Connecticut United for Research Excellence, Inc.
The Center of Connecticut's BioScience Cluster

For immediate release

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Connecticut Stem Cell Research Active and Multifaceted on Eve of StemCONN 09

New Haven, Conn., March 23, 2009 – Stem cell research in Connecticut is active and multifaceted, according to a review conducted by CURE (Connecticut United for Research Excellence), the state bioscience organization, on the eve of StemCONN 09, the international stem cell symposium taking place in New Haven March 23-24.

In the wake of its pioneering legislation in 2005 committing $100 million over 10 years to human embryonic and adult stem cell research, Connecticut has funded a variety of research, including projects aimed at building stem cell research infrastructure, projects to improve understanding of stem cells' unique ability to self-renew and differentiate, and projects that take early steps toward utilizing stem cells to develop therapies for specific diseases.

"Bioscience is a driver of Connecticut's current economy, and stem cell research is a driver of Connecticut's current bioscience," said Paul Pescatello, president and CEO of CURE. "The State's decision to make a proactive commitment to stem cell research is proving to have been very wise indeed."

At StemCONN 09, Connecticut stem cell researchers are joining other top scientists from around the United States and the globe to report the latest research findings. The gathering is one of the first in the United States since President Obama reversed limitations on Federal support of stem cell research.

Connecticut research universities have used state funding to build up stem cell research infrastructure. Yale has established the Yale Stem Cell Center in New Haven. The University of Connecticut and Wesleyan University have established a Stem Cell Core, and UConn is establishing a Stem Cell Institute at a new facility in Farmington. UConn scientists at the Stem Cell Core recently generated two new human stem cell lines.

Its funding program and encouraging attitude toward stem cell research have enabled Connecticut to attract top stem cell researchers and promising junior scientists to the State.

Although at this stage most research is still basic and being carried out in the universities, at least one Connecticut company, CellDesign of New Haven, has begun to market products based on stem cell technology.

When Governor M. Jodi Rell signed Connecticut's stem cell bill into law on June 15, 2005, Connecticut became just the third state in the nation to provide public funding in support of human embryonic and adult stem cell research. The act established advisory and peer review committees, with the Commissioner of Public Health as chair. Commissioner J. Robert Galvin is among the speakers at StemCONN 09.

State funded projects aimed at building up Connecticut's stem cell research infrastructure include:

- *Human Embryonic Stem Cell Core Facility at Yale Stem Cell Center*, Yale University, **Haifan Lin**, Principal Investigator
- *Human ES Cell Core at University of Connecticut and Wesleyan University*, University of Connecticut Health Center, **Ren-He Xu**, Principal Investigator

- *Flow Cytometry Core for the Study of hESC*, University of Connecticut Health Center, **Hector Leonardo Aguila**, Principal Investigator

  Flow cytometry is a technique for identifying and isolating cell types. It requires specialized instrumentation. This project includes purchase of a sophisticated cell-sorting instrument.

Connecticut research aimed at improving general understanding of the unique capabilities of stem cells includes:

- *Molecular Control of Pluripotency in Human Embryonic Stem Cell*, Yale Stem Cell Center, **Natalia Ivanova**, Principal Investigator

  Stem cells have a unique ability to transform into other cell types. This project studies the molecular components and pathways that control such transformations.

- *Molecular function of Lin28 in human embryonic stem cells*, Yale University, **Yingqun Huang**, Principal Investigator

  Human skin cells can be reprogrammed to act like stem cells. It is known from mouse models that Lin28 is an important factor in this reprogramming. This project extends study of Lin28 to human stem cells.

- *VRK-1-mediated Regulation of p53 in the Human ES Cell Cycle*, Yale University, **Valerie Reinke**, Principal Investigator

  As they grow, stem cells sometimes develop into tumors instead of normal tissue due to damaged DNA. This project seeks ways to limit DNA damage in cell cultures by turning on a tumor suppressor protein called p53.

- *The Role of the piRNA Pathway in Epigenetic Regulation of hESCs*, Yale University, **Qiaoqiao Wang**, Principal Investigator

  The goal of this project is to understand some of the fundamental mechanisms that control stem cells' ability to self renew and to differentiate into other cell types. In particular, the project investigates the roles played by a certain kind of protein (Piwi proteins) and a certain kind of RNA (piRNA).

