POLSKY Center for Entrepreneurship and Innovation
THE UNIVERSITY OF CHICAGO

PET Imaging Agent for Diagnosis and Monitoring of Multiple Sclerosis and Traumatic Brain Injury

SUMMARY

Multiple sclerosis (MS) is thought to affect more than 2.3 million people worldwide. Current imaging technologies used for diagnosis and management only allow visualization of potential lesions in the brain and spine, and cannot definitively determine that any observed damage is due to MS or other demyelinating disorders. The University of Chicago has developed an imaging approach using 4-AP, which is FDA approved and already prescribed to MS patients to improve walking. In addition to demonstrating imaging of demyelinated regions using radiolabeled 4-AP, the investigators have developed novel derivatives of this molecule with increased penetrance of the blood-brain barrier that can also be used for imaging.

KEY RESULTS

Radiography experiments have demonstrated localization of labeled 4-AP and derivatives to demyelinated areas in a mouse model. Some derivatives have increased penetrance of the blood-brain barrier as compared to 4-AP. PET imaging experiments to demonstrate correct localization of labeled 4-AP in non-human primate subjects are currently underway.

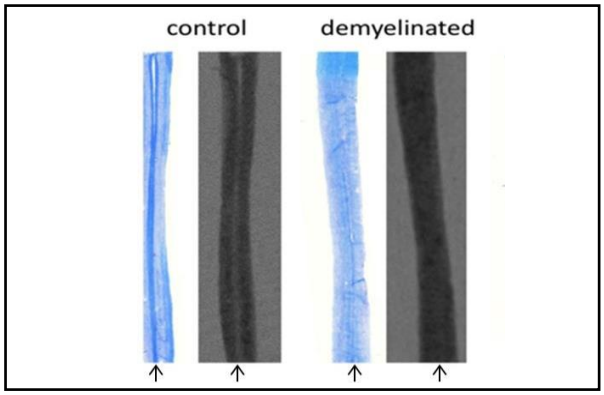
ADVANTAGES

- Imaging compounds derived from 4-AP (already FDA approved).
- Utilizes existing equipment framework (PET imaging).
- Enables definitive visualization of underlying pathology.
- Some derivatives have increased metabolic stability and brain delivery as compared with 4-AP.

APPLICATIONS

- Imaging of nerve demyelination associated with multiple sclerosis and traumatic brain injury.

Uptake of 4-AP in Spinal Cords from Mice



Left panels represent luxol fast blue staining for myelin; right panels are radiograph images using 14C labeled 4-AP. The region indicated with arrows is labeled only in spinal cords with demyelination.

TECHNICAL DESCRIPTION

Investigators have shown that radioisotope-labeled 4-AP targets potassium channels revealed in demyelinated axons, allowing clinicians the ability to visualize demyelinated areas in the central nervous system. They have gone on to make a series of novel fluorinated 4-AP derivatives in an effort to improve stability of the compound and increase penetration through the blood-brain barrier. One of the derivatives, 3-F-4-AP, has demonstrated superior stability and delivery to the brain and may prove promising for sensitive imaging of demyelinated axons. The approach is currently being tested in the PET modality in primates.

REFERENCE
UCHI 2112, 2250

DEVELOPMENT STAGE
Pre-clinical

THERAPEUTIC AREAS
Multiple Sclerosis; Traumatic Brain Injury

PUBLICATION
Synthesis of meta-substituted [18F]3-fluoro-4-aminopyridine via direct radiofluorination of pyridine N-oxides
P. Brugarolas,*a R. Freifelder,b S.-H. Chengb and O. DeJesusc
Show Affiliations
Chem. Commun., 2016,52, 7150-7152

INTELLECTUAL PROPERTY
14/329,597
Counterparts in Europe, Australia, and Canada
A second provisional application is pending.

INVENTOR(S)
Dr. Brian Popko, PhD has a long-standing interest in the myelination process and his laboratory is funded by the National Institutes of Health, the National Multiple Sclerosis Society and the Myelin Repair Foundation. Drs. Applebaum, MD and Chen, PhD are part of the Department of Radiology; Dr. Applebaum has a specific interest in neurologic PET imaging.

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