Billing Code 4140-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Jeffrey Thruston at 301-594-5179 or *jeffrey.thruston@nih.gov*. Licensing information may be obtained by communicating with the Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, 5601 Fishers Lane, Rockville, MD 20852; tel. 301-496-2644. A signed Confidential Disclosure Agreement will be required to receive copies of unpublished information related to the invention.

SUPPLEMENTARY INFORMATION: Technology description follows:

Tau RT-QuIC: Ultrasensitive Assays for the Detection of Tau Seeding Activity Associated with Tauopathies

Description of Technology:

Tauopathies are a category of neurodegenerative diseases defined by the abnormal accumulation of misfolded tau protein aggregates (often in the form of amyloid

filaments) within the brain. Tau proteins exist in six isoforms, three of which contain three microtubule binding regions (3R), and the remainder contain four microtubule binding regions (4R). Tauopathies are characterized, in part, based on the ratio of 3R/4R misfolded tau proteins that make up the aggregates. This technology enables rapid, ultrasensitive and economical differentiation of self-propagating tau aggregates associated with tauopathies in crude biospecimens. The assays use recombinant, truncated 3R, 4R, or 3R+4R tau protein substrates as indicators of tau aggregates. Specifically, misfolded tau aggregates (contained in a biological sample) seed the polymerization of either 3R, 4R, or 3R+4R tau substrates, and the polymers (amyloid fibrils) are detected as an amplified indicator of even extremely low concentrations of tau aggregates within the biological sample and aid in identification of the tauopathy. In its current embodiment, this assay has been used to detect tau seeds in brain tissue from patients with Alzheimer's disease, Pick disease, chronic traumatic encephalopathy, corticobasal degeneration, progressive supranuclear palsy, certain frontotemporal dementias, and other tauopathies. For several of these diseases, tau RT-QuIC assays have also detected tau seeding activity in patients' cerebrospinal fluid.

This technology is available for licensing for commercial development in accordance with 35 U.S.C. 209 and 37 CFR Part 404.

Potential Commercial Applications:

- Diagnosis of tauopathies, including: Alzheimer's disease, Pick disease, corticobasal degeneration, chronic traumatic encephalopathy, progressive supranuclear palsy, and frontotemporal dementias with tau deposition.
- Measurement of levels of pathological tau aggregates in biospecimens.

- Analysis of tauopathy-associated disease progression
- Clinical trial / drug development companion diagnostic

Competitive Advantages:

- Uses a consistent, concentrated source of truncated tau protein
- Rapid and economical
- Highly sensitive and specific

Development Stage:

- Research Use.

Inventors: Byron Caughey (NIAID), Eri Saijo (NIAID), Allison Kraus (NIAID), Michael Metrick II (NIAID)

Publications:

Saijo, Eri et al. "Ultrasensitive and selective detection of 3-repeat tau seeding activity in Pick disease brain and cerebrospinal fluid". *Acta Neuropathologica* vol. 133 (2017):751-765.

Kraus, Allison et al. "Seeding selectivity and ultrasensitive detection of tau aggregate conformers of Alzheimer disease". *Acta Neuropathologica* vol. 137, 4 (2019): 585-598.

Metrick II Michael et al., "Million-fold sensitivity enhancement in proteopathic seed amplification assays for biospecimens by Hofmeister ion comparisons". *Proc Natl Acad Sci USA* vol. 116, 46 (2019):23029-23039.

Saijo, Eri et al. "4-repeat tau seeds and templating subtypes as brain and CSF biomarkers of frontotemporal lobar degeneration". *Acta Neuropathologica* vol 139, 4(2020):63-77.

Metrick II, Michael et al. "A single ultrasensitive assay for detection and discrimination of tau aggregates of Alzheimer and Pick diseases**".** *Acta Neuropathologica Communications* vol. 8, 1 (2020):22.

Licensing Contact: To license this technology, please contact Jeffrey Thruston at 301-594-5179 or *jeffrey.thruston@nih.gov,* and reference E-015-2017-0.

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Wade W. Green,

Acting Deputy Director,

Technology Transfer and Intellectual Property Office,

National Institute of Allergy and Infectious Diseases.

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