U-M announces its first human embryonic stem cell line

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University of Michigan researchers have created the state's first human embryonic stem cell line, achieving a long-sought goal that provides the foundation for future efforts to develop innovative disease treatments.

The new cell line, known as UM4-6, is the culmination of years of planning and preparation at U-M and was made possible by Michigan voters' November 2008 approval of a state constitutional amendment permitting scientists here to derive embryonic stem cell lines using surplus embryos from fertility clinics.

"This historic achievement opens the door on a new era for U-M researchers, one that holds enormous promise for the treatment of many seriously debilitating and life-threatening diseases," said U-M President Mary Sue Coleman. "This accomplishment will enable the University of Michigan to take its place among the world's leaders in every aspect of stem cell research."

Work on UM4-6 began in May, and detailed characterization of the line was completed in late September. The project was conducted without federal funds, using private gifts to U-M's Consortium for Stem Cell Therapies and internal U-M resources. With the derivation of UM4-6, U-M joins a select group of fewer than a dozen U.S. universities that have created human embryonic stem cell lines.

"The real importance of today's announcement is that the ability to derive new embryonic stem cell lines will allow us to take the next step:

disease-specific research that could someday lead to new treatments," said Gary Smith, leader of the derivation project at the U-M Consortium for Stem Cell Therapies.

The consortium will distribute UM4-6 samples to stem cell researchers across campus and to their collaborators statewide. In addition, U-M researchers hope—pending the resolution of a federal court case that seeks to bar federal funding for human embryonic stem cell research—to submit UM4-6 to the U.S. National Institutes of Health for inclusion in the national registry of human embryonic stem cell lines that are eligible for federal research funding.

"We've spent a lot of time making sure that our entire process is in compliance with the NIH guidelines for registering embryonic stem cell lines so that other scientists will be able to use these lines to conduct NIH-funded research," said Smith, co-director of the consortium and a professor of obstetrics and gynecology at the Medical School.

UM4-6 was derived from a cluster of about 30 cells removed from a donated five-day-old embryo roughly the size of the period at the end of this sentence. That embryo was created for reproductive purposes but was no longer needed for that purpose and was therefore about to be destroyed.

The embryonic stem cells were extracted and placed in a culture dish containing nutrients that nourished them while preventing them from differentiating into specialized cell types. The cells divided and spread over the surface of the dish. When they began to crowd the dish, the cells were gently removed and placed into several fresh culture dishes, a process called re-plating. The re-plating process was repeated every seven to 10 days.

Once cell colonies have been successfully re-plated many times over

several months, a new embryonic stem cell line—a collection of millions of genetically identical cells generated from a single embryo—has been established. Various tests are then performed to confirm that the cells display all the traits of normal embryonic stem cells, including the ability to form the body's specialized cell types. Conducting those tests is called characterizing an embryonic stem cell line.

While the creation of Michigan's first human embryonic stem cell line stands as a research milestone, the many steps that led to the achievement were nearly as important.

"We have addressed all the regulatory issues and have derived this line according to the highest ethical standards. We have a laboratory equipped with cutting-edge equipment and people with the know-how," Smith said. “All our efforts have finally started to bear fruit, so now the truly exciting and novel work can begin."

In March 2009, four months after voters approved the state constitutional amendment, U-M announced the creation of a consortium to establish new human embryonic stem cell lines that will aid in the search for disease treatments and cures.

Based at the Medical School, the A. Alfred Taubman Medical Research Institute's Consortium for Stem Cell Therapies secured funding commitments of nearly $2 million to start the program. Lab space totaling 1,254 square feet was obtained in the Biomedical Science Research Building, and the labs were outfitted with state-of-the-art equipment. Four new research associates were hired to do the work.

Throughout much of last year, U-M researchers worked to ensure that their proposed embryo-donation and cell-line derivation projects would comply with federal law and the Michigan Constitution, as well as extensive new regulations established last summer by the National

Institutes of Health.

The project required approval by U-M's Human Pluripotent Stem Cell Research Oversight Committee and the Medical School's Institutional Review Board. Both committees are composed of physicians, scientists, ethicists, attorneys and community members who evaluated whether the project would be conducted ethically, legally and to the benefit of patients.

In November 2009, the U-M Consortium for Stem Cell Therapies received final approval to begin accepting donated embryos created for reproductive purposes but no longer needed or unsuitable for clinical use. Many Michigan couples, as well as some from outside the state, have contacted the university and expressed the desire to donate their surplus embryos—which would otherwise be discarded—for human embryonic stem cell research.

In March, the first attempts were made to establish an embryonic stem cell line, a process called derivation. After several attempts, the consortium team succeeded with UM4-6, using a 5-day-old embryo known at that stage as a blastocyst.

In addition to deriving new embryonic stem cell lines, consortium researchers spent much of this year refining recently developed techniques to convert adult skin cells into induced pluripotent stem cells, known as iPS cells. These reprogrammed cells display many of the most scientifically valuable properties of embryonic stem cells while enabling researchers to bypass embryos altogether.

Earlier this year, the consortium established its first iPS cells, using skin samples donated by healthy individuals and by patients with diseases including amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease) and several ataxias, said Sue O'Shea, a professor of cell

and developmental biology at the Medical School and co-director of the Consortium for Stem Cell Therapies. Consortium workers are now attempting to grow iPS cell lines that will be used to study disease mechanisms.

"There are few university programs in the United States deriving disease-affected embryonic stem cell lines," O'Shea said. "Our special niche will be creating, studying and understanding normal and abnormal development of disease-affected stem cell lines—both embryonic and iPS cell lines."

"These efforts represent the culmination of several years of work to bring Michigan laws into line with the laws of other states and expand the University of Michigan's facilities for pluripotent stem cell research, so we can follow the science wherever it leads and get to new treatments sooner rather than later," said Sean Morrison, director of the Center for Stem Cell Biology at U-M's Life Sciences Institute.

In the months and years ahead, consortium researchers will use genetically abnormal embryos to create cell lines that carry genes for diseases such as cystic fibrosis, Huntington's disease, Rett syndrome, spinal muscular atrophy and Tay-Sachs disease.

"We are extremely gratified that we are now able to make new embryonic stem cell and iPS cell lines available to researchers everywhere, who will put them to use in the discovery of effective treatments for a wide variety of human diseases," said Dr. Eva L. Feldman, director of the Taubman Institute. "It demonstrates the wisdom of the voters of the state of Michigan, who put their faith and confidence in the work of their scientific community. It is also a tribute to Alfred Taubman, who donated his time, his money and his leadership to make this day possible."

Embryonic stem cells are the body's master cells; they can replicate endlessly and form all of the more than 200 cell types in the human body. Scientists hope these remarkably versatile cells—and the iPS cells that mimic them—can someday replace faulty cells or diseased tissues in failing organs. This fledgling field is known as regenerative medicine, and the U-M Consortium for Stem Cell Therapies intends to play a leadership role in this research.

Provided by University of Michigan