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BAND-aid for PD and AD

By Michael J. Haas, Senior Writer

Spurred by emerging evidence of biological overlaps between Parkinson's disease and Alzheimer's disease, **The Michael J. Fox Foundation for Parkinson's Research**, the **Alzheimer's Association** and **The W. Garfield Weston Foundation** have launched a grant program to jump-start cross-disease research. The partners are soliciting project proposals and expect to announce awards in July.

The Biomarkers Across Neurodegenerative Disease (BAND) initiative will award grants of up to $150,000 to about 6 projects this year, according to MJFF CEO Todd Sherer. The funded projects would run for one to two years and could focus on marker discovery, assay standardization, genetic profiling, imaging modalities, or diagnostic or therapeutic development, he said.

Heather Snyder, director of medical and scientific operations at the Alzheimer's Association, said that the partners will decide on a per-project basis how much each organization would contribute to the award.

Snyder said that her association has allocated a total of $500,000 to BAND.

Sherer declined to disclose how much MJFF has allocated. He noted that funds from Weston will be for Canadian researchers. The foundation is a not-for-profit organization that supports science, education and land conservation in Canada.

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>
> ***—Todd Sherer, The Michael J. Fox Foundation for Parkinson's Research***

Getting the BAND together

BAND projects must use existing data or biological samples from two large-scale clinical studies—the Parkinson's Progression Markers Initiative (PPMI) and the Alzheimer's Disease Neuroimaging Initiative (ADNI).

MJFF launched the five-year PPMI in 2010 to identify biological markers of PD. PPMI initially enrolled about 150 patients and age-matched controls in the U.S. and EU[1] and later expanded to include about 600 patients and controls at 24 sites in the U.S., EU and Australia.[2]

A public-private partnership that includes the Alzheimer's Association and the **Foundation for the National Institutes of Health** launched the ADNI in 2004 to identify markers for early detection of AD and for monitoring disease progression. The study has enrolled more than 1,000 participants, including patients with AD or mild cognitive impairment (MCI), individuals at risk of developing AD and controls who have no memory problems.[3]

Indeed, the genesis of the BAND program was presentations related to the two studies at the Alzheimer's Association International Conference last July that hinted at biological overlaps between PD and AD.

The most convincing link came from Kenneth Marek, who reported preliminary data from the first 100 participants in PPMI and drew comparisons between those findings and results from ADNI. For example, cerebrospinal fluid levels of β-amyloid (Aβ) were lower in both PD and AD patients than in healthy controls, whereas cerebrospinal fluid levels of microtubule-associated protein-τ (MAPT; tau; FTDP-17) were lower in PD patients but higher in AD patients than in healthy controls. Together, these findings suggest that Aβ and tau play roles in both diseases.[2]

Marek is a clinical professor of neurology at **Yale University** and senior scientist at the university's Institute for Neurodegenerative Disorders. The preliminary PPMI data—but not the ADNI comparisons—were published in *JAMA Neurology* in October.[4]

Snyder said that Marek's presentation—as well as other presentations at the meeting that drew on both ADNI and preliminary PPMI data—stimulated discussions between MJFF and the Alzheimer's Association about leveraging the two datasets and led to the development of the grant program.

At that time, MJFF and the W. Garfield Weston Foundation were discussing plans for a grant program to fund research into PD markers, said C. Alexandra Stewart, executive director of neuroscience at Weston. Once MJFF pointed out the shared interests of the three organizations, "we all agreed a three-way program would be beneficial," she said.

Opening acts

The guidelines for BAND highlight several areas on which funded projects could focus—such as analyzing cross-talk between PD and AD markers and investigating common mechanisms across PD, AD and other neurodegenerative diseases. However, Snyder and Sherer said that these are just suggestions and do not reflect the partners' expectations or priorities for funded projects.

"We all agree that the highlighted areas are important, but we don't want to rank them or give priority to any one of them," Snyder said. "We know researchers will have innovative ideas for leveraging the datasets."

With the BAND program, "we are trying to break down the silos around research into each disease," Sherer said. "We want researchers to use these large datasets from PPMI and ADNI and find out whether

the data could change how we think about and define each disease from a biological perspective."

Sherer said that the partners have two broad goals for research that will be funded by the program: identifying commonalities between PD and AD, and drawing distinctions between PD, AD and the natural processes of aging.

"Identifying a common factor between the diseases might lead to the discovery that something previously considered only as a therapy for Parkinson's disease might actually treat a subset of both Parkinson's and Alzheimer's patients," he said. "Finding a distinguishing factor between the diseases could lead to better differential diagnoses or targeted therapies for each disease."

The well-characterized age-matched controls in PPMI and ADNI "will also allow researchers to take a close look at normal aging and neurodegeneration, which could help make distinctions between changes that are part of natural aging and changes that result from pathological disease mechanisms," said Sherer.

Snyder added that cross-disease research funded by the BAND program could lead to new treatments for other neurodegenerative disorders. She also said that the partners have not yet decided whether BAND will continue beyond the launch phase.

Sherer said that PPMI is now recruiting individuals who have one of three risk factors for PD: loss of the sense of smell, REM sleep behavior disorder (loss of normal motor inhibition during REM sleep) or mutations in either *leucine-rich repeat kinase 2* (*LRRK2*) or *α-synuclein* (*SNCA*).

"We want to look at markers in these groups of individuals and see whether we can predict who might convert to a diagnosis of PD in the future," he said. He added that a paper reporting full baseline data from the original cohort of 600 PPMI participants is in the press.

Snyder said that ADNI began its third phase, ADNI-2, in 2011 to identify individuals at risk of AD, track disease progression and develop tests to measure the effectiveness of treatments. The third phase will conclude in 2016.

BAND is not the only program that could lead to new ways of classifying PD and AD.

Last month, the **Innovative Medicines Initiative** (IMI) and the **European Federation of Pharmaceutical Industries and Associations** (EFPIA) launched Aetionomy, a consortium of 17 pharmas, research institutions and clinical centers that seeks to develop new classification systems for PD and AD based on the underlying mechanisms specific to each disease and then validate each new system in the clinic. The consortium does not aim to develop a single classification system that would encompass both diseases on the basis of their shared biology.

IMI and EFPIA have each contributed €8 million ($10.8 million) to fund Aetionomy over the next 5 years.

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COMPANIES AND INSTITUTIONS MENTIONED

Alzheimer's Association, Chicago, Ill.
European Federation of Pharmaceutical Industries and Associations, Brussels, Belgium
Foundation for the National Institutes of Health, Bethesda, Md.
Innovative Medicines Initiative, Brussels, Belgium
The Michael J. Fox Foundation for Parkinson's Research, New York, N.Y.
The W. Garfield Weston Foundation, Toronto, Ontario, Canada
Yale University, New Haven, Conn.