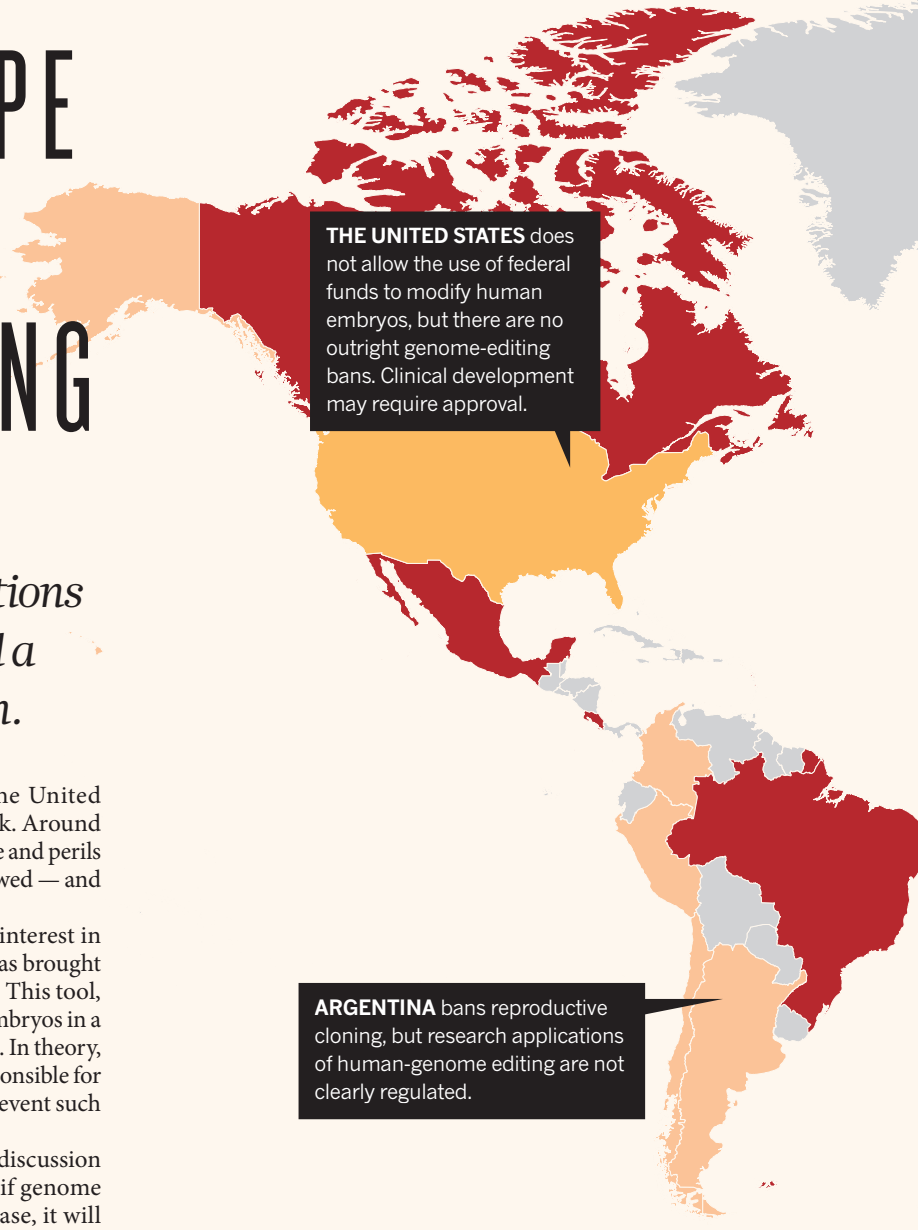
THE LANDSCAPE FOR HUMAN GENOME EDITING

BY HEIDI LEDFORD

A view of international regulations suggests where in the world a CRISPR baby could be born.



SOURCE: M. ARAKI & T. ISHII *REPROD. BIOL. ENDOCRINOL.* **12,** 108 (2014)

They are meeting in China; they are meeting in the United Kingdom; and they met in the United States last week. Around the world, scientists are gathering to discuss the promise and perils of editing the genome of a human embryo. Should it be allowed — and if so, under what circumstances?

