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RESEARCH FOUNDATION

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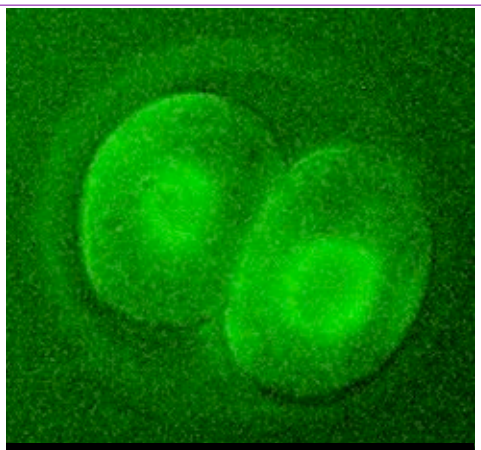
Stem Cells For *Every*Body

Twenty-Six Years of Progress

Bedford Research Foundation is TWENTY SIX

Founded in 1996 to conduct research that the NIH cannot fund because of the Dickey-Wicker amendment, Bedford Research scientists have achieved groundbreaking milestones:

- **1998** Special Program of Assisted Reproduction (SPAR) designed to protect wives and babies of HIV-infected men from infection during conception
- **2000** World's first program of human egg donation for stem cell research
- **2001** Report on artificially activated human eggs (parthenotes)
- **2002** First Activated Egg Symposium
- **2006** Research program with The University of Athens to understand human egg parthenogenesis



Green fluorescent protein glow in the nuclei of a two-cell mouse embryo provides new insights for deriving stem cells from artificially activated eggs.

- **2008** First detection of prostate cancer genes in semen
- **2009** Discovery that circadian rhythms may be important for human egg activation
- **2009** First Spinal Cord Workshop "What are the Barriers to Cure?"
- **2010** First International Meeting on Spinal Cord and Neuro-degenerative Diseases inTaiwan
- **2012** First circadian microscope to observe activated mouse egg development for five days.
- **2014** First observations of active circadian rhythm genes in early mouse embryos
- **2017** Discovery of method in a mouse model system to derive "universal" stem cells.
- **2018** Development of ethical guidelines for women to donate frozen eggs for research.
- **2019** First Symposium on Circadian Rhythms and Development (Boston)
- **2020** Development of PCR test to assist health care facilities with COVID19
- **2021** Development of unique transport medium for unfertilized human eggs for stem cell research
- **2022** Beginning of the unique "Ginterscope" design to study circadian rhythms in stem cells

This work cannot be federally funded because of the 1996 Dickey-Wicker Amendment to the National Institutes of Health budget. BRF scientists rely on private donations for research to develop "universal" stem cells for *Every* BODY.

Donate to the Foundation **Your donations could help everyone you know**

Donations accepted by mail at: Bedford Research Foundation, PO Box 1028 Bedford MA 01730

Colleagues from Rome, UMass Amherst, UMass Medical and Harvard Medical School


Dr. Oliver Rando

Dr. Corrado Spadafora was a visiting professor from Rome for the month of September. He was the first to report 33 years ago that sperm influence embryo development in more ways than just providing male chromosomes. Many colleagues from the Boston area were anxious to meet him, so we held a mini-symposium at BRF. Dr. Spadafora's insights into egg activation processes guided our pilot experiments to detect the activation of a specific set of genes, LINE1, pictured in the two cell mouse embryo on the front page. This exciting result opens a new path to improve human parthenote stem cell development.


L to R: Drs. Corrado Spadafora, Pablo Visconti, Maia Elizagaray, Maria Battistone, Ann Kiessling, Ferran Villalonga, Maria Gervasi

Staff Updates:

Dr. David Albertini, Professor of Developmental Cell Biology, Bedford Research Foundation, is also Editor-in-Chief of the Journal of Assisted Reproduction and Genetics, and visiting scientist at The Rockefeller University and Center for Human Reproduction. Dr. Albertini's most recent studies at BRF have verified the research value of human eggs rejected for human fertility treatments and usually discarded. His unique microscopy skills have confirmed the viability of the rejected eggs after their transport to Bedford thus ensuring their potential to activate into human parthenote stem cells. The work has also provided new insights into human egg responses to the hormone treatments used for fertility treatments. These studies are ongoing with the help of a generous donation of microscope funds from the ESHE foundation.

