

Japan relaxes human stem-cell rules

But scientists fear it is too late to regain lost ground.

A long-sought loosening of Japan's guidelines on human embryonic stem-cell research came into effect on 21 August. But some say the new rules are too little, too late for a struggling field that was once a source of national pride.

On the surface the previous guidelines, set in 2001, were permissive. They allowed scientists to derive new human embryonic stem (ES) cell lines and research both home-grown and imported cell lines. But that could be done only after the research was approved, and the approval process was the stumbling block. Proposed projects needed to be approved twice — first by a local institutional review board and then by a science-ministry committee. And researchers working on human ES cells had to use separate facilities from other stem-cell research.

The upshot was a slowing down of research, some say. Roughly 50 groups have passed the application process, says Hirofumi Suemori of Kyoto University's Institute for Frontier Medical Sciences. But that is only about a quarter of the number that he estimates originally wanted to use human ES cells, based on the number of groups that work with mouse ES cells or request materials derived from human ES cells.

Some charge that the regulations cost the country leadership in the field. It was Shinya Yamanaka of Kyoto University who, in 2006, created induced pluripotent stem (iPS) cells for the first time (K. Takahashi and S. Yamanaka *Cell* **126**, 663–676; 2006) — produced from normal adult cells, iPS cells have the potential, like ES cells, to generate any cell type in the body. But it soon became clear that expertise with ES cells was essential for advancing iPS-cell technology, and further experiments such as comparing the properties of iPS cells and ES cells were done outside Japan. Even in the United States, where until this year federal funding was limited to ES-cell lines derived by August 2001, ES-cell research moved ahead, says Suemori. “Researchers there were able to press forward, and with that as the foundation, they also stole the lead in iPS-cell research,” he says.

The Japanese government has been slowly trying to change the restrictions. In April, a new



Until April, Japanese scientists had to run separate facilities for human embryonic and other stem cells.

section in the explanatory material for the old guidelines erased the requirement for separate facilities. The latest guidelines also remove the secondary approval step for working with ES cells: a local review committee must still approve the work, but researchers then need only notify the science ministry of this.

Yet some burdensome restrictions remain, says Suemori. For example, the notification must include “word-for-word” minutes of the local review committee's meeting.

And the two-stage approval process remains for deriving new cell lines. Norio Nakatsuji, director of Kyoto University's Institute for Integrated Cell-Material Sciences, who created all five of Japan's human

ES-cell lines, has given up plans to make any more. “I would summarize the change as being from absurd to excessively strict,” he says. “These irrational guidelines have done and will probably continue to do great damage to all related research fields in Japan.”

Last December, Yamanaka was widely quoted for remarks made at a science-ministry assembly in which he appraised Japan's 2008 record against

other iPS-cell research groups, mostly in the United States: “One win, and about 10 losses,” he said.

The new regulations were pushed through by the Council for Science and Technology Policy, a 15-person group chaired by the prime minister that stands as the country's highest science-policy body. Junichi Iwata, of the science ministry's life-science division, says the changes were targeted at the use of human ES cells and

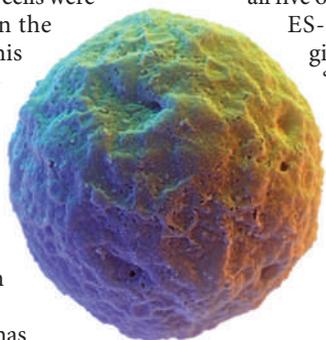
not their derivation, explaining that only two groups are licensed to derive such cells.

Asked why the reform didn't go further in addressing researchers' criticisms, he says: “The new guidelines just went into effect, so we'll see how things go. If need be, we'll change them again.”

But it might be too late to make a difference. Most of Japan's stem-cell researchers have already been pushed into iPS-cell research through targeted funding programmes and are unlikely to go back to the ES-cell basics. “I do not expect a dramatic increase in ES-cell research,” says Shin-Ichi Nishikawa, a stem-cell researcher at the RIKEN Center for Developmental Biology in Kobe.

Suemori likewise sees little change and fading hope. “It will be very difficult for us to catch up now,” he says. ■

David Cyranoski



Future hope: a human embryonic stem cell.