The meetings have been prompted by an explosion of interest in the powerful technology known as CRISPR/Cas9, which has brought unprecedented ease and precision to genetic engineering. This tool, and others like it, could be used to manipulate the DNA of embryos in a dish to learn about the earliest stages of human development. In theory, genome editing could also be used to 'fix' the mutations responsible for heritable human diseases. If done in embryos, this could prevent such diseases from being passed on.

The prospects have prompted widespread concern and discussion among scientists, ethicists and patients. Fears loom that if genome editing becomes acceptable in the clinic to stave off disease, it will inevitably come to be used to introduce, enhance or eliminate traits for non-medical reasons. Ethicists are concerned that unequal access to such technologies could lead to genetic classism. And targeted changes to a person's genome would be passed on for generations, through the germ line (sperm and eggs), fuelling fears that embryo editing could have lasting, unintended consequences.

Adding to these concerns, the regulations in many countries have not kept pace with the science.

Nature has tried to capture a snapshot of the legal landscape by querying experts and government agencies in 12 countries with histories of well-funded biological research. The responses reveal a wide range of approaches. In some countries, experimenting with human embryos at all would be a criminal offence, whereas in others, almost anything would be permissible.

Concerns over the manipulation of human embryos are nothing new. Rosario Isasi, a legal scholar at McGill University in Montreal, Canada, points to two key waves of legislation over the years: one sparked by concerns about the derivation of embryonic stem cells, which was largely deemed acceptable; the other about reproductive cloning, which was largely prohibited for safety reasons.

The current regulatory mosaic is their legacy. Tetsuya Ishii, a bioethicist at Hokkaido University in Sapporo, Japan, spent nearly a year analysing relevant legislation and guidelines in 39 countries, and found that 29 have rules that could be interpreted as restricting genome editing for clinical use (M. Araki and T. Ishii *Reprod. Biol. Endocrinol.* **12,** 108; 2014). But the 'bans' in several of these countries — including Japan, China and India — are not legally binding. "The truth is, we have guidelines but some people never follow them," said Qi Zhou, a developmental biologist at the Chinese Academy of Sciences Institute of Zoology in Beijing, at a meeting hosted by the US National Academy of Sciences in Washington DC last week. Ishii considers the rules in nine other countries — among them Russia and Argentina — to be "ambiguous". The United States, he notes, prohibits federal funding for research involving human embryos, and would probably require regulatory approval for human gene editing, but does not officially ban the use of the technique in the clinic. In countries where clinical use is banned, such as France and Australia, research is usually allowed as long as it meets certain restrictions and does not

