129Xe biosensors for molecular imaging in lungs and brain and potential early detection of breast cancer

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Technology description

Cell-compatible cryptophanes and functionalized 129Xe contrast agents for in vivo highly sensitive NMR and MRI measurements of cancer cells

Problem

Current breast cancer screening strategies rely on identifying morphological changes in tissue. There is not a single biomarker to identify early breast cancer, complicating biochemical and genomic diagnostic efforts.

Solution

Researchers in the Dmochowski lab have developed hyperpolarized 129Xe magnetic resonance imaging (MRI) contrast agents that can be used to measure the concentration, location, and function of multiple proteins in the breast to improve the accuracy of early diagnosis. Imaging in the lungs and brain via inhalation of hyperpolarized 129Xe into the lungs and rapid transport to the brain could also be conducted. Hyperpolarization involves optical pumping to align the nuclei, resulting in higher signal detectability than non-hyperpolarized gases. An enzyme-responsive 129Xe NMR biosensor has been synthesized by attaching the consensus peptide substrate for matrix metalloproteinase-7 (MMP-7), an enzyme upregulated in many cancers, to a xenon-binding organic cage, cryptophane. The enzyme cleaves the peptide covalently attached to the Xe biosensor, resulting in a change in the chemical shifts of 129Xe detected by NMR. Xe agents attached to numerous peptides can be used to detect multiple chemical shifts in NMR, and tri-functionalized sensors have been generated in the lab.

(A) Process of producing hyperpolarized 129Xe

(B) Schematic representation of hyperpolarized 129Xe NMR spectrum showing resonances of free Xe gas in aqueous solution, Xe-encapsulated biosensor bound to bioreceptor, and Xe-encapsulated in free biosensor. Biosensor is comprised of molecular cage, linker, and recognition moiety.

Application area

- Monitor multiple breast cancer markers simultaneously in vivo
- Imaging in lungs and brain via inhalation of hyperpolarized 129Xe
- Study mechanisms of drug efficacy
- Develop better diagnostic screens for breast cancer

Advantages

• Superior sensitivity, specificity, and multiplexing capability of hyperpolarized 129Xe
• Detect enzymatic activity rather than stoichiometric binding to matrix metalloproteases
• Monitor multiple chemical shifts rather than single intensity change associated with gadolinium agents
• Soluble in biological fluids
• Deliver hyperpolarized 129Xe by inhalation

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