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Empowering Ideas

A genetically encoded β-lactamase reporter for ultrasensitive ^{129}Xe NMR and MRI in mammalian cells

Brief Description

Hyperpolarized xenon chemical exchange saturation transfer (CEST) contrast agent for molecular imaging

Inventor

Ivan Dmochowski, Professor of Chemistry

STATE OF DEVELOPMENT

- Proof-of-concept
- *In vitro* and *in vivo* testing

INTELLECTUAL PROPERTY

Provisional pending

REFERENCE MEDIA

Wang Y. et al. Angew. Chemie, 2016.
Roose B.W. et al. ACS National Meeting, March 2016. Single-protein reporter for hyperpolarized xenon magnetic resonance imaging.
Dmochowski, I.J. et al. ACS National Meeting, March 2016. Xenon: new applications in materials chemistry and biosensing.

DESIRED PARTNERSHIPS

- License
- Co-development

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Problem

While genetically encoded optical reporters have enabled biomolecular imaging, the strong scattering of light by tissue is problematic. Optical reporters are limited to examining single cells and transparent model organisms. Alternate non-invasive imaging methods, such as magnetic resonance imaging (MRI), are needed for monitoring gene expression and cell migration *in vivo*. Furthermore, despite excellent spatiotemporal resolution, ^{1}H MRI reporter genes are limited by low detection sensitivity.

Solution

Researchers in the Dmochowski have developed a genetically encoded, single protein reporter for hyperpolarized ^{129}Xe NMR and MRI with high saturation contrast for use in molecular imaging applications. Hyperpolarized xenon provides enhanced detection sensitivity. Because ^{129}Xe is nontoxic, it can be safely delivered via inhalation or injection *in vivo*. Furthermore, its small size and hydrophobicity allow for interactions with proteins, occupying hydrophobic cores, substrate-binding sites, and channel pores, enabling the study of biological phenomena. ^{129}Xe chemical exchange saturation transfer (CEST) occurs between the aqueous solvent and β-lactamase, either in solution or inside a cell. Xenon CEST interactions with β-lactamase yield a distinct saturation peak and chemical shift. The x-ray crystal structure of the binding of xenon to β-lactamase has been elucidated, which will inform the design of additional CEST agents.

Advantages

- Nontoxic, readily deliverable to cells and *in vivo*
- High molecular sensitivity
- Noninvasive imaging method
- High contrast

Applications

- Molecular imaging
- Contrast agents
- Elucidate biological processes, normal and diseased physiological states
- Study cryptic pockets in proteins