

THE J. DAVID GLADSTONE INSTITUTES

1650 Owens Street, San Francisco, CA 94158 Telephone: 415.734.2000 www.gladstone.ucsf.edu
in affiliation with the University of California, San Francisco



GLADSTONE INSTITUTE OF CARDIOVASCULAR DISEASE NEWS

CONTACT:

Valerie Tucker, 415-734-2019

E-mail: vtucker@gladstone.ucsf

Web: www.gladstone.ucsf.edu

For Immediate Release

YAMANAKA ELIMINATES VIRAL VECTOR IN STEM CELL REPROGRAMMING

Gladstone Researcher Makes Progress in Improving Safety

SAN FRANCISCO, CA – October 9, 2008—Shinya Yamanaka MD, PhD, of Kyoto University and the Gladstone Institute of Cardiovascular Disease (GICD) has taken another step forward in improving the possibilities for the practical application of induced pluripotent stem (iPS) cell technology.

Previously, Yamanaka had shown that adult cells can be reprogrammed to become embryonic stem cell-like using a cancer-causing oncogene as one of the four genes required to reprogram the cells, and a virus to transfer the genes into the cells. In the last year, Dr. Yamanaka and other labs showed that the oncogene, c-Myc, is not needed. However the use of viruses that integrate into the genome prohibit use of iPS cells for regenerative medicine because of safety concerns: its integration into the cell's genome might activate or inactivate critical host genes.

Now Dr. Yamanaka's laboratory in Kyoto has eliminated the need for the virus. In a report published this week in *Science*, they showed that the critical genes can be effectively introduced

without using a virus. The ability to reprogram adult cells into iPS cells without viral integration into the genome also lies to rest concerns that the reprogramming event might be dependent upon viral integration into specific genomic loci that could mediate the genetic switch.

Yamanaka

2-2-2

“The iPS field and stem cell research in general is progressing rapidly,” said GICD Director Deepak Srivastava, MD. “But, as Shinya has shown, each step forward reveals a new set of challenges.”

Dr. Yamanaka’s team began this series of experiments by replacing the retrovirus with an adenoviral vector. While transfections with the genes on separate vectors didn’t work, they did work when the genes were arranged in a specific order on a single vector. The same arrangement worked when the genes were incorporated into a plasmid.

To determine if the plasmid-mediated reprogrammed cells were pluripotent, the scientists transplanted the cells under the skin of immunocompromised mice. The resulting tumors contained a wide variety of cell types from all three germ layers. iPS cells injected into embryos resulted in chimeric mice with the injected cells contributing to almost all cell types.

Still, other problems remain to be solved. The efficiency of the gene transfer with the plasmid was lower than with the retrovirus. Nevertheless, this significant step moves us closer to realizing the promise of stem cells in the understanding and eventual cure of diseases.

Okita K, Nakagawa M, Hyenjong H, Ichisada T, Yamanaka S. Generation of mouse induces pluripotent stem cells with viral vectors. *Science*, In press.

About the Gladstone Institutes

The J. David Gladstone Institutes, affiliated with the University of California, San Francisco (UCSF), is dedicated to the health and welfare of humankind through research into the causes and prevention of some of the world’s most devastating diseases. Gladstone is comprised of

the Gladstone Institute of Cardiovascular Disease, the Gladstone Institute of Virology and Immunology and the Gladstone Institute of Neurological Disease. More information can be found at *www.gladstone.ucsf.edu*.

#