BEDFORD STEM CELL RESEARCH FOUNDATION

Massachusetts 501(c)(3) not for profit organization

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NEWSLETTER

CLOCK GENES
Foundation scientists discover that genes controlling the body's response to light/dark cycles, circadian rhythm, are also turned on in human embryo cells that give rise to embryonic stem cells

INSIDE THIS ISSUE

Genes called *circadian oscillators* control the body's response to light and dark

BSCRF Discovers Stem Cells Have A Clock

All living things respond to the earth's light/dark cycle. Many scientists believe that early organisms survived better if they replicated their genetic material, DNA, at night to avoid damage inflicted by ultra-violet rays from the sun. Darkness is accompanied by decreased temperatures, so all living things also go through daily (circadian) temperature changes, some imposed by environment (e.g. things that live in water), some by core body temperature changes stimulated by the brain.

The response of humans to circadian changes is controlled by light stimulation of sensors in the eye that coordinate the release of hormones by the brain. Patterns of sleep and wake are the best studied circadian responses.

More recent research has revealed that in addition to the circadian rhythm of the brain, all tissues in the body have their own circadian rhythm. Thus, the new findings indicate that every cell in the body has its own internal Clock, kept in synchrony by cycles of light and dark.

Bedford Research Foundation stem cell scientists have used new technologies to study the human embryo cells that give rise to embryonic stem cells. The goal of the work is to fill information gaps about how stem cells multiply and differentiate into all the tissues in the body. These studies have revealed CLOCK genes may play an important role in stem cell biology, suggesting that new ways to culture stem cells in laboratories are urgently needed.

What is a Stem Cell?

A reserve cell with the capacity to multiply when needed to replace dead or damaged adult cells. Reserve stem cells do not exist for many vital tissues, including: heart, spinal cord, brain and pancreas.

Key Term "Pluripotent"

The capacity to become any cell in the body.

Embryonic stem cells are pluripotent, adult stem cells are not.

Types of Pluripotent Stem Cells

1) Embryonic stem cells from fertilized eggs are good models for research, but they have ethical issues, and will have tissue rejection problems (similar to bone marrow and kidney transplants).

2) Parthenote stem cells (derived from unfertilized eggs) are as pluripotent as embryonic stem cells, and have been the focus of BSCRF scientists for several years. Studies using monkey parthenote stem cells to treat Parkinson's disease in monkeys have been very promising.

- Parthenotes do not have the potential tissue rejection problems faced by stem cells derived from *fertilized* eggs.
- Unlike adult stem cells, parthenotes can become any cell in the body.
- Less controversial than stem cells that are derived from *fertilized* eggs.

3) Induced pluripotent stem cells (derived from adult skin cells) were first reported by a Japanese research team in 2007. The genes of normal human cells can be manipulated in the laboratory to acquire properties of embryonic stem cells. Termed induced pluripotent stem cells, these cells have been useful research tools, but their gene manipulations limit their use for patient therapies. Many laboratories are studying ways to derive induced pluripotent stem cells without manipulating genes.

(See the 1 minute video at www.bedfordresearch.org)

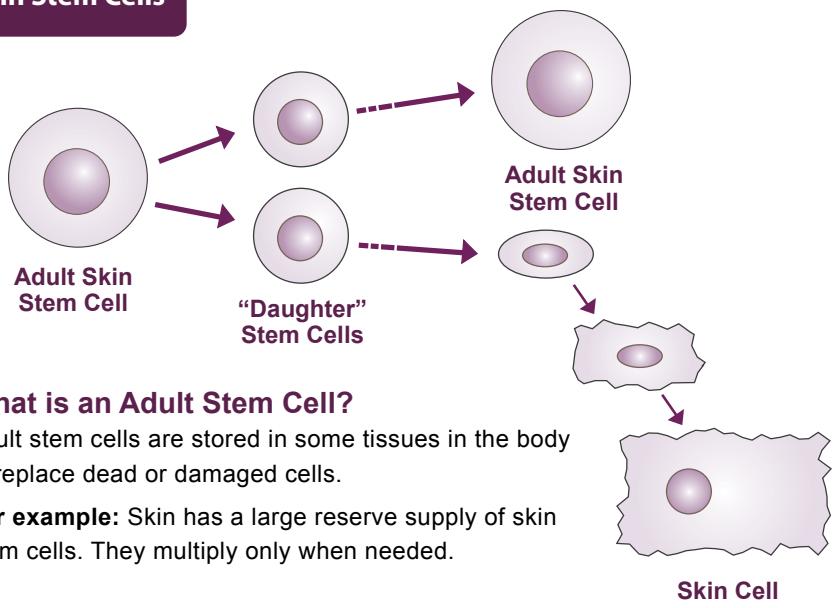
What Is An Embryonic Stem Cell?

