

LifeCell – Daily News Update

October 6, 2009

Key Industry News:

Publication	the-scientist.com
Headline	<u>Nanoparticles spur stem cells?</u>
Gist of the article	<p>Nanoparticles may prove effective tools for improving stem cells therapy, new research suggests. Chemical engineers have successfully used nanoparticles to enhance stem cells' ability to stimulate regeneration of damaged vascular tissue and reduce muscle degeneration in mice, they report in a study published online today (October 5) in Proceedings of the National Academy of Sciences.</p> <p>"This is an intriguing finding," said Arnold Kriegstein, a regenerative biologist at the University of California, San Francisco, who was not involved in the study. "But it would need to be explored a good deal further before one could really be excited about this new approach."</p> <p>Researchers studying the role of stem cells in stimulating new blood vessel formation have found that after implantation into a living organism, cells typically do not continue to renew tissue effectively enough to keep the tissue alive. The cells require help from performance-enhancing genes, which promote growth in the target tissue. Researchers generally rely on viral vectors to deliver these therapeutic genes to stem cells. "We hypothesized that with the right DNA delivery system, we could [better] enhance the therapeutic utility of stem cells," said Daniel Anderson of the Massachusetts Institute of Technology, lead author on the study.</p> <p>Anderson and his team cultured stem cells from mouse bone marrow and then introduced nanoparticles containing positively charged polymers that can bind to and deliver DNA to cells to the culture medium. Specifically, the nanoparticles carried the gene for vascular endothelial growth factor (VEGF), a signaling molecule known to stimulate the growth of new blood vessels. The modified stem cells containing the DNA were then implanted into eight mice in areas with damaged tissue. The researchers believe that cells engulf the gene-carrying nanoparticles with their cell membrane and the molecules release DNA inside the cell, Anderson said in an email, though he noted that "[t]he precise mechanism by which these [nanoparticles] deliver DNA is not clear yet."</p> <p>The MIT researchers found that after two weeks, the cells transfected with VEGF had two to four times more blood vessel density around the damaged tissue than cells without the gene or cells that received the gene using a common delivery molecule. Four weeks after injection, the modified stem</p>

	<p>cells continued to boost the growth of new blood vessels while reducing muscle degeneration in the mice.</p> <p>"We think it's an important demonstration that biodegradable polymers can be used to temporarily modify stem cells and enhance their therapeutic performance," Anderson wrote in an email.</p> <p>Kriegstein said, however, that he worries the reported benefits using nanoparticles may be transient. In the study results, he noted, there was a significant increase in VEGF levels in mouse muscle two days following cell grafting, but VEGF levels produced by the cells dropped sharply after four days.</p> <p>Kriegstein suggested that using an adenoviral vector to deliver the growth gene would make more sense than using nanoparticles. Though there have been some safety concerns, he said, studies have shown the viral vector approach can last longer and produces greater gene activity than the nanoparticle method.</p> <p>Although the study authors acknowledge the advantages of a viral delivery method, they believe that using nanoparticles is much safer than a viral vector and, with more tweaking, has great potential for long-term therapeutic benefits for stem cell therapy, Anderson said.</p> <p>Looking forward, "I think these nanoparticles will be useful not just to modify stem cells, but also to treat cancers and genetic diseases," Anderson said.</p>
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Publication	thebulletin.us
Headline	Cardiac Stem Cell Trial Seeks To Treat Some Heart Attack Patients
Gist of the article	<p>Researchers at UCSF Medical Center have begun enrollment for an early-stage clinical trial to evaluate the safety and efficacy of an adult stem cell therapy for patients who have just experienced their first acute myocardial infarction, or heart attack. The trial is part of a multi-center national study.</p> <p>The cells used, known as mesenchymal stem cells, were obtained from the bone marrow of healthy adult donors. Depending on their location in the body, mesenchymal stem cells give rise to bone, cartilage, fat, muscle and connective tissue.</p> <p>The experimental therapy is intended to combat the symptoms related to heart damage that continue to develop following a heart attack, including low pumping capacity, inflammation and increased scar tissue. Although the exact mechanisms of the stem cells' actions in this setting are not yet known, previous studies have suggested that they could reduce the amount of scar tissue and inflammation caused by heart attack.</p> <p>A previous UCSF study on the impact of bone marrow-derived stem cells on heart attacks in mice provided evidence that stem cells work by assisting in</p>

tissue repair on the cellular level, resulting in less damage and improved function.

The new clinical trial is the first stem cell clinical trial in cardiology at UCSF.

