

# Gene tests suggest acid-bath stem cells never existed

Cells purportedly made with 'STAP' method came from the wrong mice, tests show.

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Asahi Shimbun via Getty Images

Teruhiko Wakayama alleged yesterday that Haruko Obokata, his co-author of two controversial *Nature* papers, switched mice in experiments to create stem cells.

A co-author on two controversial papers claiming a new kind of embryonic-like stem cell has presented genetic data showing that the cells used to make the claim were not what they were said to be. The finding was supported by a second source, which suggested that cells made with so-called stimulus triggered acquisition of pluripotency (STAP) were probably nothing more than normal embryonic stem cells, possibly the product of switched samples.

Both announcements, made on 16 June, increase pressure on the papers' lead author, biologist Haruko Obokata of the RIKEN Center for Developmental Biology in Kobe, to prove that the STAP phenomenon does exist.

Obokata and others have [agreed to retract two papers](#) describing the STAP techniques they had published in *Nature*<sup>1,2</sup> in January after numerous problems were identified. [*Nature's* news and comment team is editorially independent of its research editorial team.] But the question remained of whether the phenomenon — in which stresses such as acid exposure or physical pressure are enough to turn bodily cells into embryonic-like cells — was real, as Obokata has steadfastly maintained.

Teruhiko Wakayama, a pioneering mouse cloner currently at Yamanashi University, headed the RIKEN CDB laboratory where Obokata claimed to have created STAP cells. During the experiments, Wakayama gave Obokata newborn mice from his laboratory. She claims to have taken spleen cells from these mice, exposed them to acid to create STAP cells, and handed them to Wakayama. Wakayama took the purported STAP cells and made self-renewing stem cell lines. He also injected them into mouse embryos to make 'chimeric' mice, thus purportedly demonstrating the cells' pluripotency, or ability to turn into all of the body's cell types.

After various problems in the papers emerged, Wakayama started to wonder whether the cells he received had truly been made by the STAP method (see '[Mismatch alleged in acid-bath stem-cell experiment](#)'). He sent the eight stem-cell lines that had been presented in the paper to the National Institute of Radiological Sciences (NIRS) in Chiba, just east of Tokyo, to be analysed. Geneticists at the NIRS targeted the sites where a green fluorescent protein (GFP), used by researchers to mark the expression of certain genes, had been

inserted into the mice genomes.

In the mice that Wakayama gave to Obokata, the GFP gene was on the 18th chromosome. But in the purported STAP cells, it was on the 15th chromosome. This strongly suggests that different mice were used. “In my laboratory, there are neither mice nor embryonic stem cells with GFP on the 15th chromosome,” Wakayama told *Nature*.

Wakayama is cautious on the interpretation of the results. “We cannot say with certainty that STAP cells never existed. While the management of experimental mice is extremely strict at CDB, it is always possible that Obokata brought in baby mice from somewhere,” he says.

But similar tests carried out by RIKEN CDB and published at the same time further call into question the origin of the STAP cells. The CDB looked at GFP insertion sites and genetic background in six other purported STAP cell lines that Obokata had kept in her laboratory. “The results are in agreement with the results of the analyses of samples held by Prof. Wakayama,” CDB director Masatoshi Takeichi wrote in an announcement posted on the centre's website on 16 June. Takeichi notes that the cells with GFP in the 18th chromosome are “of unknown provenance”. The CDB is now investigating the source of these cells.

In response, Obokata has been quoted as saying, through her lawyer Hideo Miki, that such a mix up was impossible. “She doesn’t think it could have happened, not intentionally or mistakenly,” says Miki.

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## References

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1. Obokata, H. *et al.* *Nature* **505**, 641–647 (2014).
2. Obokata, H. *et al.* *Nature* **505**, 676–680 (2014).