Correspondence

Stem-cell treatment: Japan responds

As director-general of the Pharmaceutical Safety and Environmental Health Bureau of Japan's Ministry of Health, Labour and Welfare, I cannot accept your criticism of our approval of stem-cell treatment for spinal-cord injuries (see *Nature* **565**, 535–536; 2019 and *Nature* **565**, 544–545; 2019).

Your criticism is based on the absence of double-blind studies for this treatment. But in this therapy, known as Stemirac, stem cells from the patient's bone marrow are cultured externally and then returned to the patient. A double-blind study is therefore structurally impossible, and performing a sham operation on a control group would raise ethical issues.

In such cases, properly designed clinical studies can still test efficacy — as demonstrated for drugs approved by the US Food and Drug Administration as well as in Japan. Given the convincing response to Stemirac by the group of paralysed people under discussion, it could be unethical to withhold approval and deny treatment. The rationale for the safety, efficacy and quality of the product, and for the ethics of its approval, is given in the evaluation report by Japan's Pharmaceuticals and Medical Devices Agency (see go.nature.com/2uzyqk9; in Japanese).

You also criticize Japan for marketing products with 'questionable' efficacy and for making patients bear the costs of clinical studies. However, under the terms of the country's conditional and time-limited approval for regenerative medical products, such products are granted marketing authorization only when efficacy can be demonstrated in post-marketing studies within a specified period. And, because Stemirac is covered by national health insurance, patient payments are fixed at a feasible level.

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Germline editing: medical tourism

We question some aspects of Eric Lander and colleagues' proposed moratorium, although — like most in the bioethics and science-policy communities — we are also deeply concerned about experimentation with human germline editing (see *Nature* **567**, 165–168; 2019).

For example, the authors emphasize that they do not mean a permanent ban. On the basis of our extensive analysis of other moratoriums aimed at human reproduction in the United States, however, we have found that what started as a temporary pause can quickly become stuck (for details, see R. A. Spivak *et al. J. Law Health* **30**, 20–54; 2017 and R. A. Spivak *et al. J. Health Biomed. Law* **14**, 5–26; 2018). The Dickey–Wicker Amendment, which prohibits federal funding for research in which human embryos are "knowingly subjected to risk of injury or death greater than that allowed … *in utero*" and has never been seriously revisited, is a cautionary tale.

Lander *et al.* further argue that genome editing is unnecessary because couples at risk of transmitting a heritable disease already have safe ways to avoid doing so. However, that can require third-party sperm or ova, which might not be available in some countries. Even if gametes are available, there is still the ethical question of whether a couple's interests in having genetically related children should give way to state regulation (see also H. König *Nature* **568**, 458; 2019).

Also, countries that shape their own variants of the ban would have to decide whether to forbid citizens from going abroad to access such technologies. Patients have, for example, gone to other countries for mitochondrial replacement therapy (see I. G. Cohen *Indiana J. Glob. Leg. Stud.* **25**, 439–462; 2018).

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Sex differences help precision medicine

In her review of Gina Rippon's book *The Gendered Brain*, Lise Eliot uses the term "neurosexism" to describe the "myth" of brain differences in men and women (*Nature* **566**, 453–454; 2019). Although the field is indeed rife with misinterpretation and methodological flaws, that is no justification for dismissing sex differences in neuroscience (see also R. Voskuhl and S. Klein *Nature* **568**, 171; 2019).

A variety of neurological and psychiatric conditions demonstrate robust differences between the sexes in their incidence, symptoms, progression and response to treatment (see, for example, M. T. Ferretti *et al. Nature Rev. Neurol.* **14,** 457–469; 2018). When properly documented and studied, sex and gender differences are the gateway to precision medicine.

This year's International Forum on Women's Brain and Mental Health (www.forum-wbp.com) will feature panel discussions with patients and worldwide leaders. It will assess sex and gender differences in basic and clinical neuroscience, the role of such differences in disease management and clinical trials, sex and gender biases in digital medicine, and how artificial intelligence could exploit sex differences for precision medicine.

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Call on research-integrity officers

As a first step in answering the call for a national research-integrity policy board (see C. K. Gunsalus *et al. Nature* **566**, 173–175; 2019), a US National Academy of Sciences meeting last month discussed what the role of that board should be. As research-integrity officers (RIOs) at four big US universities, we would urge the proposed board to draw on the advice of RIOs. We are uniquely placed to understand the problems facing research today.

Universities have formal, publicly available policies that lay out comprehensive processes for handling allegations of research misconduct, often carried out with federal oversight. The Association of Research Integrity Officers (see go.nature.com/2ub9clq) shares best practices and strategies for handling misconduct proceedings and promoting ethical research, and has productive partnerships with regulatory agencies and journals, and with the Committee on Publication Ethics.

The viewpoints of RIOs are invaluable when overseeing research-misconduct proceedings. Also, their positioning in institutions provides them with insight into who commits research misconduct and how it is managed. This understanding enables them to advise on best practices for preventing misconduct and on other important issues relating to research integrity.

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**On behalf of 4 correspondents (see go.nature.com/2ltr1l for full list).*