SENSORS AND PROBES

Genetic tools for magnetic resonance imaging

Genetically encoded reporters can be used for noninvasive cell tracking or molecular imaging with magnetic resonance imaging technologies.

Tracking cells with magnetic resonance imaging (MRI) has traditionally relied on exogenous contrast agents, but genetically encoded reporters have also been available. Reporter genes have the advantages of not being diluted by cell divisions and of only being expressed in viable cells. Kevin Brindle and colleagues at Cambridge University and Alan Jasanoff and colleagues at the Massachusetts Institute of Technology in Cambridge have added to the repertoire of tools by developing genetic reporters that employ different mechanisms to generate contrast in MRI.

Brindle's team chose to use the urea transporter UT-B, which increases water exchange across the plasma membrane when expressed in cells. Elevated water transport can be imaged with filter exchange imaging, an MRI modality that 'removes' signal from fast-diffusing extracellular water and instead focuses on water exchange between the extracellular and the intracellular compartments (Schilling *et al.*, 2017). UT-B generates contrast an order of magnitude higher than that of previously described reporter genes. The researchers applied their strategy to image xenografts of UT-B-expressing cells in mouse flanks.

Jasanoff and colleagues usurped the vasculature for their reporter strategy (Desai *et al.*, 2016). The reporter they developed is the calcitonin gene-related peptide (CGRP), which leads to vasodilation upon expression and secretion. Vasodilation can be imaged with echo-planar imaging. The researchers showed that they could readily detect reporter-gene-expressing cells that were injected into the rat brain. Alternatively, CGRP could be modified to act as a sensor for enzymatic processes. For example, the researchers developed protease sensors which consisted of GFP, a protease cleavage site and CGRP. When injected into the brain, CGRP was released in the presence of the cognate protease, resulting in an increase in MRI contrast.

Both sensors expand the toolkit of genetically encoded sensors for MRI applications. Besides their utility for noninvasive cell tracking, the sensors, driven by an appropriate promoter, could be used to monitor cellular differentiation states. It will also be interesting to see whether the CGRP reporter strategy can be further developed to detect endogenous signaling processes.

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RESEARCH PAPERS

Schilling, F. *et al*. MRI measurements of reporter-mediated increases in transmembrane water exchange enable detection of a gene reporter. *Nat. Biotechnol.* **35**, 75–80 (2017).

Desai, M. *et al*. Molecular imaging with engineered physiology. *Nat. Commun.* **7**, 13607 (2016).