NEUROTECHNIQUES

Pumping iron

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Magnetic resonance imaging detects expression of an iron-binding transgene in mice.

According to some medical dramas on television, almost anything is visible in magnetic resonance imaging (MRI) scans. Although real-life technology is not there yet, new techniques promise magnetic resonance images of molecular events in the whole animal. Cohen *et al.* report MRI detection of an inducible reporter transgene in mice in a recent article in *Nature Medicine*.

Researchers use iron compounds as contrast agents in MRI. Ferritin binds iron molecules inside cells. Each ferritin molecule contains 24 polypeptide chains surrounding an empty core pocket that can bind and store large amounts of iron. Mice lacking [ferritin heavy chain](#), which catalyzes iron binding, die *in utero*, whereas mice overexpressing ferritin heavy chain show reduced programmed cell death induced by reactive oxygen species relative to wild-type mice.

Mice expressing ferritin heavy chain under the control of the vascular endothelial cadherin promoter (bottom) showed increased magnetic resonance signal relative to controls (top).

The authors generated transgenic mice expressing ferritin heavy chain tagged with a hemagglutinin epitope. In these mice, hemagglutinin-positive cells contained iron (stained by the dye Prussian blue), suggesting that ferritin heavy chain binds iron *in vivo*.

MRI detected transgene expression in small, scattered cell populations. Vascular endothelial cells localize to blood vessels and cells scattered throughout most tissues. Mice expressing ferritin heavy chain under the control of the vascular endothelial cadherin promoter showed increased magnetic resonance signal in discrete brain structures, like the hippocampus, relative to control mice.

Fetal mice express vascular endothelial cadherin in liver and heart starting on embryonic day 13.5. The authors imaged pregnant dams carrying transgenic pups on gestational day 13.5. Relative to littermates that did not express the transgene, transgenic pups showed increased magnetic resonance signal and increased postmortem Prussian blue staining in heart and liver, suggesting that MRI could be used to genotype reporter mice *in utero*, according to the authors.

What are the potential applications of this technique? The authors designed the ferritin heavy chain transgene to be suppressed in the presence of tetracycline, so that the reporter could be switched on and off. They propose that MRI could be used to track migrating or differentiating cells expressing the ferritin heavy chain reporter under the control of a promoter of

interest. They also believe that the reporter might allow transcriptional regulation of gene promoters to be observed by MRI.

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1. Cohen, B. *et al.* MRI detection of transcriptional regulation of gene expression in transgenic mice. *Nature Medicine* (2007).