

Scientists create personalized bone substitutes from skin cells

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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.

More information: Engineering bone tissue substitutes from human induced pluripotent stem cells:

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