

Tri-functionalized cryptophane biosensors for biomolecular imaging and MRI diagnostics

Cryptophanes with high xenon affinity enable ultrasensitive detection of analytes in solution using Xe-129 NMR/MRI

Inventors

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STATE OF DEVELOPMENT

In vitro proof-of-concept testing

INTELLECTUAL PROPERTY

[USSN 8,222,022](#)

REFERENCE MEDIA

Riggle B.A. et al. [JACS](#), 2015, 137(16), p. 5542-5548.

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Co-development

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Technology

The Dmochowski lab has developed biosensors comprised of tri-functionalized cryptophane with high affinity for hyperpolarized ^{129}Xe . These biosensors can be designed to detect molecular markers associated with cancer and other disease. More specifically, a biosensor has been synthesized that detects matrix metalloproteases (MMPs), which are frequently upregulated in many cancers. The MMP enzyme cleaves the peptide covalently attached to the ^{129}Xe biosensor, resulting in a change in the chemical environment of ^{129}Xe readily detectable by a 0.5 ppm chemical shift in NMR. The features of these tri-functionalized cryptophanes enable the detection of picomolar concentrations of cryptophane biosensors by a technique known as Hyper-CEST NMR/MRI. Additional xenon biosensors have been designed to target integrin receptors, folate receptor, and carbonic anhydrase. In most cases, binding the cryptophane biosensor to its protein target produces a measureable change in the Xe-129 NMR chemical shift.

Advantages

- Tri-functionalized cryptophanes well-solubilized in water
- Highest known affinity for xenon
- Very favorable Xe exchange kinetics
- Ultrasensitive analyte detection
- Tri-functionalized cryptophane biosensors can be designed that each yield distinct ^{129}Xe NMR chemical shifts and can be targeted to different biomarkers

Applications

- Biosensors
- ^{129}Xe MRI diagnostics next-generation platform
- Biomolecular imaging and enhancement of existing ^1H MRI technology

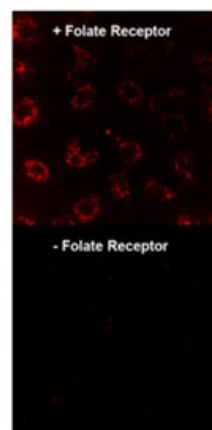
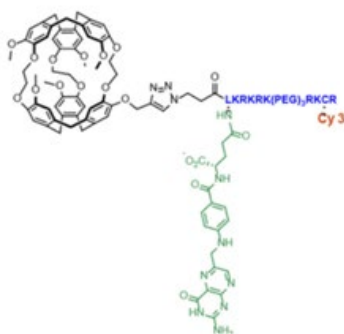


Image Caption:

From Khan et al, 2015. Folate-conjugated cryptophane to target cryptophane to membrane-bound folate receptors that are over-expressed in many human cancers.