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Transferrin receptor expression in iron oxide-labeled

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Editor:

In the August 2007 issue of *Radiology* Dr Schafer and colleagues (1) reported the upregulation of transferrin receptor (CD71) on rat mesenchymal stem cells (MSCs) labeled with superparamagnetic iron oxide nanoparticles (SPION). The authors should be commended for studying changes in the iron metabolism or storage to ensure safety of SPION cell labeling. However, their results and conclusions cannot be generalized to all SPION and transfection agents (TA) used for cells labeling.

The authors report the upregulation of CD71 on late passage (i.e., 7–16) rat MSC after labeling with ferucarbotran. Several reports had shown that after multiple passages, human and mouse MSCs are prone to genetic instability with consequent malignant transformation (2,3). Later passage (> 5) is not biologically relevant since human (h) MSCs become senescent after 20–40 population doublings in culture (4). Human MSCs are positive for the transferrin receptor (5,6), however the authors showed no CD71 expression in control rat MSCs. Ferumoxides-protamine sulfate labeled hMSCs have an expected transient decrease in CD71 mRNA and protein levels when compared to unlabeled cells (6). The upregulation of CD71 in the ferucarbotran labeled rat MSC (figure 3) cannot be extrapolated to human MSCs since control rat MSC do not express the transferrin receptor (1).

The authors avoided comparing their findings to magnetic labeling of MSCs with ferumoxides and transfection agents (TA) such as poly-L-lysine (PLL) or protamine sulfate (Pro) (7–12). The authors report that the ferucarbotran complexed to DOSPER or jetPEI coated the cell surface but were not internalized. Ferumoxides complexed to PLL (12) or Pro (8,9) are located in endosomes in hMSCs and in other cells.

The authors suggest labeling MSCs with SPION may affect homing capability of the stem cells. We and others have shown that ferumoxides-TA labeled hMSC will home to liver (7) tumors (11) or heart (13) by MRI and or by histology. The author's concern about the alteration in cell homing is not warranted especially when the SPION-TA complexes are localized in endosomes. Although the authors describe their study limitations, they overstate the clinical relevance and potential translation of their results. The author's advances in knowledge statement that SPIO-TA or USPIO-TA complexes only coats the MSC is not applicable to ferumoxides-TAs complexes and human MSC. The concerns raised by the author's are only pertinent to their study and are incorrect when ferumoxides is complexed to protamine sulfate.

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