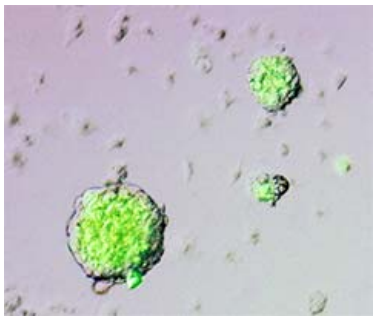
January 29, 2014

This article was withdrawn from the website on July 2 as the paper it was based on has been retracted.

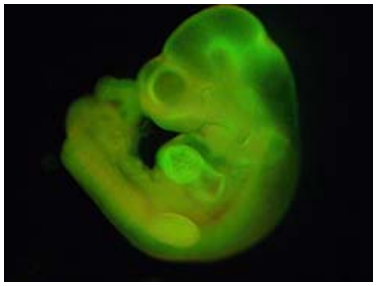
Stress turns ordinary cells pluripotent



STAP cells derived from lymphocytes

Breakthrough findings by Haruko Obokata and colleagues at the RIKEN Center for Developmental Biology (CDB) look to upset the canonical views on the fundamental definitions of cellular differentiation and pluripotency. In a pair of reports in *Nature*, Obokata shows that ordinary somatic cells from newborn mice can be stripped of their differentiation memory, reverting to a state of pluripotency in many ways resembling that seen in embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs).

The conversion process, which Obokata has named STAP (stimulus-triggered acquisition of pluripotency), requires only that the cells be shocked with a dose of sublethal stress, such as low pH or mechanical force, in order to trigger a remarkable transformation, in which the cells shrink, lose the functional characteristics specific to their somatic cell type, and enter a state of stem cell-like pluripotency. Such STAP cells show all the hallmarks of pluripotency, and contribute to chimeric mice and germline transmission when injected into early stage embryos.



Mouse embryo generated from STAP cells

Even more interestingly, STAP cells show a level of plasticity that exceeds that even of ESCs and iPSCs, in that they can give rise to cells of both embryonic and extraembryonic lineages; other pluripotent stem cells typically only generate embryonic lineage cells. STAP cells also differ from stem cells in their lower ability to proliferate in culture, but Obokata found that by adding different factors to STAP culture medium, she was able to cause them to transform into either 'STAP stem cells,' which behaved very much like embryonic stem cells, or a second form of stem cell capable of both generating extra-embryonic lineages and long-term culture.

"It's exciting to think about the new possibilities these findings open up, not only in areas like regenerative medicine, but perhaps in the study of cellular senescence and cancer as well," says Obokata. "But the greatest challenge for me going forward will be to dig deeper into the underlying mechanisms, so that we can gain a deeper understanding of how differentiated cells can covert to such an extraordinarily pluripotent state."

This work was done in collaboration with Charles Vacanti's lab at Brigham and Women's Hospital, Harvard University, Masayuki Yamato's lab at Tokyo Women's Medical University, and the laboratories for Genomic Reprogramming, Pluripotent Stem Cell Studies, and Organogenesis and Neurogenesis at the RIKEN CDB.

The reports are published in *Nature* DOI:10.1038/nature12968 and DOI:10.1038/nature12969

Pluripotent cells generated by STAP. Lymphocytes exposed to low-pH conditions are reprogrammed to a pluripotent state within 3 days. GFP shows expression of pluripotency marker Oct4, which is activated within about 2 days.

STAP cells contribute to embryonic development. On injection into a mouse blastocyst, STAP cells contribute to embryonic development. Using tetraploid complementation, it is possible to generate chimeric mice in which 100% of the embryo's somatic tissues are derived from STAP cells.

RIKEN

2-1 Hirosawa, Wako, Saitama 351-0198, Japan
Tel: +81-(0)48-462-1111
Fax: +81-(0)48-462-1554