koene, an engineer and ethicist at the University of Nottingham, UK. They tend to consider the direct damage to an individual involved in research, rather than a project's potential to do widespread harm to society. That debate flared up in September when artificial-intelligence researchers at Stanford University in California posted a preprint of research that predicted whether someone is gay from their photo; it used pictures sourced from an online dating site (see https://osf.io/zn79k). The study was approved by Stanford's IRB, but provoked condemnation from some advocacy groups for lesbian, gay, bisexual, transgender and queer (LGBTQ) people, which branded it dangerous. The study's lead author, Michal Kosinski, said the work aimed to protect people by exposing an existing threat from widely used technology. Kosinski and his colleague, Yilun Wang, discussed their results afterwards with representatives of the LGBTQ community, but Koene says that the discussion should have happened beforehand and the paper should have addressed their comments.

Computer science is a flashpoint for Internet-research ethics. Researchers in this field are not used to working with human study participants and often don't consider the ethical impact of their work, says Koene, who has surveyed approaches to ethics in different disciplines. A major concern, academics agree, is how companies use online data for research — much of which they have proprietary access to. In 2014, for example, Facebook altered users' newsfeeds without telling them, to study how this affected their emotions. A public backlash prompted Facebook to publish some details of its internal review process (M. Jackman and L. Kanerva *Wash. Lee Law Rev. Online* **72,** 442; 2016) — but there is little transparency overall about how this works, says Koene.

A major concern is how companies use online data for research.

Researchers may not want to see their science slowed by formal ethical review, which can be time-consuming and opaque. Better ethics training is one solution, says Koene. But a failure to align data science with public perceptions of what is acceptable could generate a severe reaction, he warns. "The public will see us as no different from corporate or other special-interest groups pursuing a hidden agenda," he says. ■

POLICY

Another US travel ban

Trump moves to limit visas.

BY SARA REARDON

The latest version of US President Donald Trump's travel ban could make it harder for researchers from several countries to enter the United States to attend scientific meetings, perform research or visit relatives.

On 24 September, Trump announced permanent travel restrictions on citizens of Chad, Iran, Libya, North Korea, Somalia, Syria, Venezuela and Yemen. That list includes five Muslim-majority countries that were targeted in the White House's first and second travel bans, which Trump signed in January and March. Those policies, which were designed as temporary measures, have been limited by a series of federal court rulings.

Although the latest ban largely exempts students from any travel restrictions, its provisions seem poised to limit visits to the United States by working scientists. The rules vary by country; Iranians, for instance, can enter the United States only on student visas or temporary 'J' work visas, which are common among foreign postdocs in the United States. Citizens of Libya and Yemen can no longer enter the United States on business or tourist visas, and North Koreans are barred in all circumstances.

The impact is likely to be greatest for Iran, which produces more scientists and engineers than the other countries included in the policy, says Russell Harrison, a senior legislative representative for IEEE-USA in Washington DC, which advocates for US members of the Institute of Electrical and Electronics Engineers. The travel policy will tighten security for Iranian students and for researchers who already hold J visas, subjecting them to "enhanced screening and vetting requirements" if they travel outside the United States and attempt to re-enter the country.

The White House says that the ban will stay in place until the affected countries improve their processes for screening travellers. But on 29 September, the policy drew its first legal challenge: in a federal district court in Maryland, civil-liberties groups asked to amend their lawsuit over the March travel ban to include complaints about the latest policy. Meanwhile, on 25 September, the US Supreme Court cancelled hearings for a lawsuit over the first two bans, which were partly overturned because they seemed to target Muslims. The court has asked both sides to clarify whether the latest ban negates such concerns. ■