- *Production and Validation of Patient-Matched Pluripotent Cells for Improved Cutaneous Repair*, University of Connecticut Center of Regenerative Biology, **Theodore Rasmussen**, Principal Investigator

  Regenerative medicine rests upon the ability to transplant immunologically matched cells into prospective patients. For this reason, substantial interest and effort has been focused upon the nuclear reprogramming of somatic cells, a process that can revert a patient's own cells to a state resembling an earlier developmental stage. This project uses novel approaches to produce directly reprogrammed human cells from human fibroblasts.

- *DsRNA and Epigenetic Regulation in Embryonic Stem Cells*, University of Connecticut Health Center, **Gordon G. Carmichael**, Principal Investigator

  The goal of this project is to understand some of the fundamental mechanisms that control stem cells' ability to self renew and to differentiate into other cell types. In particular, the project focuses on a special RNA molecule in the nucleus called NEAT-1. This type of RNA might help in converting ordinary (somatic) cells to pluripotent cells (cells with stem cell-like properties).

- *SMAD4-based ChIP-chip Analysis to Screen Target Genes of BMP and TGF Signaling in Human ES Cells*, University of Connecticut Health Center, **Ren-He Xu**, Principal Investigator

  The goal of this project is to understand some of the fundamental mechanisms that control stem cells' ability to self renew and to differentiate into other cell types. In particular, the project focuses on the effects of two

substances, transforming growth factor beta and bone morphogenic protein, that facilitate the ability of stem cells to transform.

- *Tyrosine Phosphorylation Profiles Associated with Self-Renewal and Differentiation of hESC*, University of Connecticut Health Center, **Bruce Mayer**, Principal Investigator

  The aim of this project is to understand how and when stem cells decide whether to self renew or to differentiate. It is known that one of the mechanisms controlling the process is tyrosine phosphorylation. In this project a new method called SH2 profiling will be used to study phosphorylation patterns.

- *Alternative Splicing in Human Embryonic Stem Cells*, University of Connecticut Health Center, **Brenton R. Graveley**, Principal Investigator

  A process called alternative splicing is one of the most important mechanisms by which gene expression is regulated. The main goal of this project is to identify the alternative splicing events that occur in undifferentiated human embryonic stem cells and in such cells undergoing differentiation into different cell types, as well as the roles of specific RNA binding proteins in controlling alternative splicing events.

- *Pragmatic Assessment of Epigenetic Drift in Human ES Cell Lines*, University of Connecticut, **Theodore Rasmussen**, Principal Investigator

  The purpose of this project is to develop methods for determining and monitoring the quality of stem cells grown in the laboratory before they are used in cell-based therapies.

- *Lineage Mapping of Early Human Embryonic Stem Cell Differentiation*, University of Connecticut, **Craig E. Nelson**, Principal Investigator

  The primary objective of this project is to create a "roadmap" of early human embryonic stem cell differentiation that can guide the efficient production of cells for regenerative medicine and cell replacement therapy.

- *Early Differentiation Markers in hESCs: Identification and Characterization of Candidates*, University of Connecticut Center for Regenerative Biology, **Mark G. Carter**, Principal Investigator

  Stem cell cultures may contain mixtures of cells at different stages, so it is important to find methods of identifying and distinguishing the stages. This project focuses on transcription factor genes, which are known to participate in regulatory networks that control the decision points in early development.

- *An Integrated Approach to Neural Differentiation of Human Embryonic Stem Cells*, Yale University, **Michael P. Snyder**, Principal Investigator

  This project investigates the process of neural cell differentiation and seeks to identify key components of the process. One of its goals is to establish techniques for identifying the genes and proteins involved that can be used by researchers throughout Connecticut.

- *Directed Isolation of Neuronal Stem Cells from hESC Lines*, Yale University School of Medicine, **Eleni A. Markakis**, Principal Investigator

  The aim of this project is to make human embryonic stem cells easier to work with, and more productive of neural stem cells, so that more labs will be able to study them**.** Expertise developed with adult-derived neural stem cells will be applied to try to isolate embryonic neural stem cells and to simplify their culture.

