The sturdier sex? Study finds female stem cells work better

April 9 2007

Female stem cells derived from muscle have a greater ability to regenerate skeletal muscle tissue than male cells, according to a study at Children's Hospital of Pittsburgh of UPMC.

The study, which is being published in the April 9 issue of the *Journal of Cell Biology*, is the first ever to report a difference in regenerative capabilities of muscle stem cells based on sex.

This finding could have a major impact on the successful development of stem cells as viable therapies for a variety of diseases and conditions, according to the study's senior author, Johnny Huard, PhD, director of the Stem Cell Research Center at Children's and the Henry J. Mankin Professor and Vice Chair for Research in the Department of Orthopaedic Surgery, University of Pittsburgh School of Medicine.

"Regardless of the sex of the host, the implantation of female stem cells led to significantly better skeletal muscle regeneration," said Dr. Huard, also the deputy director of the McGowan Institute of Regenerative Medicine. "Based on these results, future studies investigating regenerative medicine should consider the sex of the stem cells to be an important factor. Furthermore, investigations such as ours could lead to a better understanding of sex-related differences in aging and disease and could explain, at least partially, the high variability and conflicting results reported in the literature on stem cell biology."

Dr. Huard's team, and the study's first author, Bridget Deasy, PhD,

director of the Live Cell Imaging Lab at Children's Stem Cell Research Center, made the discovery while working with a population of stem cells they isolated in the lab while searching for a cure for Duchene muscular dystrophy (DMD). DMD is a genetic disease estimated to affect one in every 3,500 boys. Patients with DMD lack dystrophin, a protein that gives muscle cells structure. Using an animal model of the disease, his laboratory is using stem cells to deliver dystrophin to muscles.

In this study, Dr. Huard's team injected female and male muscle-derived stem cells into dystrophic mice and then measured the cells' ability to regenerate dystrophin-expressing muscle fibers.

They then calculated the regeneration index (RI) – the ratio of dystrophin-positive fibers per 100,000 donor cells. Only one of the 10 male populations of implanted stem cells had an RI over 200. In contrast, 40 percent of the female stem cell populations had an RI higher than 200, and 60 percent of the female populations of stem cells had an RI higher than the mean RI of the male cells (95).

This difference may arise from innate sex-related differences in the cells' stress responses, according to Dr. Deasy, an assistant professor in the Departments of Orthopaedic Surgery and Bioengineering at the University of Pittsburgh School of Medicine and School of Engineering, respectively.

The investigators examined several aspects of stem cell behavior. They screened for differences in thousands of genes, and they also looked for differences related to estrogen. In many ways the male and female stem cells were similar, Dr. Deasy said.

"The major difference was what we observed after exposing the cells to stress or after cell transplantation in the animals that have muscular

dystrophy. Transplantation of female cells leads to a much more significant level of skeletal muscle regeneration," she said. "The male cells exhibited increased differentiation after exposure to oxidative stress, which may lead to cell depletion and a proliferative advantage for female cells after cell transplantation."

Source: Children's Hospital of Pittsburgh