TECHNOLOGY

Targeted Delivery of Imaging Probes for In Vivo Cellular Imaging

OVERVIEW

Electron paramagnetic resonance (EPR) imaging is a technique for studying molecules that have one or more unpaired electrons, such as organic and inorganic free radicals or complexes with a transition metal ion. EPR may be thought of as analogous to MRI, except that it measures the excitation of electron spins instead of atomic nuclei. Given that most stable molecules have all their electrons paired, EPR is less widely used than MRI. However, EPR can be a very specific measurement technique with use of the right probe. The UMB inventors designed nitroxide ester-based probes to be retained in the cell longer at physiological conditions, and this innovation helps make in vivo EPR imaging feasible. The present UMB invention expands on a related technology (UMB ref: JK-2007-064), with the addition of new compounds, including isotopically labeled versions of the probes, and encapsulation of the probes inside liposomes for in vivo cellular imaging by EPR. In the liposome, the nitroxides are concentrated and their EPR signal is quenched so that the liposome is "dark" from an imaging perspective. Upon release from the liposome into the cell, nitroxides produce a strong signal that can be accurately correlated with local oxygen concentration, microviscosity, and other cellular properties. In applying this technology to tumor imaging, the surface of the liposome is decorated with antibody domains specific for antigens on the surface of tumor cells. This strategy has been nicely demonstrated by the UMB inventors in a cell line overexpressing HER2, which showed bright intracellular signaling after incubation with anti-HER2 immunoliposomes delivering the probe, versus no signal observed in control cell lines. The inventors envision use of this targeted imaging technology to detect tumors and metastases and to measure physiological properties of tumor cells.

APPLICATIONS

Imaging biomarkers are increasingly recognized as important and useful tools to be applied across the spectrum of drug discovery and development (e.g., target validation, pharmacokinetic assessment, or prognostic indicator). An imaging biomarker may even be developed as a companion diagnostic. A new industry emphasis is highlighted by creation of the Society for Nuclear Medicine's Clinical Trials Network in 2008, with over 200 biomarker manufacturers and 230 imaging centers registered by end of 2010. The goal is to establish standardized protocols and to provide a resource of IND applications that will be available for cross-reference in clinical trials. Another collaborative effort is the Biomarkers Consortium, a public-private partnership managed by the Foundation for the National Institutes of Health. Three of the consortium's ongoing projects involve imaging biomarkers, such as the evaluation of fluorodeoxyglucose-positron emission tomography (FDG-PET) as a clinical biomarker in non-small cell lung cancer and non-Hodgkin's lymphoma. Imaging is often used in oncology clinical trials to determine the size of a tumor, or to assess its proliferation and metabolism, which can be related to treatment response. Emerging areas also include measurements of tumor angiogenesis, levels of hypoxia, and apoptosis.(Business Insights report, July 2010).

ADVANTAGES

Targeted delivery of nitroxide probes to enable new imaging modalities for quantitative physiological measurements.

STAGE OF DEVELOPMENT

In vivo proof-of-concept of liposome delivery in progress to demonstrate efficacy for tumor imaging in xenograft models. Several novel nitroxide probes have proven useful in animal models for quantification and mapping of oxygen status in the brain. Isotopically labeled nitroxide probes have recently been tested and show further enhanced sensitivity.

R&D REQUIRED

Completion of in vivo proof-of-concept of liposome delivery to further develop as pre-clinical tool. For ultimate clinical use, a clinical-grade device for EPR measurement will be required.

LICENSING POTENTIAL

UMB seeks development partner for advancing this technology into pre-clinical or clinical use.

CONTACT INFO

Office of Technology Transfer
620 W Lexington St., 4th Floor
Baltimore, MD 21201
Email: ott@umaryland.edu
Phone: (410) 706-2380

Additional Information

INSTITUTION

University of Maryland, Baltimore

PATENT STATUS

U.S. CIP Patent, 10,202,342 , issued 02/12/2019

CATEGORIES

- Research Tools, Antibodies, & Reagents
- Diagnostics

INVESTIGATOR(S)

Joseph Kao
Gerald Rosen
Scott Burks

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