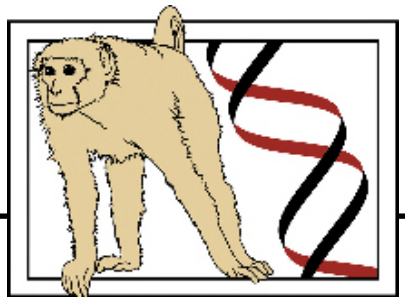
Stem Cell Resource Unit

Wisconsin National Primate Research Center
University of Wisconsin-Madison



The Stem Cell Resource Unit facilitates non-human primate (nhp) embryonic stem cell (ES cell) research. Specifically, the unit:

1) Stores frozen, genetically defined rhesus macaque and common marmoset monkey ES cell lines.

2) Develops genetically modified nhp ES cells and their derivatives.

3) Generates reagents that support the growth of nhp ES cells and their derivatives.

4) Develops strategies to differentiate and purify specific nhp ES cell derivatives.

5) Provides large-scale production of nhp ES cells and their derivatives for transplantation and *in vitro* studies.

6) Coordinates and assists animal procedures for ES cell transplantation studies.

The Stem Cell Resource Unit, with assistance from the Primate Center's Centralized Protocol Implementation Unit and WiCell Research Institute* (see next page), provides frozen nhp ES cells and training to interested investigators. This unit helps investigators pursue nhp ES cell culture in their own laboratories, to compliment their work with human ES cells, and as a prelude to using the rhesus monkey as a transplantation model.

Additionally, the stem cell resource unit provides zebrafish bFGF, a recombinant protein important for culturing nhp ES cells. Unit members also plan to use Mauritian cynomolgus macaque embryos to create new ES cell lines.

James Thomson heads the WNPRC Stem Cell Resource Unit and collaborates with several campus investigators on stem cell and regenerative medicine research. Thomson and his research teams became the first to successfully isolate and culture nonhuman primate ES cells (1995 *PNAS*), human ES cells (1998 *Science*), and induced pluripotent stem cells, or iPS cells, which act like ES cells but without the need to destroy an embryo (2007 *Nature,* with **Junying Yu**). At the same time, at Kyoto University, Shinya Yamanaka published similar results in *Science*.

In 2008, the Stem Cell Resource Unit provided iPS cell derivation for disease-specific cell lines to UW-Madison investigators. Three disease cell lines were used for iPS cell generation and a total of 29 cloned cultures were frozen for future use.

In 2009, unit members Yu and Thomson were authors on a paper detailing genetic reprogramming of cells cultured from a donor afflicted with a specific disease: "Induced pluripotent stem cells from a spinal muscular atrophy patient." (Ebert *et al*, *Nature,* 2009).

Campus investigators work with pluripotent and adult stem cells, human and nonhuman primate stem cells. Their collaborations and shared expertise are the keys to advancing all avenues of stem cell research:

• Several investigators at the Primate Center and on campus are collaborating on attempts to direct stem cells into becoming dopaminergic neurons to treat Parkinson's Disease. They include **Thomson, Clive Svendsen, Su-Chun Zhang, Joe Kemnitz, and Marina Emborg.**

• **Su-Chun Zhang** at the Waisman Center is researching neural-based stem cells and their potential for treating multiple sclerosis, amyotrophic lateral sclerosis (ALS), spinal cord injury and other diseases and disorders.

•**Ted Golos** is a reproductive biologist using stem cells and nonhuman primate embryos to study the basic biology of placental development. His long-

term goal is to improve pregnancy success and maternal and fetal health.

• Transplant surgeon **Jon Odorico** has guided stem cells into becoming pancreatic cells. These cells might someday be able to manufacture natural insulin for people with diabetes.

• UW-Madison researchers have derived many types of blood and immune system cells from pluripotent stem cells. Transplants of adult stem cells from bone marrow have effectively treated many cancers such as leukemia, lymphoma and multiple myeloma. Yet these therapies are hindered by limited cell quantities and not enough matched donors. UW researchers are planning to do ES or iPS cell-derived blood transplants in monkeys within a few years.

A larger supply of fresh healthy blood cells from pluripotent stem cells may also someday be transplanted into patients with sickle cell anemia, hemophaelia and other genetic diseases of the blood. Such transplants could theoretically improve, or even cure these patients. Generating platelets, red blood cells, white blood cells, and other blood components from ES or iPS stem cells might also help alleviate blood bank shortages. **Igor Slukvin** and **Peiman Hematti** are exploring these hematopoetic (blood-related) stem cell potentials.

• **Timothy Kamp** is a cardiologist aiming to use cardiac muscle cells from human ES and iPS cells to help restore cardiac function in patients who have heart disease. He is also studying cardiomyocytes *in vitro* as a method of preclinical safety testing for new heart drugs. Kamp co-directs the Stem Cell & Regenerative Medicine Center on campus.

• **Tenneille Ludwig** is a researcher at WiCell who, along with Thomson in 2006, grew two new lines of human ES cells without using animal products as growth factors. Ludwig trained with Thomson at the Primate Center before joining WiCell and deriving this "feeder-free" gold standard cell culture method.

• **Rupa Shevde** is a scientist at WiCell studying the growth of bone cells from ES and iPS cells. She also collaborates with the Primate Center and other departments to conduct stem cell outreach.

• **Ian Duncan** is a neuroscientist working with ES and iPS cells to study brain repair in the central nervous system. His research has implications for treating multiple sclerosis.

• **Sean Palacek** is a chemical and biological engineer working on better stem cell preservation methods. He is also interested in developing skin cells from ES cells to develop a skin substitute for burn victims and others who need skin transplants.

• **Clive Svendsen**, co-director of the Stem Cell & Regenerative Medicine Center, is collaborating with numerous investigators on various types of stem cell research and modeling diseases such as Fragile X, ALS, Parkinson's disease, Down's Syndrome and spinal cord injury.

• **Ronald Kalil** in Opthalmology and Visual Sciences is researching neural repair. The adult brain does not produce new neurons in response to brain injury. Neurons grown from stem cells might someday help the injured brain repair itself.

*WiCell is a private research institute off campus operated under a collaborative agreement with the UW-Madison. Directed by **Erik Forsberg**, WiCell allows the sharing of the unique resources at the Primate Center, the UW Hospital Transplant Program, and the Waisman Clinical BioManufacturing Facility. WiCell-trained scientists conduct ES and iPS cell research throughout the world.

WiCell also houses the U.S. National Stem Cell Bank, directed by **Derek Hei**. The NIH established this bank in October 2005 to consolidate many of the federally funded eligible human embryonic stem (ES) cell lines in one location, reduce the costs that researchers have to pay for the cells, and maintain quality control over the cells.

For more stem cell and regenerative medicine center information, please visit the UW-Madison Stem Cell & Regenerative Medicine Center website at *stemcells.wisc.edu*.

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