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Could investment in biosafety research be leaving the public more at risk?

“We need more infectious-disease research, not less,” he says.

Despite reservations expressed at the hearing, the expansion of bioterror-related research continues. Congress might still use its control of budgets to push for greater oversight, though, and Stupak and others have asked the government to assess the overall programme. ■

Ewen Callaway

research grants should be awarded, in part, on the basis of applicants' compliance with biosafety standards. It also puts forward a Europe-wide system for the accreditation of research facilities suitable for work on potentially dangerous pathogens. And it asks whether it would be feasible to accredit individual researchers.

In their responses, the EBSA and EuropaBio backed the accreditation of facilities but said that it would be much more difficult to accredit individual researchers without running into problems regarding discrimination or personal privacy. Both groups broadly welcomed the idea of making grants conditional on compliance with biosafety standards. ■

Daniel Cressey

1. Jackson, R. J. *et al. A. J. Virol.* **75**, 1205–1210 (2001).
2. Tumpey, T. M. *et al. Science* **310**, 77–80 (2005).

Doubts raised over stem-cell marker

Two papers published this week challenge the validity of using the protein Oct4 as a marker for adult stem cells. The protein maintains embryonic stem cells in an undifferentiated state, called pluripotency, but the papers question whether it has the same function in adult stem cells.

Oct4 controls gene expression during the early stages of embryo formation, but switches off in somatic cells shortly thereafter. It thus seems logical that Oct4 might also control adult stem cells, and more than 60 studies have used Oct4 expression as a marker of these cells.

But now, Rudolf Jaenisch's lab at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, has used several approaches to test for Oct4 expression in adult stem cells in mice¹. All came up negative. “It's hard to prove beyond any doubt that something is not expressed or doesn't have a function,” says author Christopher Lengner, also from the Whitehead Institute. “That's why we had to use overlapping methods. We beat the thing to death.”

Lengner and his colleagues aren't alone. Several years ago, Lorenza Lazzari, of the Maggiore Foundation Hospital in Milan, Italy, and her colleagues detected low levels of Oct4 expression in adult stem cells, but their negative controls, which did not contain stem cells, yielded the same result.

Lazzari had found it difficult to publish her work, but eventually succeeded earlier this year². “The dogma of Oct4 as a stem-cell marker was stated by several scientists working on somatic stem cells and it has been very difficult to convince editors,” says Lazzari, who says that she has had several manuscripts

on the topic rejected. Many published papers showing Oct4 expression simply didn't include a negative control, Lengner says.

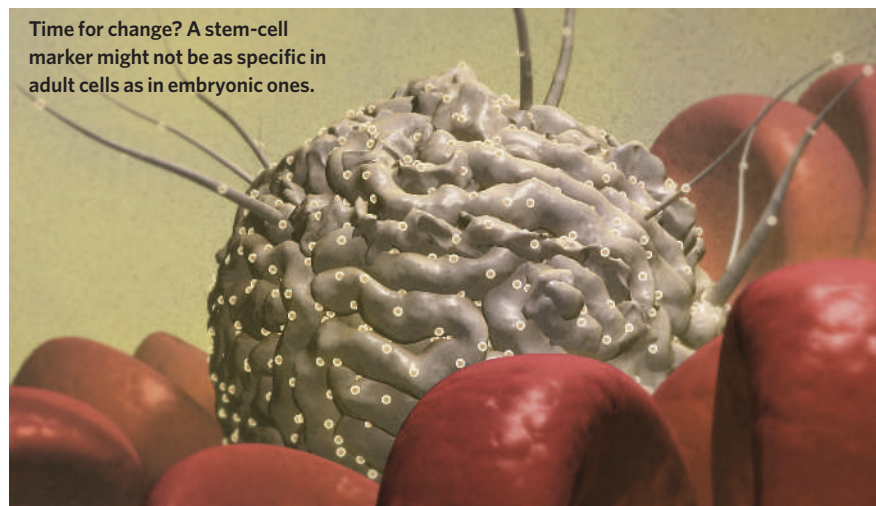
Lazzari's false-positive results could be due to the presence of several *Oct4*-related genes that do not code for functional protein, says Gesine Kögler of the Heinrich-Heine University in Düsseldorf, Germany. Kögler and her colleagues found that many approaches used to detect Oct4 cannot distinguish between the functional *Oct4* gene and its related pseudogenes³. Lengner also says that many papers relied on stem cells that had been maintained as cell cultures for many generations, and may no longer reflect what occurs in live animals.

This doesn't necessarily mean that adult stem cells are not pluripotent, notes Leendert Looijenga, a pathologist at the Erasmus Medical Center in Rotterdam, the Netherlands. It does, however, suggest that they are regulated differently from embryonic ones.

Looijenga and his colleagues have tested more than 3,600 cancer tissue samples, representing more than 100 cancers. They found that Oct4 was often expressed in gamete-producing tissue, but not in other types of tissue, supporting the link between pluripotency and the protein. Researchers were driven by the idea that Oct4 ought to be present in adult stem cells and stem-cell-derived cancers, says Looijenga. “It's a logical idea,” he says, “but logical ideas aren't always right.” ■

Heidi Ledford

1. Lengner, C. J. *et al. Cell Stem Cell* **1**, 403–415 (2007).
2. Zangrossi, S. *et al. Stem Cells* **25**, 1675–1680 (2007).
3. Liedtke, S., Enczmann, J., Waclawczyk, S., Wernet, P. & Kögler, G. *Cell Stem Cell* **1**, 364–366 (2007).
4. Looijenga, L. H. J. *et al. Cancer Res* **63**, 2244–2250 (2003).



Time for change? A stem-cell marker might not be as specific in adult cells as in embryonic ones.

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