


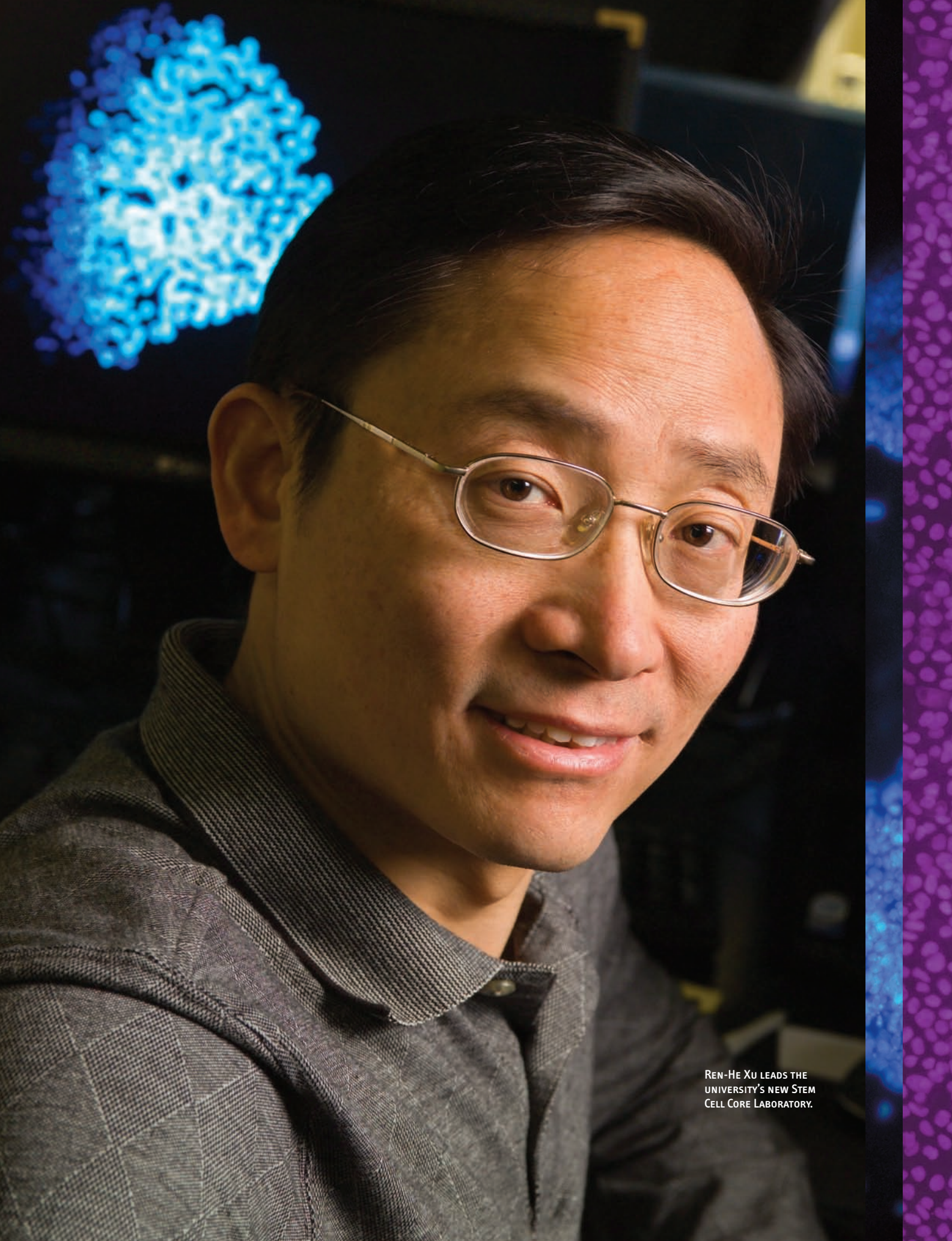
# UConn health center

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Unlocking the  
**Secrets**  
of  
Embryonic  
**Cells Stem**

UNIVERSITY PROPOSES NEW HOSPITAL ♦ CENTER FOR POISON PREVENTION



REN-HE XU LEADS THE UNIVERSITY'S NEW STEM CELL CORE LABORATORY.