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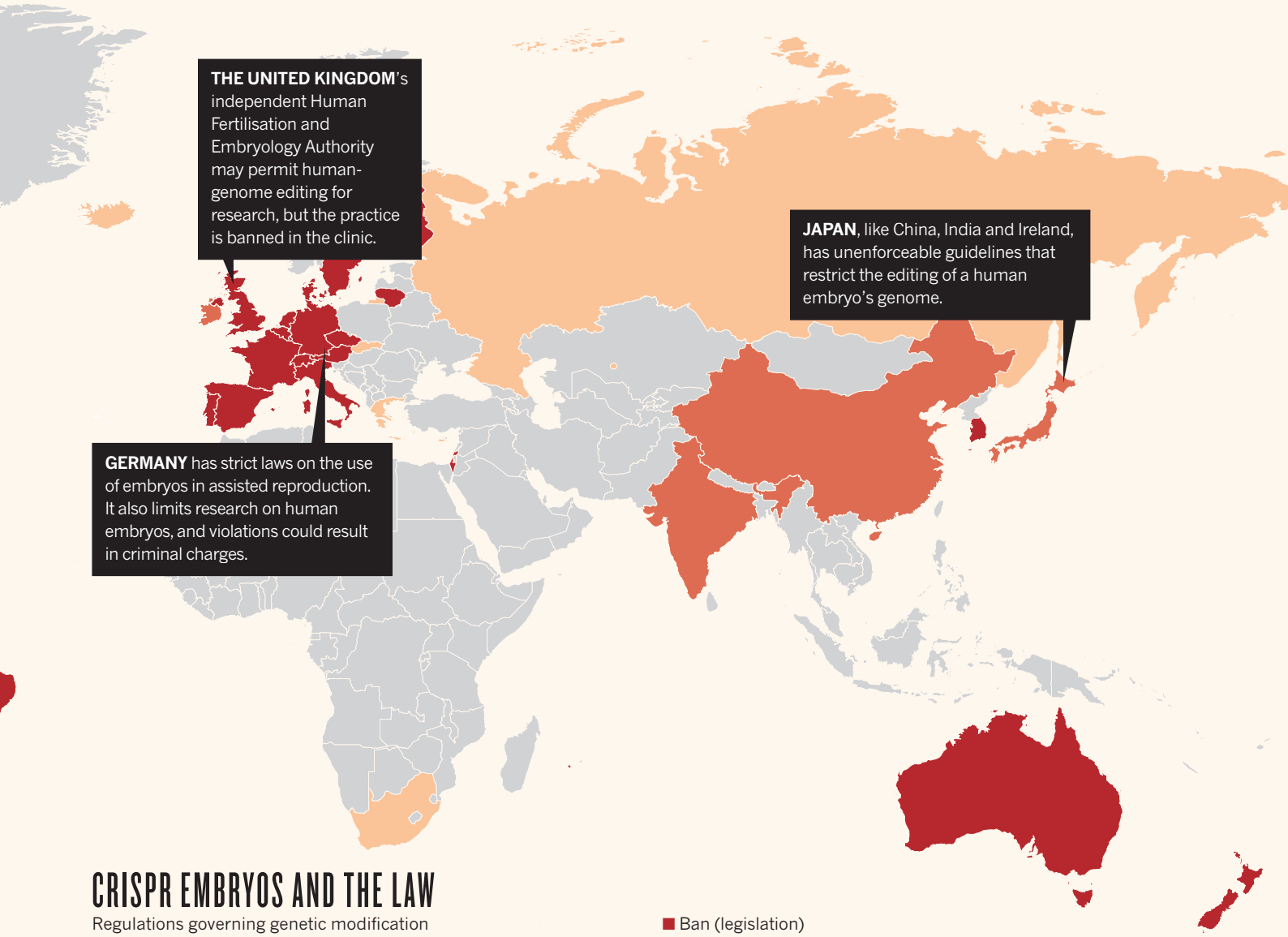

CRISPR EMBRYOS AND THE LAW

Regulations governing genetic modification in human embryos vary. Some countries ban the practice through legislation that carries criminal penalties; others have unenforceable guidelines.

attempt to generate a live birth (see 'CRISPR embryos and the law').

Many researchers long for international guidelines that, even if not enforceable, could guide national lawmakers. Developing such a framework is one of the aims of ongoing discussions; the US National Academy, for example, plans to hold an international summit in December and then produce recommendations for responsible use of the technique in 2016.

But the research has already begun, and more is coming. Scientists in China announced in April that they had used CRISPR to alter the genomes of human embryos, albeit ones incapable of producing a live baby (P. Liang *et al. Protein Cell* **6,** 363–372; 2015). Xiao-Jiang Li, a neuroscientist at Emory University in Atlanta, Georgia, who has used the technique in monkeys, says he has heard rumours that several other Chinese laboratories are already doing such experiments. And in September, developmental biologist Kathy Niakan of the Francis Crick Institute in London applied to the UK Human Fertilisation and Embryology Authority for permission to use the technique to study errors in embryo development that can contribute to infertility and miscarriage. No one so far has declared an interest in producing live babies with edited genomes, and initial experiments would suggest that it is not yet safe. But some suspect that it is only a matter of time.

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Ishii predicts that countries with high rates of *in vitro* fertilization will be the first to attempt clinical applications. Japan, he says, has one of the highest numbers of fertility clinics in the world, and has no enforceable rules on germline modification. The same is true for India.

Guoping Feng, a neuroscientist at the Massachusetts Institute of Technology in Cambridge, hopes that with improvement, the technique could eventually be used to prevent genetic disease. But he argues that it is much too soon to be trying it in the clinic. "Now is not the time to do human-embryo manipulation," he says. "If we do the wrong thing, we can send the wrong message to the public — and then the public will not support scientific research anymore." ■

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