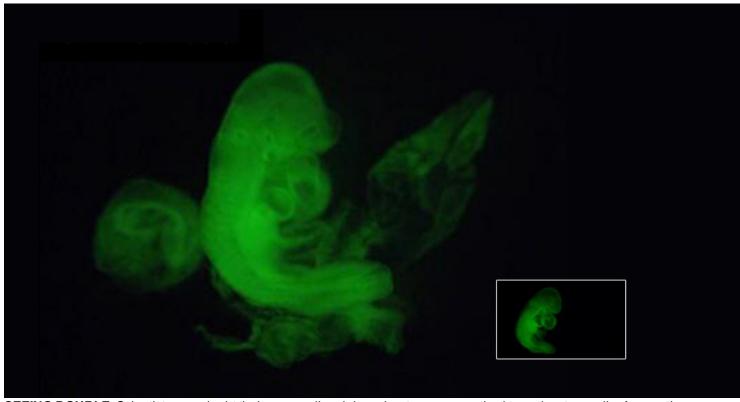


News: Cells

Dramatic retraction adds to questions about stem cell research

Researchers admit mistakes and question whether STAP cells exist

By Tina Hesman Saey 11:36am, July 7, 2014



SEEING DOUBLE Scientists now doubt their own earlier claims about an easy method to make stem cells. Among the errors identified in their papers were two pictures of a single embryo created from STAP cells (green) that had been represented as depictions of two different embryos (large image with placenta, inset without placenta).

Rising doubts about easy-to-make stem cells have hit a crescendo: The researchers who claimed to have discovered STAP cells have pulled their papers from the journal *Nature*. The scientists say that mistakes in the work now make them question the existence of such cells. The original publication described making STAP stem cells simply by stressing mature cells with a squeeze or with a brief plunge in acid.

Other scientists worry that the combination of early enthusiasm about the papers quickly followed by revelations of misconduct will mar the reputation of stem cell research.

"We apologize for the mistakes," the team of STAP cell researchers <u>writes</u> in the July 3 *Nature*. "These multiple errors impair the credibility of the study as a whole and we are unable to say

without doubt whether the [STAP cell] phenomenon is real."

When they were announced in January, STAP cells were greeted with both hope and skepticism that easy techniques could turn back the developmental clock and reset cells to a primordial state rivaling that of embryonic stem cells (<u>SN: 2/22/14, p. 6</u>). The cells, named stimulus-triggered acquisition of pluripotency cells or STAP for short, could purportedly generate any type of tissue in a mouse's body and could even produce placenta, something that other stem cells generally can't do.

Researchers in other labs attempted to replicate the results but were unsuccessful. "Hundreds of postdocs and graduate students have tried to do this in their labs because it was supposed to be so easy. They have had zero success," says Jeanne Loring, a stem cell researcher at the Scripps Research Institute in La Jolla, Calif.

Within days of publication, scientists also noted that images and passages of text appeared to have been copied, sparking an investigation by RIKEN, the research institute in Japan where much of the work was done (<u>SN Online: 3/10/14</u>). That investigation found instances of plagiarism and data manipulation, and concluded that the study's lead author, Haruko Obokata, was guilty of misconduct (<u>SN Online: 4/1/14</u>).

The institute is still attempting to replicate the work. Japanese media reported that in early July, Obokata began a planned five months of experiments with the aim of demonstrating that STAP cells do exist. She is working under close supervision, including video surveillance, the *Japan Times* reported. Loring, however, thinks it unlikely that anyone would adopt the method now even if RIKEN demonstrates the cells are real.

Study coauthor Charles Vacanti, a stem cell researcher at Brigham and Women's Hospital and Harvard University was one of the originators of the idea that stimuli such as mechanical or chemical stress could reprogram adult cells to form stem cells. Vacanti declined to speak to news reporters but stood behind his original idea. He <u>said on his website</u> that the misconduct investigation did not cast doubt on the existence of STAP cells. But he agreed to retract the papers because, he said, "I am concerned that the multiple errors that have been identified impair the credibility of the manuscript as a whole."

While researchers have used cocktails of chemicals to reprogram cells into stem cells (*SN Online: 7/18/13*), Leonard Zon, director of the stem cell program at Boston Children's Hospital, says he always doubted the papers' assertion that a single stressor, like acid, could completely change a cell's fate.

Stem cell scientist Paul Knoepfler of the University of California, Davis, agrees. "The concept of STAP cells doesn't make a whole lot of sense to me," he says. "Sure, stress might be able to influence cell fate, but to entirely reprogram it seems highly unlikely." If mild stresses could make mature cells revert back to the ultraflexible state of cells in an embryo, he says, "we'dhave stem cell tumors sprouting up inside of us all the time."

The evidence to support STAP cells' existence is, if anything, only weakening as scientists look more deeply into the original reports.

In the retraction notice, the authors list five newly identified errors, including pictures — other than the ones previously found — of a single cell or embryo labeled as multiple cells or embryos.

Nature contends in a July 3 editorial that its editors and reviewers could not have discovered

those and other fatal flaws during the peer review process.

But Loring finds that argument specious. "There has to be some responsibility somewhere," she says.

Nature has marked the papers as retracted but the journal continues to host them on its website. "In our opinion, to take down retracted papers from journal websites amounts to an attempt to rewrite history, and makes life needlessly difficult for those wishing to learn from such episodes," the editorial says.

The incident has tainted the reputation of stem cell research, Loring and Zon say. But scientists are drawing on the experience to educate young researchers. Zon points to a recent session on scientific integrity for junior investigators at the International Society for Stem Cell Research meeting as an example. "We're trying to be responsible as a field," he says.

As for Loring, she's tired of the controversy. Her favorite alternative for what the acronym STAP might stand for is "Stop Talking About the Papers." The field can move past the incident, she says, "There's enough really excellent work to swamp it out."

Citations

Editorial. <u>STAP retracted</u>. *Nature*. Vol. 511, July 3, 2014, p. 5. doi:10.1038/511005b.

- H. Obokata et al. <u>Retraction: Bidirectional developmental potential in reprogrammed cells with acquired pluripotency</u>. *Nature.* Vol. 5II, July 3, 2014, p. 112. doi:10.1038/nature13599.
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Embattled researcher Obokata arrives at Riken to prove STAP cells. Japan Times, July 2, 2014.

- C. Vacanti. <u>Statement for news media</u>. July 2, 2014.
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 <u>Nature paper retractions</u>. Knoepfler Lab Stem
 Cell Blog. July 2, 2014.

Further Reading

- T. H. Saey. A little acid or a tight squeeze can turn a cell stemlike. Science News. Vol. 185, February 22, 2014, p. 6.
- T. H. Saey. <u>Acid-bath method for making stem cells under fire</u>. Science News Online, March 10, 2014.
- T. H. Saey. <u>Misconduct found in Japanese stem cell research</u>. Science News Online, April 1, 2014.
- A. Yeager. <u>Stem cell scientist reportedly</u> <u>agrees to retract controversial paper</u>. Science News Online. May 28, 2014.
- L. Guterman. <u>Questions raised about new</u> method for making stem cells. Science News Online. February 19, 2014.
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