# Unlocking the Secrets of Embryonic Stem Cells

By Jim Smith

University scientists collaborate on broad research initiatives designed to harness human embryonic stem cells to meet specific therapeutic needs.

**L**iisa Kuhn, Ph.D., opens a package, empties the contents into a dish, adds some liquid and agitates. In a few minutes she's "cooked up" a sticky, translucent blob that resembles nothing so much as turquoise gelatin.

But this isn't a kitchen. It's a laboratory at the UConn Health Center. And the stuff isn't jello. It's a polymer, one of many materials Kuhn and her colleague, A. Jon Goldberg, Ph.D., director of the Center for Biomaterials, are currently testing as they prepare for some of the most intense – and most intensely scrutinized – research ever conducted.

The materials are "scaffolds," a term used in the world of regenerative medicine. Scaffolds are delivery systems, which doctors will use to deliver or implant stem cells into people, in just a few years, if all goes well.

Stem cells are chameleons. Unspecialized, they are the progenitors of all animal cells;

that is, they have the remarkable capacity to mature into any of the 220 tissue and cell types in the human body. From brain and liver tissue to bone and skin, stem cells can transform into the myriad specialized cells the body requires for specific functions.

Sometimes referred to as medical "magic seeds," their discovery is touted as one of the great milestones in the advancement of medicine. They are popularly envisioned as a cure-all for nearly every disease imaginable.

Unlocking their storied potential is no simple matter, however. They can live indefinitely, under the right conditions; but they are notoriously unstable. In fact, they may be the primal forerunners of every human cell form; but they yearn to make something of themselves, and they will swiftly proliferate into one cell line or another at the least provocation.

Harnessing them and compelling them to grow according to specific medical needs has proven to be difficult, but it is absolutely essential if they are going to become more than a dream. The UConn researchers are at the very forefront of the attempt to unlock their potential, figuring how to manage them and grow them reliably and efficiently, according to specific therapeutic need.

## Focus on Regenerative Medicine

Two years ago, when the Connecticut General Assembly authorized public financing of human stem cell research, UConn had already made its wholehearted commitment to regenerative medicine. At the Storrs campus, the university already had opened a new state-of-the-art Center for Regenerative Biology. There, Xiangzhong "Jerry" Yang, Ph.D., one of the world's foremost animal biotechnologists, oversees a group of five scientists recruited to staff the new center and drive basic science research in the field.

Then, last year, UConn recruited Ren-He Xu, Ph.D., to head a new state-of-the-art Stem Cell Core Laboratory near the Health Center's Department of Genetics and Developmental Biology. A renowned expert on growing human embryonic stem (ES) cells, Xu was a founding member of the prestigious WiCell Research Institute, the center where human embryonic stem cells were first developed.

"We knew we needed someone with real expertise to move forward with a serious commitment to research that involves human embryonic stem cells," says Marc Lalande, Ph.D., chairman of the Department of Genetics and Developmental Biology, and chairman of the university's stem cell work group.

Last fall, when Connecticut disbursed \$20 million for stem cell research – becoming the first state in the nation to release public funds for research banned by the federal government – UConn researchers received some \$12 million, fully 60 percent of the total to support 23 principal investigators in a collaborative, cross-campus team. They are studying stem cells from many different perspectives, hoping to crack their code in the interplay.

These scientists and their research are laying the foundation for what Lalande hopes will soon be a formal Stem Cell Institute collaborating actively with stem cell researchers throughout the country and the world.

