MRI contrast agents change stem cell proliferation

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When researchers tested three different labeling agents on three different stem cell populations to determine what effect the labeling agents had on stem cell phenotype, biological behavior and migration abilities, they found changes in stem cell proliferation depending on the type of contrast agent used.

The team of researchers from Belgium and Spain tested USPIO (ultra small superparamagnetic iron oxide) contrast agents Resovist, Endorem and Sinerem on mouse embryonic stem cells (mESC), rat multipotent adult progenitor cells (rMAPC) and mouse mensenchymal stem cells (mMSC). Their study is published in the current issue of Cell Transplantation (19:8), now freely available on-line at http://www.ingentaconnect.com/content/cog/ct/.

The researchers found the labeling efficiency with each of the (U)SPIOs varied significantly when different stem cell populations were compared.

"This means that labeling methods will likely need to be optimized for every cell type," said Dr. Crabbe. "Over time we saw a dilution of (U)SPIOs and a decrease of iron in the cells."

Non-invasive imaging plays an important post-transplantation role in stem cell research, but questions regarding whether the contrast agents used to track transplanted stem cells in vivo via MRI have an impact on the cells had largely gone unanswered until this study.

On the issue of whether (U)SPIO labeling has a biological affects on cells, the researchers discovered "no significant alterations" in cell phenotypes and that the label "does not significantly alter stem cell differentiation."

"Sinerem decreased proliferation of mMSC while both Sinerem and Endorem affected the proliferation rate of rMAPC, although prolonged culture, until seven days, resulted in restoration of the proliferation rate," noted Dr. Crabbe. "We also found that higher concentrations of Sinerem ® and Endorem ® were needed for cell labeling to achieve similar MRI detectability."

The researchers concluded that it will be necessary to evaluate the efficiency of cell labeling for every new contrast agent combination aimed at being followed in vivo by MRI. Also, the effect on biological behavior of cells should be examined. They noted that their results were limited to examining the effects of labeling on proliferation, not differentiation.

"Although labeling of stem cells with MRI is promising, there are some limitations," concluded Dr. Crabbe. "More optimal particles are needed that can be taken up without the need of potentially toxic agents. Also, there is the problem of particle dilution over time as cells divide. When grafted cells continue to proliferate, loss of signal occurs."

According to Dr. Julio Voltarelli, professor of clinical medicine and clinical immunology at the University of Sao Pãulo, Brazil and section editor for Cell Transplantation there has been a knowledge gap regarding the survival and distribution of stem cell populations used for in vivo therapy.

"Many studies have tried to close this gap by using radioactive or nonradioactive labeling of the cells in order to follow their fate in the

organism," said Dr. Voltarelli. "However, this paper demonstrates that such labeling may alter stem cell behavior, such as proliferative potential, and give biased information when compared to nonlabeled cells."

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