(13) C magnetic resonance spectroscopy measurements with hyperpolarized [1-(13) C] pyruvate can be used to detect the expression of transgenic pyruvate decarboxylase activity in vivo.

Abstract:

Dissolution dynamic nuclear polarization can increase the sensitivity of the (13) C magnetic resonance spectroscopy experiment by at least four orders of magnitude and offers a novel approach to the development of MRI gene reporters based on enzymes that metabolize (13) C-labeled tracers. We describe here a gene reporter based on the enzyme pyruvate decarboxylase (EC 4.1.1.1), which catalyzes the decarboxylation of pyruvate to produce acetaldehyde and carbon dioxide. Pyruvate decarboxylase from Zymomonas mobilis (zmPDC) and a mutant that lacked enzyme activity were expressed using an inducible promoter in human embryonic kidney (HEK293T) cells. Enzyme activity was measured in the cells and in xenografts derived from the cells using (13) C MRS measurements of the conversion of hyperpolarized [1-(13) C] pyruvate to H(13) CO3-. Induction of zmPDC expression in the cells and in the xenografts derived from them resulted in an approximately two-fold increase in the H(13) CO3-/[1-(13) C] pyruvate signal ratio following intravenous injection of hyperpolarized [1-(13) C] pyruvate. We have demonstrated the feasibility of using