Biomarkers Across Neurodegenerative Diseases

Program Objectives: The Alzheimer’s Association (ALZ), Alzheimer’s Research UK (ARUK), The Michael J. Fox Foundation for Parkinson’s Research (MJFF), and the Weston Brain Institute (Weston) announce a global Request for Applications (RFA). The main objective of BAND is to stimulate analyses across Alzheimer’s disease (AD), Parkinson’s disease (PD) and other neurodegenerative diseases to increase understanding of pathogenesis similarities and differences. Analyses from this program may support, for example, biomarker discovery, assay standardization, genetic profiling, harmonization of existing data set phenotypes, cross-disease analysis of existing genetic data, inclusion of other neurodegenerative diseases related to PD and AD, and imaging development. The RFA aims to build on existing momentum to leverage similar activities and increase impact across the neurodegenerative disease spectrum. It also builds on recent evidence suggesting substantial overlap between AD, PD, and other neurodegenerative diseases pathologically, but also potentially biologically. The RFA is designed to enable preliminary pilot research or proof-of-principle studies utilizing data and/or samples from large biomarker studies of neurodegenerative disease cohorts, including but not limited to the Alzheimer’s Disease Neuroimaging Initiative (ADNI), the Parkinson’s Progression Markers Initiative (PPMI), and a Frontotemporal Lobar Dementia (FTLD) cohort study in order to garner further research support from other funding agencies. Proposed projects must use resources from at least one either AD or PD cohort such as ADNI or PPMI. Data may come from investigator-chosen cohorts, including other neurodegenerative disease studies.

Background: Although AD and PD are clinically distinct entities, research has hinted at underlying pathological, physiological, and possibly genetic linkages between these two diseases across the neurodegenerative continuum. Recent data reported at the 2013 Alzheimer’s Association’s International Conference stimulated discussion in the research community about the possible cross talk between AD and PD. For example, underlying pathologies/biomarkers, such as cerebrospinal fluid (CSF) alpha-synuclein, have been measured in the sample sets collected for both diseases to help understand similarities and differences in these diseases. Furthermore, similar imaging modalities, such as MRI and PET, are being employed to interrogate changes that occur with disease progression. As therapeutic approaches are developed that may be disease-modifying for several neurodegenerative diseases, stratification of clinical trial populations based on biomarker profiles may increase the probability of success in demonstrating a beneficial effect.

Potential Areas of Study: Several areas of study worthy of further research may focus on projects that utilize existing data/samples to interrogate high-impact questions related to aging and neurodegeneration. Applications that are innovative, high-risk, high-reward and tackle critical scientific, diagnostic and therapeutic questions in AD, PD, FTLD and other neurodegenerative diseases are encouraged. All proposals must include either an AD or PD cohort and must include at least one additional neurodegenerative disease. The study of existing well-annotated and defined cohorts is
a requirement. Grant proposals could address, but are not limited to, the following areas of study:

1. **Analysis of existing neurodegenerative disease datasets.** Research projects in this category could engage in analyses of control and disease populations that test hypotheses related to aging and neurodegenerative disorders. The ADNI, PPMI and FTLD datasets, and potentially other datasets include clinical, imaging and biologic data in publicly accessible databases that can be aggregated together in order to enhance our understanding of the unique and overlapping changes occurring in different neurodegenerative diseases. For instance, building on the whole genome sequencing of the ADNI 1 dataset, researchers could investigate PD-related genetic correlations (e.g., DJ-1) and assess prevalence of AD-related genetic markers (e.g., APOE4) in PD-specific datasets. Applicants are encouraged to draw on other cohort studies to complement the datasets mentioned above. To this end, applicants have the opportunity to bring other robust datasets to the partners attention as potential tools to ask questions.

2. **Standardization of data acquisition/methods/quality control/assays.** Research projects in this category should focus on cross-standardization efforts between biochemical biomarkers (e.g., possible coordination of alpha-synuclein analyzed in both ADNI and PPMI), the identification of other panels/ pathways that may be duplicative in disease mechanisms (e.g., targeted analysis of inflammation or apoptosis), and the standardization of existing MRI methods/data acquisition.

