

Summary Report on STAP Cell Research Paper Investigation II

1. Circumstances

In response to doubts raised concerning the two STAP papers published in Nature and then retracted on July 2, 2014, and a related paper shown below, RIKEN carried out a preliminary inquiry. Based on the results of this preliminary investigation, RIKEN decided to carry out a full investigation, and an Investigative Committee consisting of 7 people from outside RIKEN was established on September 3, with Isao Katsura serving as Chair.

Nature **505**, 641–647 (2014); doi:10.1038/nature12968

Nature **505**, 676–680 (2014); doi:10.1038/nature12969

Protocol Exchange (2014); doi:10.1038/protex.2014.008

2. Individuals investigated

Haruko Obokata

At the time of submission: Research Unit Leader, Laboratory for Cellular Reprogramming, RIKEN Center for Developmental Biology

Teruhiko Wakayama

At the time of submission: Team Leader, Laboratory for Genomic Reprogramming, RIKEN Center for Developmental Biology

Professor, Faculty of Life and Environmental Sciences, University of Yamanashi

Hitoshi Niwa

At the time of submission: Project Leader, Laboratory for Pluripotent Stem Cell Studies, RIKEN Center for Developmental Biology

3. Investigation methods

- 1) DNA samples prepared from the following materials in the Obokata and Wakayama laboratories were analyzed using various methods, including a next-generation sequencer.

Analyzed materials

STAP stem cells, FI stem cells, ES cells, frozen STAP cell extracts, fixed teratoma specimens, and STAP cell-generated chimera mice DNA

- 2) The following materials were examined and analyzed: Laboratory notebooks, documents, and e-mail records provided by the individuals concerned, and data remaining in the CDB Genome Resource Analysis Unit (GRAS) and in equipment used in the experiments.
- 3) Facts were confirmed with the individuals concerned through face-to-face interviews and questionnaires.

4. Results of the investigation and opinions

- 1) Investigation of samples from the Obokata and Wakayama laboratories
The following conclusions were reached based on analyses of SNP distribution, specific deletions, inserted GFP gene, and other factors.

- a) The three STAP stem cells, FLS, GLS, and AC129, were actually derived from the three ES cells FES1, GOF-ES, and 129B6F1-ES1, respectively.
- b) The FI stem cell CTS was actually derived from an ES cell FES1.
- c) It is highly probable that the chimera mice claimed to be developed from STAP cells were actually developed from ES cells FES1.
- d) It is highly probable that the teratomas claimed to be developed from STAP cells were actually developed from ES cells FES1.
- e) The STAP cell samples given to GRAS for Chip-seq analysis were actually 129B6F1-ES1 cells.

Opinion

It is unlikely that there was accidental contamination by three different ES cells, and it is suspected that the contamination may have occurred artificially. However, given the difficulty of identifying who might have contaminated the cultures, it is not possible to conclusively determine that it was artificial contamination. We cannot, therefore, conclude that there was research misconduct in this instance.

2) Investigation of published figures

- a) *Article Fig. 5c: Growth curves of STAP stem cells.* No measurements were submitted of the cell numbers, and in the interview with Obokata, it was found that she had created the figure without measuring the cell numbers.
- b) *Article Fig. 2c: DNA methylation.* It was not possible to reproduce this figure from the sequence data kept by GRAS, and in the interview with Obokata, it was found that she had created the figure with deliberately selected data.

Opinion

The STAP stem cell growth experiments were not properly performed. The figure of DNA methylation was not correctly made using original data. We therefore conclude that these two figures represent research misconduct involving fabrication. Both figures were created by Obokata and she bears responsibility for them.

5. Summary

We have concluded that there was research misconduct by Obokata on two points. More important is that all of the STAP stem cells, FI stem cells, chimera mice, and teratomas originated in cultures contaminated with ES cells, a fact that refutes all of the main conclusions of the two papers. We have been able to confirm the existence of very little original data for the figures in the papers, and the responsibility for this rests primarily with Obokata who created the figures. Nevertheless, it is a serious problem that the collaborators and co-authors overlooked this point. In particular, Wakayama who headed the laboratory in which Obokata worked, and Sasai, who played a major role in compiling the final version of the STAP cell papers, both bear heavy responsibility.