Connecticut research with links to potential therapies for specific diseases includes:

- *Directing Production and Functional Integration of Embryonic Stem Cell-Derived Neural Stem Cells*, Wesleyan University, **Laura B. Grabel**, Principal Investigator

  Long-term goals are focused on developing effective cell-based therapies for **epilepsy**, which afflicts over 60 million people worldwide. Designing embryonic stem cell therapies to treat **neurodegenerative disorders** requires identifying the signals that promote the transition of embryonic stem cells into neural stem cells. This project investigates the role of the extracellular signaling molecule Hedgehog in this transition. It also studies the fate of embryonic stem cell-derived neural stem cells transplanted into a mouse model of epilepsy. The results from these studies may help in the future design of human embryonic stem cell-based therapies used to treat **neurological disorders**.

- *Role of the Leukemia Gene MKL in Developmental Hematopoiesis Using hES Cells*, Yale University, **Diane Krause**, Principal Investigator

  This project studies the function of a gene called MKL that is mutated in the cancer cells of some patients with acute megakaryoblastic **leukemia**. The focus is on creating a cell line that will overexpress MKL on demand, so that its effect on normal megakaryocyte development and megakaryocytic leukemia can be studied.

- *Magnetic Resonance Imaging of Directed Endogenous Neural Progenitor Cell Migration*, Yale University School of Medicine, **Erik Shapiro**, Principal Investigator

  Delivery of various chemicals into the brain can alter and drive migration patterns of one's own neural precursor cells away from their normal routes, to areas of potential need. These directed cells have demonstrated significant benefits in several disease models, such as **ALS** and **Huntington's Disease**. The overall objective of this proposal is to use both magnetic resonance imaging and immunohistochemistry to evaluate the effect of combining the delivery of various chemicals into the brains of adult rats to increase cell migration to desired areas of the brain.

- *Translational Studies in Monkeys of hESCs for Treatment of Parkinson's Disease*, Yale University School of Medicine, **D. Eugene Redmond, Jr.**, Principal Investigator

  This project will advance the field toward a clinical application of stem cells, derived from embryonic stem cells, by doing important final efficacy, toxicity, and side effect studies in monkeys that are a prerequisite to human clinical trials. The project has the potential, and the investigators have the experience, to move to clinical trials in **Parkinson's Disease**, if the experiments are successful, by the end of the proposed funding period.

- *Effect of Hypoxia on Neural Stem Cells and the Function in CAN Repair*, Yale University, **Flora M. Vaccarino**, Principal Investigator

  This project will study mouse models in order to further understand the role of genetically modified human neural stem cell (NSC) lines in fostering **brain recovery after injury**. The project seeks to understand the critical genes that NSC must express in order to overcome tissue factors that obstruct **brain repair**.

- *Regulation hESC-derived Neural Stem Cells by Notch Signaling*, Yale University, **Joshua Breunig**, Principal Investigator

  This project seeks to determine the potential for repair of human embryonic stem cell-derived neural stem cells following molecular manipulation of the Notch pathway—one of the most powerful molecular mediators of cell fate (i.e., the cell's decision to remain a stem cell or generate neurons). Understanding of the Notch pathway may lead to enhanced transplantation therapies and to direct clinical applications for neural stem cells in the treatment of **traumatic brain injury**, **spinal cord injury**, and **neurodegenerative disease**.

- *Definitive Hematopoitic Differentiation of hESCs under Feeder-Free and Serum-Free Conditions,* Yale University, **Caihong Qiu**, Principal Investigator

  The purpose of this project is to develop approaches to efficiently induce human embryonic stem cells into blood cells in a system that is free of any non-human products. The focus will be on **bone marrow cells** and **red blood cells** that could be used for **transplantations** and **transfusions**, respectively.

- *Cortical neuronal protection in spinal cord injury following transplantation of dissociated neurospheres derived from human embryonic stem cells*, Yale University School of Medicine, **Masanori Sasaki**, Principal Investigator

  The mesenchyme is that part of the embryonic mesoderm from which connective tissue, bone, cartilage, and the circulatory and lymphatic systems develop. Transplantation of gene-modified human mesenchymal stem cells can contribute to repair and functional recovery in cases of **spinal cord injury**. This project uses rat models to better understand the details of the process.