3. **Biomarker cross talk between neurodegenerative diseases.** Research projects in this category should focus on the translation of novel biomarker efforts to identify shared and disparate biochemical biomarkers. Projects may investigate AD samples for PD-related biomarkers or, conversely, PD samples for AD-related biomarkers, or may suggest new biomarkers for analyses. Data of this nature will be useful in identifying subpopulations within individuals affected by AD or PD.

4. **Investigate common mechanisms across the broader spectrum of neurodegenerative diseases.** Research projects in this category will assess the commonality and potential mechanisms engaged across the disease spectrum – including AD, PD, FTLD, and other neurodegenerative diseases. The value in this area of study is the identification of high-return targets for therapeutic intervention or modification.

5. **Investigate age-related changes and risk factors for neurodegeneration.** Both ADNI and PPMI include longitudinal data from age-matched control subjects that could be used to better understand the normal distribution of biomarkers in aged populations.
**General considerations:** All proposals must have a clear focus on AD and/or PD and may also include other neurodegenerative diseases. Applicants may request support to use the ADNI and PPMI data and other existing datasets. Prospective data collection or cohort-building is not appropriate for this RFA, but use of data and/or samples from other existing cohorts is permissible. Please note: biological samples from the ADNI and PPMI datasets are not available for use under this RFA. Ultimately, the goal of this program is to translate the research into strategies to increase understanding of the similarities or differences between neurodegenerative diseases to help stratify populations and possible treatments. Therefore, animal studies are not appropriate for this RFA.

Because the principal idea is to encourage studies building on existing cohorts, bridging the neurodegenerative continuum and building diverse expertise, an interdisciplinary approach may be the most fruitful. Therefore, submissions from collaborative research teams (i.e., basic scientists and clinical researchers) that have experience across aging and neurodegenerative diseases are strongly encouraged. In addition, while novel and creative ideas are sought, proposals also need to demonstrate feasibility.

**Available Funding:** ALZ, ARUK, MJFF, and Weston anticipate funding multiple awards under this program. Applicants may request up to two years and $150,000 in total costs, inclusive of both direct and indirect costs. Exceptions for particularly unique projects or projects that span the globe will be considered, but requests that exceed $150,000 must be well justified in the Available Resources and Budget Justification section of the application – please contact staff for approval. Indirect costs may not exceed 10 percent of direct costs.

**Eligibility:** Applications are encouraged from research laboratories and teams around the world. Researchers with full-time staff or faculty appointments are encouraged to apply. Post-doctoral fellows are eligible to apply as a principal investigator (PI), but must collaborate with an administrative PI who serves as the director of the laboratory in which the research will be conducted. The administrative PI will be responsible for assisting in providing all institutional documents required for the project and will be required to sign any award contract. Training or mentoring-only proposals will not be considered.

**Letter of Intent/Application**

Letters of Intent (LOI) must be submitted through the proposalCENTRAL on-line application system at [http://proposalcentral.altum.com](http://proposalcentral.altum.com).

Letters of intent must be received by 6:00 PM EST, April 9, 2015.

For those invited to submit a full application, **applications must be received by 6:00 PM EST, June 26, 2015.**
Important Deadlines:

March 5, 2015…………………… Website access opens to application materials
March 12, 2015…………………… Informational conference call*
April 9, 2015.......................... Letters of intent due
May 19, 2015........................... Full applications invited
June 26, 2015........................... Full applications due
September 2015....................... Anticipated award announcements
October 2015.......................... Anticipated funding

*ALZ, ARUK, MJFF, and Weston will hold a 45-minute conference call at 12 p.m. ET on March 12, 2015 to clarify and explain the goals of this funding initiative and answer applicant questions. To receive call-in details, RSVP to conferencecalls@michaeljfox.org.

Budget and allowable costs:
It is required that funds awarded under this program be used for direct research support. Budgets must be appropriate and justifiable for the work described.

Funds awarded may be used for:
- Laboratory supplies
- Salary for the principal investigator, scientific (including post-doctoral fellows) and technical staff (including laboratory technicians and administrative support staff whose work is directly related to the funded project) except where individuals are paid salaries by their institutions.

Funds awarded cannot be used for:
- Tuition
- Computer hardware or software for investigators and other capital equipment
- Rent for laboratory/office space
- Construction or renovation costs
- Travel