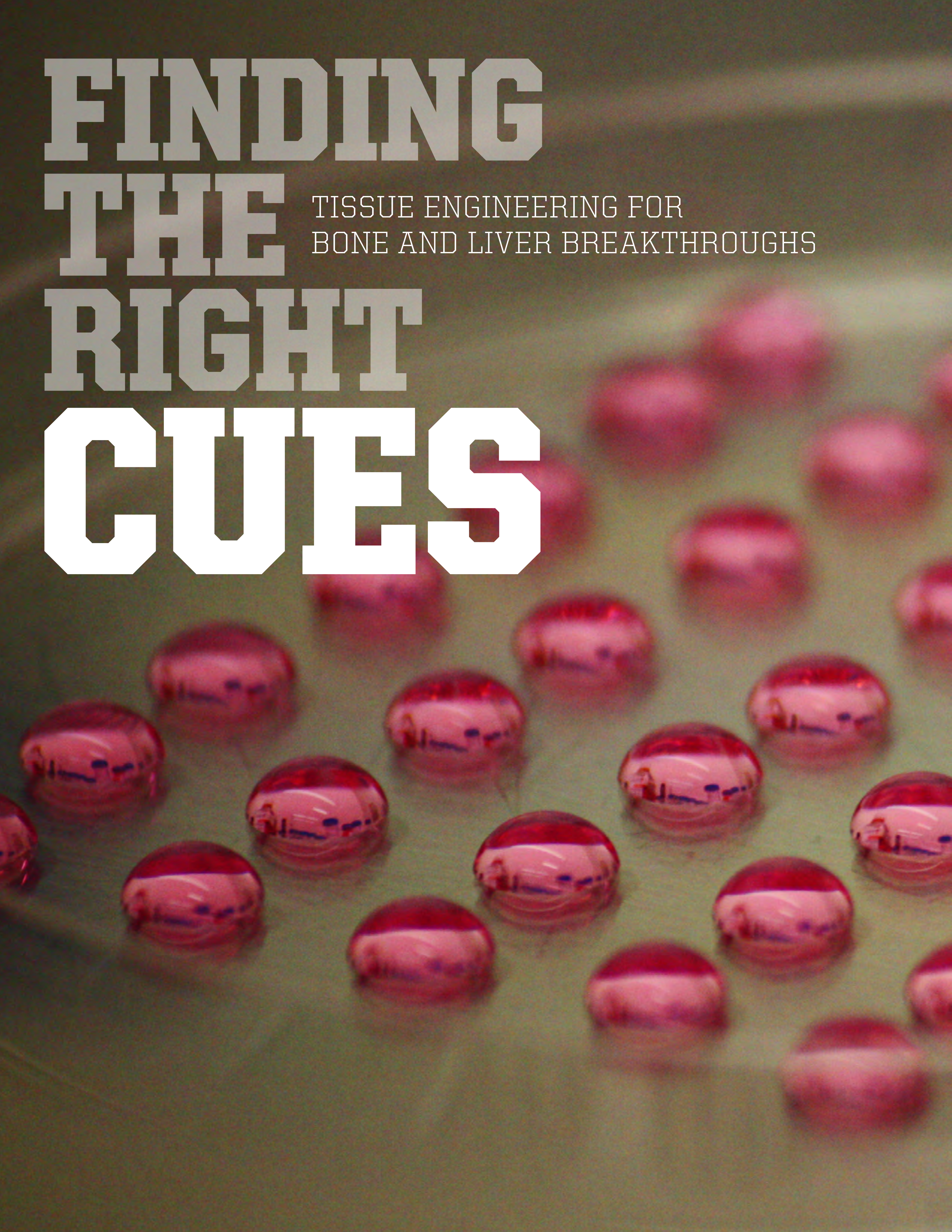
# FINDING THE RIGHT CUES

## TISSUE ENGINEERING FOR BONE AND LIVER BREAKTHROUGHS

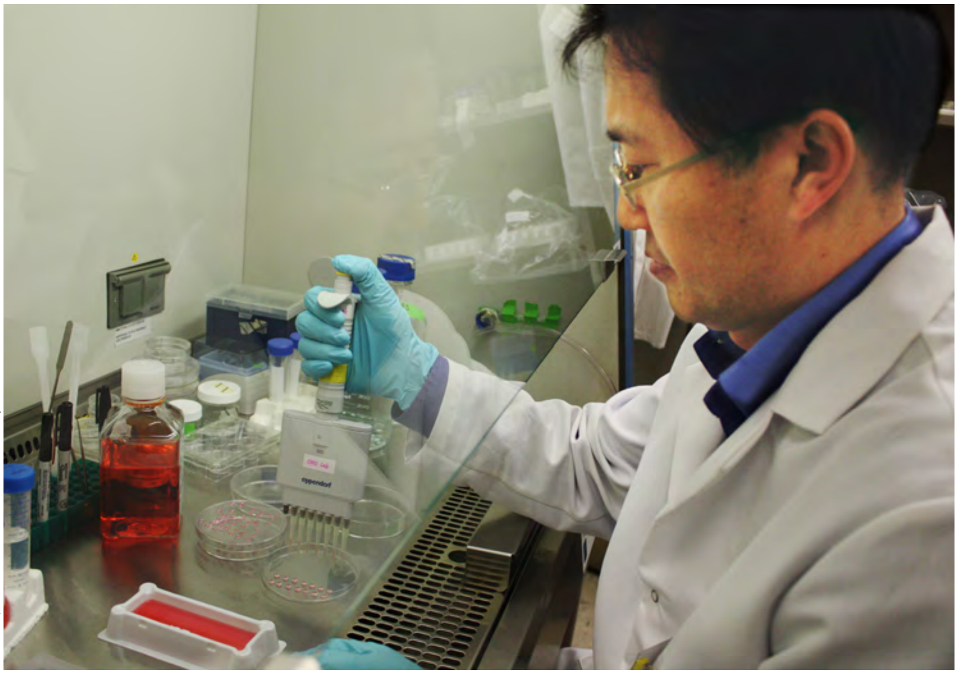


**Each year tens of thousands of people die in the U.S. from chronic and acute liver failure. Many die waiting for a liver transplant and others because there is no technology suitable for assisting the liver as it heals after physical or chemical trauma.**

**"It's a sobering statistic," says Assistant Professor of Biomedical Engineering Cheul Cho, the NJIT researcher who is working on a stem-cell based solution for this therapeutic challenge. Cho and Associate Professor Treena Arinzeh recently received Coulter Translational Research Awards that will initially give them a total of $400,000 to advance the translational, or clinical, development of leading-edge stem-cell treatments for disease and injury.**

*[continued]*

"IT'S A MATTER OF PROVIDING THE RIGHT CHEMICAL AND MECHANICAL CUES – THE CUES THAT TELL STEM CELLS WHAT TYPE OF MATURE CELLS WE WANT THEM TO BECOME AND THAT ENCOURAGE THEIR GROWTH IN A CLINICALLY USEFUL MANNER." *– Associate Professor Treena Arinzeh*



PHOTOS, RIGHT AND PREVIOUS PAGE: JOHN MICALE

*Shown close-up on pages 6-7, the hanging drop culture being prepared by Assistant Professor Cheul Cho facilitates the formation of embryoid bodies and the differentiation of embryonic stem cells.*

Although Arinzeh and Cho are pursuing different therapeutic objectives, their research has several aspects in common. Both are engaged in what is referred to as tissue engineering, and their efforts involve inducing vigorous differentiation of stem cells into functional tissues.

"It's a matter of providing the right chemical and mechanical cues – the cues that tell stem cells what type of mature cells we want them to become and that encourage their growth in a clinically useful manner," Arinzeh says. This is as true of Arinzeh's focus on bone tissue as it is for Cho's work with liver cells known as hepatocytes.