At the Health Center, David W. Rowe, M.D., director of the dental school's Center for Regenerative Medicine and Skeletal Development, is managing an ambitious nine-project research group funded by the state. "It's important to view stem cells as lineages," he says, by way of explaining the idea that animates his group. "There are interconnections and commonalities within groups of cells. All bone cells have an ES cell ancestor. So it seemed to us that studying a single kind of cell was the most efficient way to approach this work." The protocols his

## Research Oversight



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As UConn moves into the new and unfamiliar territory of human embryonic stem cell work, it is guided by a committee whose members are responsible for providing oversight of all ethical issues related to the derivation and research of human stem cell lines.

"We want to ensure that our research is ethically sensitive and well justified and that inappropriate research does not occur," says Anne Hiskes, associate professor of philosophy and chair of the university's Embryonic Stem Cell Research Oversight Committee. Other members include faculty with scientific, ethical and legal expertise from the Storrs and the Health Center campuses, two community members, and representatives from research compliance. Two members of the committee are ordained clergy.

"We'll develop principles and policies to guide the research, review and approve research protocols, and educate investigators about ethical issues related to the research," says Hiskes. "The standards we develop will apply across all of the university's schools, colleges, campuses and research centers."



RESEARCHERS COLLABORATING ON A PROJECT TO UNDERSTAND HOW TO GET EMBRYONIC STEM CELLS TO HELP REBUILD BONE, CARTILAGE, SKIN AND MUSCLE TISSUE ARE: FROM BOTTOM, A. JON GOLDBERG, DAVID ROWE AND MINA MINA, LEONARDO AGUILA AND DAVID GOLDHAMER, LIISA KUHN, DONG SHIN AND ALEXANDER LICHTLER, WILLIAM UPHOLT, ROBERT KOSHER AND CAROLINE DEALY.

team hopes to define are likely to be similar for the development of any stem cell line.

The group project's effort begins with Alexander Lichtler, who is seeking the best way to compel ES cells to become progenitors for all musculoskeletal tissue. In two related projects, Leonardo Aguila and Dong Shin will design effective methods to isolate the cells identified by Lichtler and map their wiring diagram, classifying which genes control the process by which ES cells become progenitors for bone and muscle.

In five other projects, Rowe and Mina Mina, Robert Kosher, Caroline Dealy, David Goldhamer and Stephen Clark will "test drive" the cells produced by Lichtler, seeking to ensure that they will work in specific applications. At the

center of this process will be Goldberg and Kuhn, engineers who work in the interface between medicine and engineering. The scaffolds they are testing, already commercially available, range from gels to sponges and bone-like matrices pocked with pores. Each can be used to house and nourish stem cells inserted into the body to rebuild tissue damaged by injury or disease. But Goldberg and Kuhn quickly concede that they may be called upon to design new scaffolds, depending upon what kinds of cells the team eventually produces and how those cells will be employed.

## Developing Experimental Models

**When the state of Connecticut disbursed \$20 million for stem cell research, UConn received \$12 million, 60 percent of the total, for 23 investigators in a cross-campus collaboration.**

The first phase of the group's work is expected to take one to two years, says Rowe. During that time, the researchers will develop various experimental models amenable to stem cell therapies, setting the stage for actual testing of new cells designed to treat bone disorders. By the third year, he predicts, possibly sooner, "We'll have progenitor cells ready to test in repair models."

By then, the university will have completely refurbished the 113,000-square-foot building it purchased on 24 acres of land near the Health Center campus. This will be the home of the new Stem Cell Institute and related interdisciplinary research programs, housing both research laboratories and incubator space for businesses eager to commercialize stem cell science.

Rowe is optimistic that around the time the new institute holds its open house, his group will have made sufficient progress with their progenitor cells to be in a strong position to attract the additional funding they'll need to complete the rigorous testing and documentation the Food and Drug Administration always requires before authorizing a product for use on humans. Beyond that, he is reluctant to make predictions. The world of medical research is a constantly shifting landscape.

He will go so far as to say, however, that he feels confident human ES cells will have become a useful and rapidly evolving new form of therapy within the next decade. And the university's researchers, supported by funding from a visionary legislature, are breaking new ground every day. 