

Using MagA and Modified Ferritin Subunits to Track Tumor Cell Growth

D. E. Goldhawk¹, R. Figueredo², C. Lemaire³, P. Foster⁴, S. Dhanvantari⁵, J. Koropatnick², R. T. Thompson¹, and F. S. Prato¹

¹Imaging, Lawson Health Research Institute, London, ON, Canada, ²London Regional Cancer Program, London, ON, Canada, ³Physics and Astronomy, University of Waterloo, Waterloo, ON, Canada, ⁴Imaging, Robarts Research Institute, London, ON, Canada, ⁵Diabetes and Metabolism, Lawson Health Research Institute, London, ON, Canada

Introduction We have investigated the application of gene-based contrast from overexpression of iron binding proteins, in tracking cancer cell growth using MRI. Here we compare expression of modified ferritin subunits (HF+LF), lacking iron response elements (1), with that of MagA, an iron transporter from magnetotactic bacteria (2), in a preclinical model of human cancer. These studies describe the relative potential of engineered tumor cells to differentiate *in vivo* and provide suitable contrast for MRI.

Methods Human MDA-MB-435 cells were transfected with pcDNA3.1 bearing either *MagA* or *HF+LF* inserts. Stably-expressing clones were cultured in the presence or absence of iron supplementation and transplanted into mice fed either a standard or iron-enriched diet. In each animal, parental cells injected into the opposite flank served as the control. Growing tumors were examined *in situ* at 3, 6 and 9 weeks. Endpoint analyses were performed after formalin fixation on a 3T MRI scanner and correlated with tumor histology.

Results Cells expressing MagA or HF+LF formed tumors in nude mice; however, no contrast enhancement between control and engineered cells was observed in tumors formed in the absence of iron supplementation. By 3 weeks post-injection, tumors were 100-150 mm³ and showed varying degrees of MR contrast at 3T in the engineered tumors relative to parental controls. MagA-derived contrast was optimal when iron was added to cell cultures alone (Figure 1) or in combination with dietary iron.

Discussion To enhance cell contrast for MRI, we have examined the potential of iron regulatory proteins to act as contrast agents. Both MagA and the modified ferritin subunits provide cellular contrast in response to iron supplementation, without interrupting cancer cell programming.



Figure 1. Tracking Cancer Cell Growth Using MagA Expression. A clone of MagA expressed in human MDA-MB-435 cells was cultured for 7 days in iron-supplemented media prior to subcutaneous injection of 10⁷ cells into the hind limb of immuno-compromised, nude mice. At 3 weeks, fixed mice were imaged using a 3T MRI scanner and custom-built RF coil (3). An axial cross section shows tumors derived from parental cells on the right flank (R) and from MagA-expressing cells on the left (L). Blue arrows point to each tumor. The image was obtained using 3D FIESTA software and the following parameters: TR/TE=16/8, BW=62, scan time=21 min.

References

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