Dr. María Gracia Gervasi, Assistant Professor of Reproductive Cell Biology at BRF, has implemented the continuous time lapse recordings of human eggs during recovery from transport followed by parthenogenetic activation. The dozens of time lapse movies have revealed new insights into egg activities during culture (www.bedfordresearch.org) without and with artificial activation stimulus. The work supports the notion that although artificial culture conditions can stimulate eggs to begin to synthesize new copies of chromosomes and divide into two, four and eight-cell parthenotes, most hit a road-block that prevents further development to stable stem cells. The new time-lapse results provide a non-detrimental approach to following egg responses to various stimuli to overcome the block to stable stem cells.

Dr. Lynae Brayboy, Associate Professor of Reproductive Cell Biology at BRF, has continued her sabbatical at Charite, a well-known research hospital in Germany. Dr. Brayboy is board certified in Reproductive Endocrinology with a passion for understanding egg biology: "Life begins with an egg, and we don't know very much about them." Dr. Brayboy has received grant funds to study egg defects in a mouse model of aging and infertility. Although normally fertile when young, the mice undergo premature aging and infertility. Dr. Gervasi successfully derived 19 new embryonic stem cell lines plus two parthenote stem cell lines from the mutant mice that will be used to conduct studies not possible with eggs alone, including understanding egg defects in premature aging.

From the Director…

The green-glowing mouse embryo cells on the front page bring my decades of research full circle. During my graduate school studies of retroviruses, Nobel laureate Howard Temin hypothesized that the unique enzyme in retroviruses, reverse transcriptase, responsible for the reverse flow of genetic information back to new gene sequences, was more fundamentally important than multiplying viruses, it must have a more basic biological role. He hypothesized it provided a pathway for early embryos to amplify specific genetic information important to early embryonic development. In 1979 I published the first report of reverse transcriptase in normal human cells and in 1981 I published the first report of reverse transcriptase in early mouse embryos. But research tools were not available to take the work further, this was before large-scale gene sequencing was possible. This research path took a new turn when Corrado Spadafora discovered that not only did sperm internalize all types of nucleic acids they were exposed to, they also contained a reverse transcriptase activity that could make DNA copies of RNAs. This was highly controversial, but in keeping with Temin's original hypothesis. Once all the genetic information in organisms could be sequenced, it was discovered that a large percentage of both human and mouse genes code for reverse transcriptase, including LINE1 elements, that are actually repeated hundreds of times throughout the chromosomes of all mammals. Most LINE1 genes are silent, but much research has revealed they are activated in specific conditions, such as cancer, and early embryo development. This brings us to the possibility that LINE1 activation may be needed to get through the 8-cell roadblock exhibited by the human parthenotes we are studying. Dr. Spadafora gave us the research tool to explore this possibility, as illustrated on the front page, and we will be able to also use this tool in the discarded, activated human eggs we now study routinely.

Donate Today

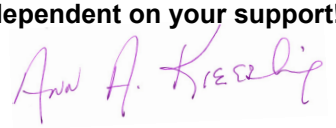
"Bedford Research scientists are developing stem cells from eggs, not from embryos, thus bypassing many of the ethical dilemmas associated with stem cell research."

-Sen. Michael J. Barrett

Our discovery in 2009 that normal 8-cell human embryos have the genes controlling circadian rhythms turned on suggests another fundamentally important pathway in the activation of human eggs. This research path has been thwarted by the lack of a circadian microscope sensitive enough to detect the low level of light output by a bioluminescent mouse model for circadian rhythm studies. Thanks to a generous donation by Tabor Gunter, we are in the process of designing the "Gunterscope", the first circadian microscope capable of detecting single photons of light output. It is still in the design phase, but the plan is to have initial images by mid-2023. This will allow us to test the hypothesis that circadian rhythms are important to normal cell divisions of both embryonic and stem cells. If this is found to be true, this would revolutionize the way all cells are cultured for research, cell therapies, and assisted reproduction, ramifications far beyond our specific research.

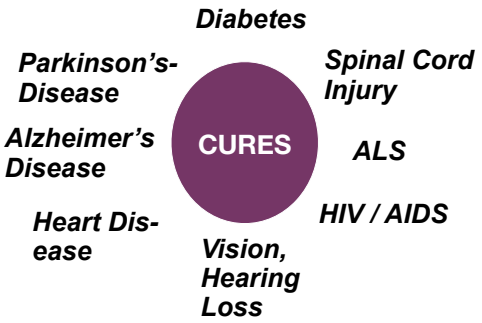
Human egg research MUST be privately funded. We appreciate your contribution to our critical work and are entirely dependent on your support!

