



EMBARGOED UNTIL: 3:00 PM EST 6 MAY 2013

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NYSCF SCIENTISTS CREATE PERSONALIZED BONE SUBSTITUTES FROM SKIN CELLS

For treatment of large bone defects and traumatic injuries

NEW YORK, NY (May 6, 2013) – A team of New York Stem Cell Foundation (NYSCF) Research Institute scientists report today the generation of patient-specific bone substitutes from skin cells for repair of large bone defects. The study, led by Darja Marolt, PhD, a NYSCF-Helmsley Investigator and Giuseppe Maria de Peppo, PhD, a NYSCF Research Fellow, and published in the *Proceedings of the National Academy of Sciences of the USA*, represents a major advance in personalized reconstructive treatments for patients with bone defects resulting from disease or trauma.

This advance will facilitate the development of customizable, three-dimensional bone grafts on-demand, matched to fit the exact needs and immune profile of a patient. Taking skin cells, the NYSCF scientists utilized an advanced technique called “reprogramming” to revert adult cells into an embryonic-like state. These induced pluripotent stem (iPS) cells carry the same genetic information as the patient and they can become any of the body’s cell types.

The NYSCF team guided these iPS cells to become bone-forming progenitors and seeded the cells onto a scaffold for three-dimensional bone formation. They then placed the constructs into a device called a bioreactor, which provides nutrients, removes waste, and stimulates maturation, mimicking a natural developmental environment.

“Bone is more than a hard mineral composite, it is an active organ that constantly remodels. Blood vessels shuttle important nutrients to healthy cells and remove waste; nerves provide connection to the brain; and, bone marrow cells form new blood and immune cells,” said Marolt.

Previous studies have demonstrated the bone-forming potential from other cell sources, yet serious caveats for clinical translation remain. A patient’s own bone marrow stem cells can form bone and cartilaginous tissue, not the underlying vasculature and nerve compartments; and, embryonic stem cell derived bone may prompt an immune rejection. The NYSCF scientists chose to work with iPS cells to overcome these limitations, comparing iPS sources with embryonic stem cells and bone marrow derived cells.

“No other research group has published work on creating fully-viable, functional, three-dimensional bone substitutes from human iPS cells. These results bring us closer to achieving our ultimate goal, to develop the most promising treatments for patients,” said de Peppo.

While severity varies, bone defects and injuries are currently treated with bone grafts, taken either from another part of the patient’s body or a donor bone bank, or with synthetic substitutes. None of these permit complex reconstruction, and they may elicit immune rejection or fail to integrate with surrounding connective tissues. For trauma patients, suffering from shrapnel wounds or vehicular injury, these traditional treatments provide limited functional and cosmetic improvement.

After a comprehensive *in vitro* analysis of the generated bone, the NYSCF team assessed stability when transplanted in an animal model to address a major concern for iPS-based cell therapies. Undifferentiated iPS cells can form teratomas, a type of tumor. The iPS cell-derived bone substitutes were implanted under the skin of immunocompromised mice. After 12 weeks, the explanted constructs matured and showed no malignancies but complete maturation of bone tissue, while blood vessel cells began to integrate along the grafts. These results indicate the stability of the bone substitutes.

The scientists caution that although these results represent a major advance, further research is necessary before skin cell-derived bone grafts reach patients. Next steps include protocol optimization and the successful growth of blood vessels within the bone.

“Following from these findings, we will be able to create tailored bone grafts, on demand, for patients without any immune rejection issues,” said Susan L. Solomon, CEO of NYSCF. “This is not a good approach, it is the best approach to repair devastating damage or defects.”

Beyond potential therapeutic relevance, these adaptive bone substitutes may be implemented to model bone development and different pathologies. Analysis could enrich current understanding and identify potential drug targets.

Other contributors to the study include: Dr. David Kahler, Dr. Linshan Shang, and Dana Alsaman of The New York Stem Cell Foundation Research Institute; and Dr. Ivan Marcos Campos and Dr. Gordana Vunjak-Novakovic of Columbia University.

Funding for this study was provided by the Leona M. and Harry B. Helmsley Charitable Trust; The New York Stem Cell Foundation; Robin Chemers Neustein; Goldman Sachs Gives, at the recommendation of Alan and Deborah Cohen; New York State Stem Cell Science Shared Facility Grant C024179; and National Institutes of Health Grants DE016525 and EB002520.

About The New York Stem Cell Foundation

The New York Stem Cell Foundation (NYSCF) is an independent organization founded in 2005 to accelerate cures and better treatments for patients through stem cell research. NYSCF employs over 40 researchers at the NYSCF Research Institute, located in New York, and is an acknowledged world leader in stem cell research and in developing

pioneering stem cell technologies, including the NYSCF Global Stem Cell Array. Additionally, NYSCF supports another 60 researchers at other leading institutions worldwide through its Innovator Programs, including the NYSCF – Druckenmiller Fellowships and the NYSCF-Robertson Investigator Awards. NYSCF focuses on translational research in a model designed to overcome the barriers that slow discovery and replaces silos with collaboration.

NYSCF researchers have achieved four major discoveries in the field, including: the discovery of a clinical cure to prevent transmission of maternal mitochondrial diseases in December 2012; the derivation of the first-ever patient specific embryonic stem cell line (#1 Medical Breakthrough of 2011 by *Time* magazine); the discovery of a new way to reprogram stem cells; and the creation of the first disease model from induced pluripotent stem cells (also named the #1 Medical Breakthrough by *Time* magazine in 2008). More information is available at www.nyscf.org.

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