



News Release

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CONTACT: Kim Guenther
(215...
kim.guenther@uphs.upenn.edu



University of Pennsylvania School of Medicine
University of Pennsylvania Health System

Penn Medicine Pathologists Pioneer Biomarker Test to Diagnose or Rule Out Alzheimer's Disease

Biomarker Signatures Predict Conversion from Mild Cognitive Impairment to Alzheimer's Disease

PHILADELPHIA, PA – A test capable of confirming or ruling out Alzheimer's disease has been validated and standardized by researchers at the University of Pennsylvania School of Medicine. By measuring cerebrospinal fluid (CSF) concentrations of two of the disease's biochemical hallmarks – amyloid beta42 peptide and tau protein – the test also predicted whether a person's mild cognitive impairment would convert to Alzheimer's disease over time. Researchers were able to detect this devastating disease at the earliest stages, before dementia symptoms appeared and widespread irreversible damage occurred. The findings hold promise in the search for effective pharmaceutical therapies capable of halting the disease.

Homing in on a previously suggested pathological CSF biomarker signature, a team of Penn Medicine researchers, led by **Leslie M. Shaw, PhD**, Co-Director of the Penn Alzheimer's Disease Neuroimaging Initiative (ADNI) Biomarker Core, found evidence of neuron degeneration – marked by an increase in CSF concentration of tau proteins – and plaque deposition, indicated by a decrease in amyloid beta42 concentration. In addition, people with two copies of the genetic risk factor for Alzheimer's disease, *APOE ε4*, had the lowest concentrations of amyloid beta42, compared to those with one or no copies. The study appears in the online edition of the *Annals of Neurology*.

“With this test, we can reliably detect and track the progression of Alzheimer's disease,” said Dr. Shaw. “Validated biomarker tests will improve the focus of Alzheimer's clinical trials, enrolling patients at earlier stages of the disease to find treatments that can at least delay –and perhaps



stop— neurodegeneration. In addition, prevention trials can test methods to delay or block mild cognitive impairment from converting to full-blown Alzheimer’s.”

Further validation studies of this research test system are underway. Additional work is needed to develop additional biomarkers, as well as identify more genetic risk factors that will help distinguish Alzheimer’s from other neurodegenerative diseases characterized by cognitive impairments.

“Thanks to the dedicated researchers and volunteers who participated in this and other Alzheimer’s disease studies through the Penn Alzheimer’s Disease Core Center and at ADNI trial sites around the US and Canada, we have validated a test where a safe, simple lumbar puncture can provide information to confirm suspected Alzheimer’s disease and predict the onset of the disease,” said **John Q. Trojanowski, MD, PhD**, Director of the Penn Alzheimer’s Disease Core Center. “Using this technique, we will further our understanding of how the disease progresses and what we can do to stop Alzheimer’s disease before it starts.”

About the Study

Cerebral spinal fluid samples contributed by 410 ADNI volunteers at 56 sites across the U.S. and Canada were included in this study. To independently establish threshold values for these biomarkers, cerebrospinal fluid samples from 52 Penn Memory Center volunteers with normal cognition and 56 people with confirmed Alzheimer’s disease based on post-mortem autopsy diagnosis were also measured. The test was based on the multiplexed xMAP microbead immunoassay system, with reagents provided by Innogenetics.

When compared with normal, healthy adults of the same age, a pattern of changes emerged in people with mild cognitive impairment or Alzheimer’s disease. In this group, tau concentrations increased, while amyloid beta42 levels decreased as the disease progressed.

- The test was 87 percent accurate overall (80 percent or above is considered clinically useful).
 - In the CSF samples from those with autopsy-confirmed Alzheimer’s disease, the amyloid beta42 concentration threshold was most sensitive and detected Alzheimer’s disease at a rate of 96.4 percent.
 - The test accurately ruled out Alzheimer’s disease in 95.2 percent of the subjects.
 - The test positively predicted the conversion from mild cognitive impairment to Alzheimer’s disease at a rate of 81.8 percent.

Data used in preparing this article were produced by the Alzheimer’s Disease Neuroimaging Initiative (ADNI) Biomarker Core at Penn or obtained from the ADNI database (www.loni.ucla.edu/ADNI). Many ADNI investigators contributed to the design and implementation of ADNI or provided information but did not participate in the analysis of the data presented here or in the writing of this report. A complete list of ANDI investigators is



available at http://www.loni.ucla.edu/ADNI/Collaboration/ADNI_Authorship_list.pdf.

The ADNI public-private partnership includes federal support from the National Institute on Aging and the National Institute for Biomedical Imaging and Bioengineering, both part of the National Institutes of Health, and the participation of the Food and Drug Administration. Private sector support comes from pharmaceutical companies and other organizations through the Foundation for NIH, which has raised more than \$25 million from both corporations and non-profits toward ADNI. Current private sector funders include Abbott Laboratories, AstraZeneca AB, Bayer Schering Pharma AG, Bristol-Myers Squibb, Eisai Global Clinical Development, Elan Corporation, Genentech, General Electric Healthcare, GlaxoSmithKline, Innogenetics, Johnson & Johnson, Eli Lilly and Co., Inc., Merck & Co., Inc., Novartis AG, Pfizer Inc, F. Hoffmann-La Roche, Schering-Plough, Synarc Inc., and Wyeth Research, as well as non-profit partners the Alzheimer's Association and the Institute for the Study of Aging.

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***PENN Medicine** is a \$3.6 billion enterprise dedicated to the related missions of medical education, biomedical research, and excellence in patient care. PENN Medicine consists of the University of Pennsylvania School of Medicine (founded in 1765 as the nation's first medical school) and the University of Pennsylvania Health System.*

Penn's School of Medicine is currently ranked #4 in the nation in U.S. News & World Report's survey of top research-oriented medical schools; and, according to most recent data from the National Institutes of Health, received over \$379 million in NIH research funds in the 2006 fiscal year. Supporting 1,700 fulltime faculty and 700 students, the School of Medicine is recognized worldwide for its superior education and training of the next generation of physician-scientists and leaders of academic medicine.

The University of Pennsylvania Health System (UPHS) includes its flagship hospital, the Hospital of the University of Pennsylvania, rated one of the nation's top ten "Honor Roll" hospitals by U.S. News & World Report; Pennsylvania Hospital, the nation's first hospital; and Penn Presbyterian Medical Center. In addition UPHS includes a primary-care provider network; a faculty practice plan; home care, hospice, and nursing home; three multispecialty satellite facilities; as well as the Penn Medicine at Rittenhouse campus, which offers comprehensive inpatient rehabilitation facilities and outpatient services in multiple specialties.

This release is available online at
http://www.uphs.upenn.edu/news/News_Releases/2009/03/csf-alzheimers-biomarker.html