A stem cell derived from eggs fertilized by sperm; these stem cells are "pluripotent." Recent research has shown that it is also possible to get pluripotent stem cells from *unfertilized* eggs (parthenotes).

What Are Cord Blood Stem Cells?

Cells in the umbilical cord are "multipotent" and can give rise to all the cells in a normal bone marrow. Scientists are working to discover if these cells can become other types of adult stem cells.

Skin Stem Cells



What is an Adult Stem Cell?

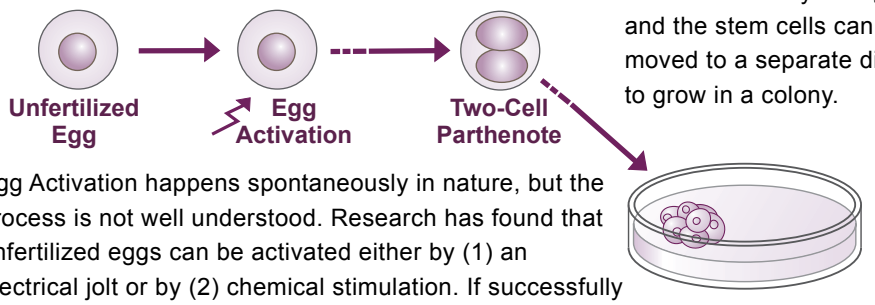
Adult stem cells are stored in some tissues in the body to replace dead or damaged cells.

For example: Skin has a large reserve supply of skin stem cells. They multiply only when needed.

Stem Cells From *Unfertilized* Eggs!!

When eggs are fertilized by sperm they become "activated," their cells divide and can be a source of embryonic stem cells. Human eggs can also be "activated" without being fertilized. *Unfertilized*, "activated" eggs are called **Parthenotes**.

Parthenote Stem Cells



After approximately 6 days the parthenote reaches the 150 cell Blastocyst stage and the stem cells can be moved to a separate dish to grow in a colony.

Egg Activation happens spontaneously in nature, but the process is not well understood. Research has found that unfertilized eggs can be activated either by (1) an electrical jolt or by (2) chemical stimulation. If successfully activated, the egg undergoes early cell divisions similar to fertilized eggs, but cannot give rise to an offspring.

Results at BSCRF are promising. We have developed laboratory conditions that lead to mouse parthenote stem cells (mPS) with the same efficiency as from fertilized mouse eggs. Our most recent mPS cells were developed entirely in laboratory conditions free of other animal cells, thus paving the way for similar development of human PS cells free of animal products.

THE 2009 ACTIVATED EGG SYMPOSIUM

On November 6, 2009, the Foundation will host it's seventh annual Activated Egg Symposium. During this one-day event researchers studying eggs for *stem cell derivation*, or *reproduction* share and discuss their research. With attendance limited to 100 the event provides a uniquely focussed environment for investigators from academia and industry to meet and form collaborations.

This year's keynote will be **Dr. Renee A. Reijo Pera**, director of Stanford's Center for Human Embryonic Stem Cell Research and Education.

THE 2009 SPINAL CORD WORKSHOP

"What are the Barriers to Cure?" the second spinal cord workshop was held on April 4th, 2009.

The workshop brought together medical and scientific expertise to identify barriers to reversal of the neurologic damage that follows spinal cord injury, and describe what is needed to overcome those barriers to cure.

The emerging field of stem cell therapy may hold special promise, but as described by the workshop participants, specifics about cell differentiation, method of delivery and outcome measures need to be developed.

Videos from this exciting day of talks are available at www.bedfordresearch.org.