### HEPATIC SUPPORT

Cho's Coulter Award will underwrite continued development of a promising technology that can help to sustain hepatic functions – the vital functions of the liver. In humans and other mammals, the liver is an engine of protein synthesis and storage. It produces urea, the main component of urine, as well as bile, and about 80 percent of the cholesterol in the human body. It stores vitamins and minerals, and has a role in maintaining a proper level of glucose in the blood. The liver also filters harmful substances, such as alcohol, from the blood.

Hepatocytes are the key to these and other processes. They constitute 70 to 80 percent of the human liver's cellular mass. The goal of Cho's research is a bioartificial liver using hepatocytes derived from embryonic stem cells that would be an extracorporeal assistive device. That is, the device would be outside of the body and provide temporary support while a patient waits for a transplantable liver or for their liver to recover from some type of trauma.

An NJIT faculty member since 2007, Cho is building on research in which he participated under the auspices of the Center for Engineering in Medicine at the Massachusetts General Hospital in affiliation with the Harvard Medical School. He was part of a team that demonstrated how a device incorporating stem-cell derived hepatocytes greatly increased the survival rate for laboratory rats experiencing liver failure induced by drugs.

One of the fundamental challenges that Cho has helped to confront involves producing hepatocytes in quantities sufficient for a clinically viable bioartificial liver. This amounts to about 10 percent of the mass of a typical human liver, or approximately 10 billion hepatocytes.

Cho is already named on a patent application covering a method that can provide not only the requisite quantity of cells, but also a level of purity that makes a bioartificial liver even more feasible. The application, titled "Homogeneous differentiation of hepatocyte-like cells from embryonic stem cells," describes a unique use of collagen gel substrates to encourage the rapid growth of functional hepatocytes. Cho anticipates that the ability to obtain the volume of hepatocytes necessary will advance his work on a patentable bioartificial liver.

### ESSENTIAL MODELS

According to Cho, the capacity to generate hepatocytes from stem cells offers additional potential for biomedical research and therapeutic discovery. His interests include investigating the creation of what he terms "three-dimensional models" of liver tissue. This involves growing layers of hepatocytes on an appropriate foundation, or scaffold. Vascularization, the growth of blood vessels, could be stimulated as part of the process, making the model an even more valuable laboratory analog of human physiology.

It's conceivable that other types of tissue could be modeled – heart tissue, for example. Such models could be very useful for basic research into cell and organ functions, as well as for developing and testing new drugs. They could yield data about human tissues that's more reliable and comprehensive than current drug-screening technologies and animal testing.

Speaking of another tissue-engineering frontier, Cho says that it may even be possible to induce a sample of one's own skin cells to revert to the stem-cell stage and then to direct them toward becoming tissue needed to treat a disease or injury. The benefits of this therapeutic possibility, he explains, include avoiding complications arising from the rejection of foreign tissue and the ethical issues that continue to surround the biomedical use of most embryonic stem cells.

## TEXTILES AND BONE REPAIR

For nearly a decade, NJIT researcher Arinzeh has been working to refine techniques for regenerating bone tissue. Her successes include the creation of calcium phosphate scaffolds that foster the transformation of adult stem cells into bone tissue. The ultimate goal is to provide replacement tissue for individuals such as cancer patients who have had tumors removed from a bone and those afflicted by fractures resulting from osteoporosis. Also very significant is Arinzeh's finding that the use of adult stem cells obtained from bone marrow eliminates the risk of implanted tissue being rejected by the recipient.

The groundbreaking nature of Arinzeh's work has been widely acknowledged. In 2003, the National Science Foundation (NSF) gave Arinzeh its highest honor, a Faculty Early Career Development Award that came with a major research grant. The following year, President George W. Bush awarded her the Presidential Early Career Award for Scientists and Engineers.

