Study finds method to improve transplant cell delivery

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(Medical Xpress) -- A new technique for improving delivery of stem cells may lead to better and faster tissue repair, a breakthrough with promise for sports medicine and military populations.

Researchers at the National Institutes of Health Clinical Center discovered a way to enhance delivery of transplant cells in rodents to a desired site by increasing presence of chemicals that attract the introduced cells. Non-destructive pulsed focused ultrasound interacts with tissue to elevate levels of naturally produced chemicals (such as cytokines, chemokines, and growth factors) on target tissues. Transplanted stem cells have receptors for these chemicals, so an increased presence attracts more of them to the desired site.

Regenerative medicine uses stem cells to replace damaged cells and tissues, and transplanting these cells intravenously is a noninvasive and easily replicated procedure. However, only 1 to 3 percent of intravenous transplanted cells make it to the desired target. By increasing the presence of chemically attractive factors, researchers in the laboratory saw 8 to 10 times more transplanted bone marrow stromal cells in a pulsed focused ultrasound-treated rodent kidney than a non-treated kidney.

“It's like your circulatory system is a series of highways. What makes you want to get off at New York City? We're putting an attraction in the middle of nowhere so the transplant cells will want to go there, to the target site,” said Joseph A. Frank, M.D., chief of the NIH Clinical

Center Radiology and Imaging Sciences Laboratory of Diagnostic Radiology Research. Frank is senior author on the findings that were published online in *Stem Cells* on March 30, 2012.

The attractive chemical agents are enhanced during inflammation or injury, but their quantity elevations last for a short time. Researchers in the laboratory showed that they can extend that window or open a new one using pulsed focused ultrasound. The ultrasound delivers energy to a targeted region, and the tissue converts the energy into the chemical attractive agents. The ultrasound increased the number of these agents expressed on endothelial or vessel wall surfaces through approximately one day and returned to control levels by day three.

An advantage of this improved delivery method is that the pulsed focused ultrasound does not cause any adverse effects to the treated tissue. Researchers also saw increased passage of stem cells into treated tissue and retention, and the focused ultrasound permeates deep so human body composition is not a limitation. Since the technique increases presence of more than 10 attractive chemical factors, the method is not cell specific and may be advantageous for a variety of cell products, such as neural cells or immune cells.

“This research shows the ingenuity of our scientists and the fostering environment at the NIH Clinical Center to run with an idea and see it through to real application for clinical practice,” said NIH Clinical Center Director John I. Gallin, M.D.

Researchers from the National Cancer Institute; Catholic University of America, Washington, D.C.; and NIH's National Institute of Biomedical Imaging and Bioengineering also contributed to these findings.

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