BAKE SALE FOR STEM CELL RESEARCH

In May of 2009 the Foundation received a donation from the members of the Purple Team Congress at Pennichuck Middle School in Nashua, New Hampshire raised during a bake sale.

"...because we know it could save many lives. Several people in our school have been affected by diseases that could be helped with further stem cell research."

The bake sale raised $175 for the Bedford Research Foundation's science programs. That is enough to cover a full day of reagents and supplies for Foundation's staff to conduct experiments, and helps to fund further breakthroughs as we lead the way in this rapidly evolving area of biomedicine.

Foundation Research Programs

Patient-Specific Pluripotent Stem Cells

Developing patient-specific pluripotent stem cells is a primary focus of the Foundation's Stem Cell Research program. Unfertilized eggs are an excellent, but under-utilized source of pluripotent stem cells because of the moratorium on federal funding for the research. The new stem cell research guidelines, developed in response to President Obama's executive order, still do not allow federal funding for research on stem cells derived from unfertilized human eggs.

Spinal Cord Injury Treatment Trials in the U.S.

The Spinal Cord Workshops in 2008 and 2009 organized by the Bedford Research Foundation with the University of Georgia and The Shepherd Center brought together clinicians and scientists in an unusually candid discussion of "What are the barriers to cure for spinal cord injury." The 2010 workshop is planned for Taiwan and will also include Chinese clinicians and scientists. The goal is to expedite safety trials for stem cell therapy of spinal cord injury in the U. S. as well as China.

Donations are urgently needed for these programs, please donate at www.bedfordresearch.org

Cell Multiplication Controlled by a Surprising Set of Genes

BSCRF Discovers Stem Cells Have A Clock

"The cells that give rise to embryonic stem cells appear to be regulated by genes that control circadian rhythm..."

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While stem cell scientists struggle to understand the therapeutic potential of the extraordinary cells that can multiply to the trillions needed for therapies, and become every tissue in the body, the public agonizes over the use of embryos to derive them. The result is a lack of federal funds for most of the work, despite President Obama's executive order to rescind former President Bush's restrictions. In fact, fewer federal dollars are available now than ever before while the National Institutes of Health (NIH) implements new guidelines. This is an enormous frustration for scientists, and an outright tragedy for patients.

Regrettably, the federal moratorium also extends to stem cells derived from eggs not fertilized by sperm, termed parthenote stem cells. It is a fact of nature that unfertilized human eggs can spontaneously (or artificially) begin to divide into cells that can also multiply to the trillions needed for therapies, and become all the types of cells in the body, but cannot become offspring. Parthenote stem cells would logically seem to avoid the dilemmas associated with stem cells from embryos, as well as provide a source of patient-specific stem cells for women. But the new NIH guidelines specifically exclude parthenote stem cells from federal funding. Therefore, the only source of funding for BSCRF's unique parthenote stem cell research program is private contributions. Every dollar counts, $175 a day funds a stem cell researcher.

Not excluded, however, is the derivation of stem cells from testis, a break-through reported by several research teams in 2009. Apparently as versatile as embryonic stem cells, testis-derived stem cells are an exciting new source of pluripotent stem cells and patient-specific cells for men.

Award-winning Bedford Foundation stem cell scientists are poised to study both testis-derived and egg-derived stem cells in 2010 to determine if circadian laboratory conditions improve the yield of therapeutic cells for diseases such as spinal cord injury, diabetes, heart failure, lung failure, Parkinson's disease, stroke, ALS, autism, Alzheimer's, and AIDS . The parthenote stem cell studies can only be supported by non-federal funds, so to avoid conflict with federal agencies, the testis-derived stem cell research must also be non-federally funded. Adequate funding is the only unmet need to move this work forward. Your support is urgently needed.

Your contribution may benefit everyone you know. Ann A. Kiessling, PhD

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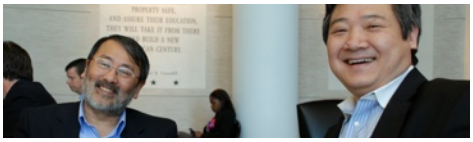
News Inside

The 2009 Activated Egg Symposium



The 2009 Spinal Cord Workshop

May 2009: Middle School Holds Bake Sale for Bedford's Research