Sincerely



Ann A Kiessling, PhD ***Director, Bedford Research Foundation***

Philanthropy Is The Key To Continued Progress



The average cost of each experiment is $95,000. Because much of our building overhead is covered by fee-for-service laboratory tests, ***92% of every dollar donated*** goes directly toward research, both stem cells for every body and prostate screening tests. This innovative funding model allows Bedford Research scientists greater flexibility to move quickly in promising new research directions.

Continued progress in all research areas requires meeting our annual funding goal of $500,000 in 2023.

This will help fund another scientist to keep our momentum going — donate today!

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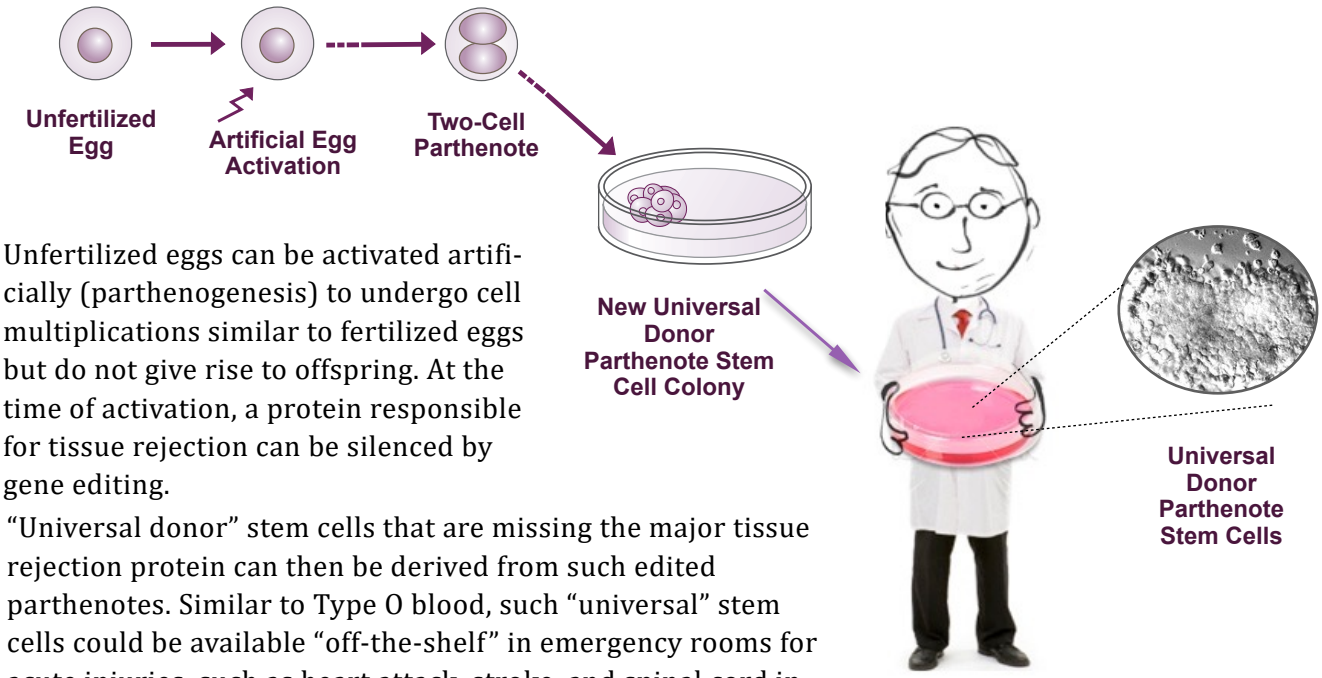
News Inside

Stem Cells for *Every*Body



Unfertilized eggs can be activated artificially (parthenogenesis) to undergo cell multiplications similar to fertilized eggs but do not give rise to offspring. At the time of activation, a protein responsible for tissue rejection can be silenced by gene editing.

"Universal donor" stem cells that are missing the major tissue rejection protein can then be derived from such edited parthenotes. Similar to Type O blood, such "universal" stem cells could be available "off-the-shelf" in emergency rooms for acute injuries, such as heart attack, stroke, and spinal cord injury. This would be a significant step forward in stem cell therapies for critical and chronic conditions.