

## A New Stem Cell Line for HD: Another Model of the Disease

Harvard Stem Cell Institute researcher George Q. Daley, MD, PhD, also associate director of the Stem Cell Program at Children's Hospital Boston, and HSCI colleagues Konrad Hochedlinger and Chad Cowan have produced a robust new collection of disease-specific stem cell lines, including one for Huntington's Disease. All were developed using the new induced pluripotent stem cell (iPS) technique.

The iPS technique involves the use of either certain types of skin cells called fibroblasts or certain types of bone marrow cells. For the HD line, skin cells were used from a young woman with Juvenile Huntington's Disease. The cells are transfected with four genes inserted into a viral vector. The four genes reprogram the cells to become stem cells with the potential to become any cell in the body.

The new iPS lines will be deposited in a new HSCI "core" facility being established at Massachusetts General Hospital (MGH), HSCI co-director Doug Melton announced. The operations of the iPS Core will be overseen by a faculty committee, which Daley will chair.



George Daley and Doug Melton at a 2007 press conference announcing the start of the project.

"We wanted to produce a large number of disease models for ourselves, our collaborators, and the stem cell research community to accelerate research," Daley said. "The original embryonic stem cell lines are generic, and allow you to ask only basic questions. But these new lines are valuable tools for attacking the root causes of disease. Our work is just the beginning for studying thousands of diseases in a petri dish," he said.

Melton said that the HSCI iPS Core will serve as a repository for iPS cells produced by HSCI scientists. "The Core will also function as a technical laboratory to produce these disease-specific lines for use by scientists around the world."

He went on to say that "The suite of iPS cell lines reported by the Daley group marks an important achievement and a very significant advance for patients suffering from degenerative diseases. These disease-specific iPS cells are invaluable tools that will allow researchers to watch the development diseases in petri dishes, outside of the patients. And we have good reason to believe that this will make it possible to find new treatments, and eventually drugs, to slow or even stop the course of a number of diseases. In years ahead, this report will be seen as opening the door to a new approach to develop therapies."

"One of our goals in creating the NIH Director's Pioneer Award programs was to enable exceptionally creative scientists to move quickly in promising new directions, thereby speeding the intellectual and technical breakthroughs needed to address major challenges in biomedical or behavioral research," said National Institutes of Health Director Elias A.

Zerhouni, M.D. "This is certainly the case for Drs. Daley and Hochedlinger, who deployed their Director's award resources to advance our ability to use induced pluripotent stem cells for disease-specific studies and drug development."

Daley and his colleagues, led by first-author and Children's researcher In Hyun Park, PhD, intentionally produced some stem cell lines for highly heritable, single-gene diseases such as Gaucher's; complex genetic syndromes such as Down's; and then complex diseases such as Parkinson's that involve genetic, cellular, and perhaps environmental components.

"The cell lines available from the iPS Core will allow stem cell researchers around the world to explore possible gene therapies for some conditions, and will aid in the development of drugs for others," Daley said.

The stem cell line for Huntington's Disease provides a welcome new model to study the development of the disease within a single cell. It could also be used to screen for and test potential new treatments. The authors note, however, that these cells could not be used for transplantation, even after the correction of the genetic defect, because of the use of the viral vectors.

Huntington's Disease is also being studied through cell models established from transgenic animals and through animals genetically engineered to develop the disease, including drosophila (fruitflies), a variety of mice models, sheep, and rhesus monkeys. Each model captures some but not all of the features of the disease. Cell models allow researchers to learn more about what is happening inside the cell. Animal models allow researchers to learn more about how Huntington's Disease progresses in a living animal and how it affects the brain as a system, including problems with how the cortex communicates with the striatum and how cells signal to each other. By studying a variety of models, researchers can gain more insight into the disease.

## **References:**

Press releases from Massachusetts General Hospital

In-Hyun Park, Natasha Arora, Hongguang Huo, Nimet Maherali, Tim Ahfeldt, Akiko Shimamura, M. William Lensch, Chad Cowan, Konrad Hochedlinger, and George Q. Daley. "**Disease-Specific Induced Pluripotent Stem Cells.**" Cell 2008 Aug 6. [Epub ahead of print].

- *Marsha L. Miller, Ph.D., August 13, 2008.*