

Fluorescent Amyloid Binding Agents for Diagnosis of Alzheimer's Disease

Tech ID: 20849 / UC Case 2010-162-0

BACKGROUND

Amyloids are insoluble fibrous protein aggregates that accumulate in various organs throughout the human body. It has been clinically proven that abnormal accumulation of beta-amyloids in the brain is associated with various neurodegenerative diseases, including Alzheimer disease. Diagnostic biomarkers currently in clinical development are limited to small radio-labeled molecules for detection of amyloidosis through PET or SPECT imaging modes. There remains a pressing need for the design and development of new imaging agents for conclusive early diagnosis of Alzheimer's disease, ideally through widely accessible detection platforms.

TECHNOLOGY DESCRIPTION

A common structural feature of known amyloid-binding agents is an electronically-polarized, extended aromatic system that is inherent to a family of fluorescent probes known as molecular rotors. Features of molecular rotors, which inherently decrease the non-radiative decay rate and increase fluorescence emission upon binding to aggregated beta-amyloids, were incorporated into a general design of novel, amyloid-binding agents.

APPLICATIONS

- ▶ Fluorescent probes are compatible with in vivo fluorescence imaging instruments.
- ▶ Generally relevant for the early diagnosis of diseases characterized by amyloid aggregates, such as Alzheimer's, Parkinson, Huntington disease, and rheumatoid arthritis.

ADVANTAGES

- ▶ Simple synthesis and chemistries amenable to modification and production at large scales.
- ▶ Fluorescence profile optimized for in vivo characterization of amyloid deposits using existing and widely accessible imaging instruments.
- ▶ These probes may be used for the monitoring of disease progression in the development of new therapeutic treatments.

STATE OF DEVELOPMENT

Proprietary methods were used to identify, synthesize, and characterize seven, novel compositions of matter. Development included in vitro evaluation for specifications relevant to use in clinical practice, including: solubility, fluorescence characteristics, ability to cross the blood-brain barrier, binding constants, and capability to detect amyloidosis in brain tissue.

INTELLECTUAL PROPERTY INFO

US and numerous foreign rights available for licensure in some fields. US application at link, below.

RELATED MATERIALS

- ▶ [Kevin Cao](#), Kevin, et al., *Aminonaphthlanene 2-Cyanoacrylate (ANCA) Probes Fluorescently Discriminate between Amyloid-β and Prion Plaques in Brain*, J. Am. Chem. Soc., Article ASAP, DOI: 10.1021/ja3063698, Publication Date (Web): August 6, 2012
- ▶ Sutharsan, J. et. al., *Rational Design of Amyloid Binding Agents Based on the Molecular Rotor Motif*, ChemMedChem, 5:1, 56-60 (2009).
- ▶ Ran, C., et al., *Design, Synthesis, and Testing of Difluoroboron-Derivatized Curcumins as Near-Infrared Probes for In Vivo Detection of Amyloid-Beta Deposits*, J. Am. Chem. Soc. 2009, 131, 15257-15261.
- ▶ Chang, W.M. et al., *ANCA: A Family of Fluorescent Probes that Bind and Stain Amyloid Plaques in Human Tissue*, ACS Chemical Neuroscience, DOI: 10.1021/cn200018v, Publication Date (Web): March 21, 2011.

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OTHER INFORMATION

KEYWORDS

neurodegenerative, Alzheimer, Parkinson, Huntington, arthritis, RA, beta-amyloid, brain, fluoroprobes, emission, fluorescent probe, amyloid, CNS, diagnostic, diagnosis, detection, therapeutic, small molecule, imaging, image, ophthalmology, ophthalmologic

CATEGORIZED AS

- ▶ **Medical**
 - ▶ Diagnostics
 - ▶ Disease: Ophthalmology and Optometry
- ▶ **Research Tools**
 - ▶ Reagents

RELATED CASES

2010-162-0, 2006-105-1, 2006-105-2, 2006-105-4, 2006-105-3, 2007-018-1, 2007-018-2

► Dutescu, R. M. et al., *Amyloid Precursor Protein Processing and Retinal Pathology in Mouse Models of Alzheimer's Disease*, Graefes Arch Clin Exp Ophthalmol (2009) 247:1213–1221.

► Cao et al. (2012), Amino Naphthalenyl-2-Cyano-Acrylate (ANCA) Probes Fluorescently Discriminate between Amyloid- β and Prion Plaques in Brain, *J. Am. Chem. Soc.*, Just Accepted Manuscript, DOI: 10.1021/ja3063698, Publication Date (Web): August 6, 2012

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,551,722	01/24/2017	2010-162
United States Of America	Issued Patent	8,940,918	01/27/2015	2010-162

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Lead Compounds for Diagnosis and Therapy of Alzheimer's Disease
- pH-"Tunable" Nano-Particle Drug Delivery System
- Ultrasensitive, Ion Channel-Based Sensors

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