Adult stem cells improve fracture healing

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In an approach that could become a new treatment for the 10 to 20 percent of people whose broken bones fail to heal, researchers at the University of North Carolina at Chapel Hill have shown that transplantation of adult stem cells can improve healing of fractures.

Adult stem cells are specialized cells with the ability to regenerate tissue in response to damage. However, many patients lack sufficient numbers of these cells and thus cannot heal properly.

Researchers have used adult stem cells in a few cases to improve fracture healing, but further studies were needed to show that this method was truly effective and safe before it can be pursued as a new treatment.

Now scientists at UNC have provided the scientific foundation for future clinical trials of this approach by demonstrating in animal models that these cells can be used to repair broken bones.

"This finding is critical to patients who lack the proper healing process and to individuals prone to broken bones, such as those with osteoporosis and the rare genetic condition known as brittle bone disease," said Dr. Anna Spagnoli, associate professor of pediatrics and biomedical engineering in the UNC School of Medicine and senior author on the study.

The study, presented Monday, June 16 at the annual Endocrine Society meeting in San Francisco by the first author, Froilan Granero-Molto,

Ph.D., post-doctoral associate researcher in UNC's pediatrics department, is the first to visualize the action of transplanted adult stem cells as they mend fractures in mice.

During normal fracture healing, stem cells migrate to the site of the break, forming the cartilage and bone needed to fuse the broken bones back together. But in more than 600,000 Americans a year, this process does not occur as it should and these bones stay broken. The result can be long periods of immobilization, pain, bone deformities and even death.

Current therapies, such as multiple surgeries with bone autografts and artificial prosthetic materials, often are not enough to cure these patients.

"Man-made materials do not address the normal bone's function, and recurrent fractures, wear and toxicity are a real problem," Spagnoli said. "There is clearly a need to develop alternative therapies to enhance fracture healing in patients with bone union failure."

Kicking stem cells into repair mode is one of the objectives of a new branch of medicine called regenerative medicine. With a little prodding, stem cells in human bone marrow – called mesenchymal stem cells – can turn into bone, cartilage, fat, muscle and blood vessel cells.

"The beauty of regenerative medicine is that we are helping the body improve its innate ability to regenerate healthy tissue on its own, rather than introducing manmade materials to try to patch up a broken bone," Spagnoli said.

Granero-Molto and other colleagues led by Spagnoli demonstrated this approach by transplanting adult stem cells in mice with fractures of the tibia, the long bone of the leg. The cells were taken from the bone

marrow of mice that produce luciferase, the same molecule that allows fireflies to glow. In addition to possessing the ability to glow, the cells were engineered to express a molecule called insulin-like growth factor 1 (IGF-1). IGF-1 is a potent bone regenerator necessary for bones to grow both in size and strength.

The researchers transplanted the cells through a simple intravenous injection and then placed the mice into a dark box so they could track the glowing stem cells as they migrated within the rodent. They found that these cells were specifically attracted to the fracture site, and that a particular molecule called CXCR4 – which acts as a homing signal – was necessary for the migration.

Using a computerized tomography (CT or CAT) scan, the researchers showed that the stem cells not only migrated to the site of the fracture, but also improved healing there by increasing the bone and cartilage that bridged the bone gap. The bone at the fracture site in the treated mice was about three times stronger than that of untreated controls.

If scientists can duplicate the results of this animal study in humans, it may lead to a new treatment for the millions of people who suffer fractures that do not heal properly, Spagnoli said. Once a physician determines that the bone has not healed, they could obtain adult stem cells from the person's bone marrow in a minimally invasive procedure and transplant them at the same time the patient is receiving a bone graft.

Spagnoli said adult stem cells may pose fewer problems than embryonic stem cells, since they are not associated with the ethical controversy that surrounds the latter. Also, they may avoid the problem of rejection by the immune system, since the patient's own cells can be used.

Source: University of North Carolina at Chapel Hill