- *Functional Use of Embryonic Stem Cells for Kidney Repair*, Yale University, **Lloyd G. Cantley**, Principal Investigator

  The purpose of this project is to develop a strategy for encouraging embryonic stem cells to become kidney progenitor cells for use in the treatment of patients with **acute renal failure**.

- *Human Embryonic and Adult Stem Cell for Vascular Regeneration*, Yale University School of Medicine, **Laura E. Niklason**, Principal Investigator

  This project will evaluate the pathways by which certain kinds of stem cells become vascular tissue. The focus is on bone marrow-derived mesenchymal stem cells as well as human embryonic stem cells. The results could pave the way for development of a novel therapy for **vascular disease**.

- *Wnt Signaling and Cardiomyocyte Differentiation from hESCs,* Yale University, **Dianqing Wu**, Principal Investigator

  Studies suggest a phenomenon known as Wnt signaling is important in the development of embryonic stem cells in heart tissue. In this project the phenomenon is studied more closely by a team that includes experts in biomaterial sciences and cardiac surgery. One goal is to establish a method for efficient cardiogenic cell production and engraftment, which lead to **cardiac function recovery** in a **heart disease** model.

- *Directed Differentiation of ESCs into Cochlear Precursors for Transplantation as Treatment of Deafness*, University of Connecticut Health Center, **D. Kent Morest**, Principal Investigator

  This project seeks to apply stem cell therapy to human hearing disorders, including **deafness**, **partial hearing loss** and **ringing in the ears (tinnitus**) due to noise, drugs, infections, and aging.

- *Development of Efficient Methods for Reproducible and Inducible Transgene Expression in Human Embryonic Stem Cells,* University of Connecticut Health Center, **Yuanhao (James) Li**, Principal Investigator

  This project seeks to develop methods for genetic modification of human embryonic stem cells. The modified lines would be used to explore new approaches to producing neurons in the inner ear for treatment of **hearing loss**.

- *Optimizing Axonal Regeneration Using a Polymer Implant Containing hESC-derived Glia*, University of Connecticut, **Akiko Nishiyama**, Principal Investigator

  This proposal seeks to generate glial (central nervous system) cells that will be used as a supportive cellular substrate to promote neuronal regeneration. Therapies that promote regeneration of damaged neurons will have a wide range of clinical applications ranging from treatment of acute spinal cord injury to chronic **neurodegenerative diseases**.

- *Human embryonic stem cells (hESC) as a source of radial glia, neurons and oligodendrocytes*, University of Connecticut, **Nada Zecevic**, Principal Investigator

  This project investigates whether human embryonic stem cells could be used as a source of human radial glia (RG) cells by comparing their cellular characteristics, and proliferation and differentiation potentials, to those of fetal RG. The project also examines factors that determine RG cell differentiation into either neurons or oligodendrocytes (OLs). OLs produce myelin sheaths damaged in **multiple sclerosis**, and thus are of particular clinical interest.

- *Modeling Motor Neuron Degeneration in Spinal Muscular Atrophy Using hESCs*, University of Connecticut Health Center, Farmington, **Xuejun Li**, Principal Investigator

  Spinal muscular atrophy, the leading genetic cause of death in infants and toddlers, is caused by an abnormal or missing gene known as the survival motor neuron gene. This project aims to model the motor neuron degeneration that occurs in spinal muscular atrophy through modifying human embryonic stem cells.

- *Migration and Integration of Embryonic Stem Cell-Derived Neurons into Cerebral Cortex,* University of Connecticut, **Joseph LoTurco**, Principal Investigator

  The cerebral cortex of the brain is the major target of several currently untreatable **degenerative and traumatic brain disorders** including **Alzheimer's Disease** and **stroke**. This project seeks to grow neuronal progenitor cells from human embryonic stem cells and explore ways to alter the stem cell-derived neurons so as to improve their migration once transplanted.We have also constructed DNA vectors that can now be used to alter the stem cell-derived neurons in ways that may improve their migration once transplanted.