"This is an important and exciting step for physicians and scientists seeking to translate research into beneficial treatments for patients," said Yerem Yeghiazarians, MD, co-director of the Adult Cardiac Catheterization Laboratory, director of the UCSF Translational Cardiac Stem Cell Program and lead investigator of the cardiac stem cell study.

"Many of us have been working for a long time to have a therapy for patients that could improve organ damage at the basic level," he added. "UCSF is one of the fastest hospitals in the nation at treating heart attack with angioplasty, according to the National Cardiovascular Data Registry. We are hoping that this stem cell therapy will prove successful in improving heart function and minimize the damage even more."

All patients arriving at UCSF's Emergency Department with heart attack will continue to be treated with standard measures. Patients who meet the medical criteria for the trial will be able to elect to receive the stem cell therapy within seven days after their heart attack.

To be eligible, male and female patients must be between the ages of 21 and 85, and have a baseline ejection fraction - the measurement of blood pumped out of the ventricles per heart beat - between 30 and 45 percent.

The stem cell therapy is delivered to patients via a one-time IV-infusion, performed on-site at UCSF. The infusion takes approximately half an hour. Patients will be followed for two years and progress will be assessed with MRI and ultrasound imaging in addition to the standard battery of cardiac measures, including electrocardiogram (ECG) and heart function monitoring.

The goal of the therapy is to prevent the permanent damage that heart attacks cause. According to the American Heart Association, more than half a million Americans will experience their first heart attack in 2009. Up to six years after a first heart attack, 18 percent of men and 35 percent of women will have another heart attack.

The two-year, Phase II trial will test the safety and efficacy of a stem cell therapy called Prochymal, developed by Osiris Therapeutics, Inc. Results from a Phase I (safety) trial - which did not involve UCSF - were announced by the company in Feb., 2009

Despite early promising cardiac stem cell studies conducted at academic medical centers nationally and internationally, researchers still have questions about how stem cells work in the body in order to benefit heart

	<p>patients.</p> <p>“This and future studies hope to answer some of these questions. For instance, how is the therapeutic benefit achieved? Do these cells differentiate into heart muscle cells? Do they minimize cell death after a heart attack or do they act by other mechanisms to improve the cardiac function?” said Yeghiazarians.</p> <p>To seek answers to these questions, UCSF launched a Translational Cardiac Stem Cell Research Program in 2003. The program includes a multi-disciplinary team of practicing clinicians and basic and translational scientists with expertise in the various aspects of cardiac development and physiology. The program is dedicated to the study of adult stem cells and their role in treating diseases of the heart and circulatory system.</p> <p>“The aim of our laboratory is to advance the basic science and to translate our findings from the lab bench to treat our patients at the bedside,” said Dr. Yeghiazarians.</p>
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Publication	timesofindia.indiatimes.com
Headline	Adult stem cells offer new fracture treatment
Gist of the article	<p>"Lack of fracture repair often leads to several surgeries, long periods of immobilization, pain, bone deformities, and sometimes death. The precise reason why a patient's fracture does not heal remains unknown in most cases," said senior investigator Dr. Anna Spagnoli, of the University of North Carolina.</p> <p>The researchers are of the opinion that a deficiency in adult stem cells, which normally become reparative cells in response to damage, may be the main reason why broken bones sometimes fail to heal.</p> <p>Spagnoli say that stem cells in human bone marrow, called mesenchymal stem cells, can become bone, cartilage, fat, muscle, and blood vessel cells, and directing these stem cells into the repair mode is one of the objectives of a new branch of medicine called regenerative medicine.</p> <p>She adds that the adult stem cells, which can be obtained from a patient's bone marrow in a minimally invasive procedure, have been reported to improve fracture healing in a few patients.</p> <p>She, however, also stresses that need for animal studies before clinical trials can begin. In a recent study, she and her colleagues took adult stem cells from the bone marrow of mice with leg fractures, and engineered them to express a potent bone regenerator, insulin-like growth factor 1 (IGF-1).</p> <p>The researchers then transplanted the treated cells into mice with a fracture of the tibia, the long bone of the leg. Upon computed tomography (CT or CAT) scanning, the team observed that the treated mice had better fracture</p>

healing than did untreated controls.

They found that the stem cells migrated to the fracture site and increased the bone and cartilage that bridged the bone gap. "Our study provided critical data needed to implement a novel therapeutic approach in patients with impaired fracture healing," Spagnoli said.

She believes that the use of adult stem cells would have several advantages over embryonic stem cells because they do not have the ethical controversy that surrounds embryonic stem cells, and they may avoid the immune rejection response, as the patient's own cells can be used.