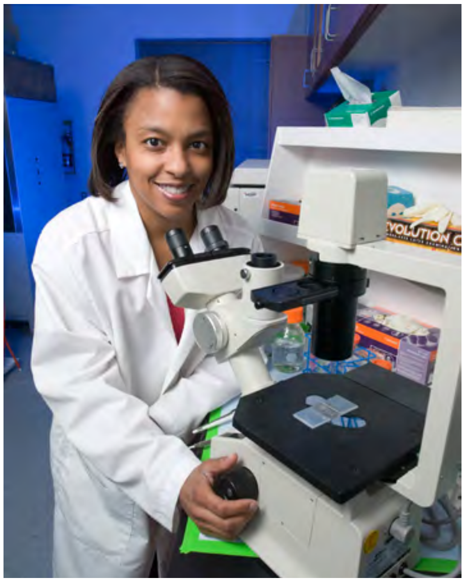
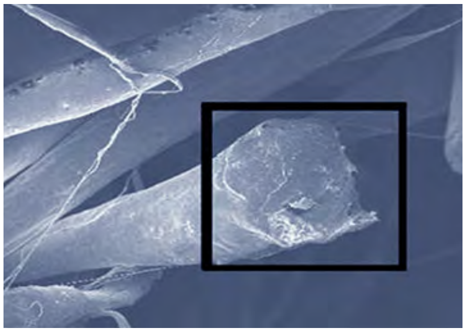


PHOTO: KAI CHAN

*Associate Professor Treena Arinzeh*



*Top: Scanning electron microscope (SEM) image of the fibrous scaffold containing nanoceramics for use in bone repair. Above: SEM image of the cross section of a single fiber.*

Arinzeh's Coulter Award affirms that her research has moved an important step forward. The key elements of this progress are highlighted in the title of the patent application that she has filed: "Electrospun ceramic-polymer composite as a scaffold for tissue repair." Essentially, Arinzeh has shown that a substantially better scaffold can be fabricated by embedding ceramic nanoparticles in polymer fibers. Electrospinning, the technique that produces the fibers, was developed commercially for the manufacture of textiles. It uses an electrical charge to draw minute fibers from a liquid. For Arinzeh's research, the fibers are deposited on a target substrate to form a superior biodegradable scaffold on which the appropriate cells will attach, migrate and form new bone.

Collaborating with Arinzeh in this initiative is Dr. Sheldon Lin, an orthopedic surgeon affiliated with the University of Medicine and Dentistry of New Jersey. Once the therapeutic technology they are developing is proven at the preclinical stage, the plan is to license it for comprehensive evaluation in a clinical setting.

Arinzeh continues to explore other promising avenues in tissue engineering. These include looking into whether scaffolds with intrinsic electrical activity encourage faster cell growth and tissue formation, work being carried out with NJIT co-investigators Research Professor Michael Jaffe and Professor Boris Khusid. Their efforts are supported by a recent NSF grant of nearly $400,000. ■

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## SCIENCE SERVING HUMANITY

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**The Coulter Principle touches our lives in many other ways, from enjoying chocolate to swallowing a pill and applying cosmetics. It is an essential tool for quality control and standardization of particles in numerous industries. NASA even uses the Coulter Principle to assess the quality of rocket fuel.**

**Throughout his life, Coulter continued to promote advances in cellular analysis. Coulter Corporation has been a leader in the development of monoclonal antibodies and technologies for assaying them. These technologies are used in the characterization and treatment of cancer, leukemia and infectious diseases.**

**Coulter's commitment to improving life through science and technology is the guiding principle of the Wallace H. Coulter Foundation, which he founded shortly before his death to support the work of established U.S. biomedical engineering departments. Through the awards given to researchers such as NJIT's Treena Arinzeh and Cheul Cho, the foundation seeks to accelerate the development of therapies that are both clinically and commercially promising.**