- *Targeting Lineage Committed Stem Cells to Damaged Intestinal Mucosa*, University of Connecticut Health Center, **Daniel W. Rosenberg** and **Charles Giardina**, Investigators

  Damage to the intestinal mucosa can occur as a result of **inflammatory bowel disease**, or even as a result of radiation therapy. This project seeks to develop new methodologies to encourage human embryonic stem cells to differentiate into multi-potent intestinal stem cells. The researchers hypothesize that such stem cells will migrate to the damaged gut wall, undergo engraftment, and ultimately form a fully repaired and functionally reconstituted epithelium, thus providing enormous therapeutic potential.

- *Differentiation of hESC Lines to Neural Crest-Derived Trabecular Meshwork-Like Cells – Implications in Glaucoma,* University of Connecticut Health Center, **Dharamainder Choudhary**, Principal Investigator

  One of the major risk factors for development of **glaucoma** is an elevated intraocular pressure. This develops due to resistance to the aqueous humor outflow in the trabecular meshwork (TM) region of the eye. This project explores how damaged TM cells might be replaced by new TM cells generated from human embryonic stem cells.

- *Cytokine-induced Production of Transplantable Hematopoietic Stem Cells from Human ES Cells*, University of Connecticut Health Center, **Laijun Lai**, Principal Investigator

  This project seeks to establish a method to generate transplantable hematopoietic stem cells (HSCs) from human embryonic stem cells that could be used for the treatment of a variety of diseases. Hematopoietic stem cell transplantation, the most common cell-based therapy applied today, is widely used in the treatment of a variety of types of **cancer**, **aplastic anemia**, complications of irradiation and chemotherapy, primary (hereditary) and secondary (acquired) **immunodeficiency disorders**, **organ transplantation**, and **autoimmunity**. Bone marrow, umbilical cord blood, and mobilized peripheral blood are the major sources of HSCs. However, especially in adult patients, transplantation therapy is frequently limited by the unavailability of sufficient freshly harvested HSCs.

- *Embryonic Stem Cell as a Universal Cancer Vaccine*, University of Connecticut Health Center, **Bei Liu**, Principal Investigator

Tumor and ES cells bear many similarities to each other. This project aims to generate **tumor vaccines** from plain embryonic stem cells. The project could potentially lead to the beginning of direct clinical testing of stem-cell based **cancer vaccine**.

- *Generation of insulin-producing cells from human embryonic stem cells*, University of Connecticut Center for Regenerative Biology, **Mark G. Carter**, Principal Investigator

  Diabetes involves the destruction of β-cells in the pancreas, which secrete insulin in response to elevated blood sugar concentrations. This project focuses on studying the roles of the two genes PDX1 and NGN1 in directing differentiation of human embryonic stem cells toward β-cell and other pancreatic lineages. A detailed understanding of lineage control points will be a requirement for efficient production of safe and effective β-cells from embryonic stem cells for clinical use.

- *Quantitative Analysis of Molecular Transport and Population Kinetics of Stem Cell Cultivation in a Microfluidic System*, University of Connecticut, **Tai-Hsi Fan**, Principal Investigator

  Precise control of the microenvironment sustaining stem cell proliferation and differentiation is important for advances in **regenerative medicine**. This project focuses on the design and analysis of biochip-based microculture systems for the culture of undifferentiated embryonic stem cells. Ultimately this could lead to better methodologies for **tissue reconstruction**.

- *Cell Cycle and Nuclear Reprogramming by Somatic Cell Fusion*, University of Connecticut Health Center, **Winfried Krueger**, Principal Investigator

  The reprogramming of ordinary (somatic) cells to get them to act like stem cells (i.e., exhibit pluripotency) is a promising area of potential therapy because the reprogrammed cells are based on somatic cells taken from each patient's own body. One way to reprogram is to fuse ordinary cells with human embryonic stem cells. Fusion may be a better strategy than other methods of reprogramming, especially in the elderly. This project compares reprogramming efficiencies and compares the potential for reprogrammability of older and younger cells. Results could be important in developing therapies for **age-related degenerative diseases**.

- *Synaptic replenishment through embryonic stem cell-derived neurons in a transgenic mouse model of Alzheimer's Disease*, University of Connecticut, **Ben Bahr**, Principal Investigator

  Over the last 15 years, drug classes have been developed that can block pathogenic pathways that are most pronounced in the aged brain. This project will test how such drug classes enhance the survival of transplanted stem cells. The results may lead to methods that increase the effectiveness of stem cells in offsetting the loss of connections between nerve cells that occurs in **Alzheimer's Disease**.

- *Directing hES-Derived Progenitor Cells into Musculoskeletal Lineages*, University of Connecticut Health Center and University of Connecticut, **David W. Rowe**, Principal Investigator

  This group grant covers nine different projects under David Rowe's auspices:

  1. *Skeletal Mesenchymal Progenitor Cells*, **Alexander Lichtler**, Investigator

     The goal of the project is to develop improved methods to get human embryonic stem cells to change into cell types that can be used to **repair defects in bone, cartilage, skin or muscle**.

  2. *Phenotyping and Isolation of hES-Derived Cells of the Musculoskeletal Lineage*, **Hector Aguila**, Investigator

     One of the best ways to identify differences between types of cells is to use antibodies that differentially recognize molecules on their surface. The main purpose of this project is to generate new antibodies that would allow the identification of stem cells capable of contributing to the regeneration of the **cartilage**, **bone**, and **muscle**.

3. *Microarray and Genetics Networks*, **Dong-Guk Shin**, Investigator

   Bioinformatics has become an essential component of modern life science research. This project develops computerized methods for analyzing stem cell data in order to shorten the time needed to evaluate the efficacy of stem cell compounds in treating patients with various injuries.

4. *Biometric Surfaces for Efficient and Stable Stem Cell Differentiation*, **Lisa Kuhn**, Investigator

   This project seeks to create biomaterial surfaces that will help direct stem cells to regenerate … needed **bone**, **cartilage**, **tendon** or **muscle** tissue. Three-dimensional, porous biomaterials carrying cells will be used to repair tissues in animal experiments.

5. *Optimizing mesoderm-derived bone cell differentiation from hES cells*, **David Rowe**, Investigator

   The researchers have developed an animal model for testing the ability of bone stem cells to repair using mouse stem cells carrying a gene that makes the cells emit a color that can be detected by a microscope. However, the steps for placing the color identification genes into human cells require a different process than that used for mice. Specialized viruses have been constructed to contain the color identification genes. The project seeks to place those genes into human embryonic stem cells so that a cell line containing the viral vectors can be used to test ways to make the cells progress to become **bone stem cells**.

6. *Optimizing neural crest-derived bone cell differentiation from hES cells*, **Mina Mina**, Investigator

   Virtually all craniofacial structures are derived from embryonic cells called neural crest cells. This project seeks to generate and identify neural crest progenitors from mouse embryonic stem cells that can be applied to human embryonic stem cells. Ultimately such cells may be used towards **regeneration of lost tissues in the craniofacial skeleton**, including the teeth.

7. *Cartilage Differentiation from hES-derived progenitor cells*, **Robert A. Kosher**, Investigator

   Treatment of **degenerative cartilage diseases** is a clinical challenge because of the limited capacity of the tissue for self-repair.This project will test the ability of human embryonic stem cells and reprogrammed (induced) stem cellsto repair damaged and diseased human cartilage from **osteoarthritic** patients.

8. *A mouse model to study the myogenic potential of human embryonic stem cells*, **David Goldhammer**, Investigator

   Cell therapies for **muscular dystrophy** have shown some promise in animal models.The purpose of this project is to evaluate and optimize the ability of human embryonic stem cell-derived progenitor cells to repair skeletal muscle and to produce muscle stem cells.

9. *Use of hES cell-derived dermal fibroblasts for therapy of cutaneous wounds*, **Stephen Clark**, Investigator

   The objective of this research program is to identify cell-based approaches to improve the **healing of cutaneous wounds**. The use human embryonic stem cells or reprogrammed patient-specific somatic cells as a source to produce large numbers of specifically selected immune cells as well as cells that create new skin tissue could be used in a clinical setting in the treatment of **chronic skin lesions**.

CURE (Connecticut United for Research Excellence) (http://www.curenet.org) is a statewide coalition of over 100 educational and research institutions, biotechnology and pharmaceutical companies and other supporting businesses. It is dedicated to promoting the growth and increasing public understanding of biomedical research and science in Connecticut.