Biomarkers Across Neurodegenerative Diseases (BAND)

**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. The intent of this RFA is to analyze across existing data; biological samples are not available for use under this RFA. Funding from this program may support but is not limited to projects that aim to develop and/or advance innovative data models, biomarker discovery, assay standardization, genetic profiling, harmonize existing data set phenotypes, analyze cross-disease or longitudinal analyses of existing data, inclusion of other neurodegenerative diseases related to PD and AD, or imaging development.

BAND aims to build on existing momentum to leverage similar activities and increase impact across the neurodegenerative disease spectrum. It also builds on 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 well-defined neurodegenerative disease cohorts (as described below), in order to garner further research support from other funding agencies. Data may come from investigator-chosen cohorts, including of other neurodegenerative disease studies.

Ultimately, the goal of this program is to translate the research into strategies to increase understanding of the similarities or differences across and between neurodegenerative diseases to help stratify populations and develop possible diagnostic tools or treatments.

**Background:** Although AD, PD and other neurodegenerative diseases are clinically distinct entities, research has hinted at underlying pathological, physiological, and possibly genetic linkages between these diseases across the neurodegenerative continuum. For example, underlying pathologies/biomarkers, such as cerebrospinal fluid (CSF) alpha-synuclein, have been measured in the sample sets collected for both AD and PD 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, DLB and other neurodegenerative diseases (e.g. MSA, PSP, vascular contributions or prodromes to these neurodegenerative diseases of aging) are encouraged. All proposals must include an AD and/or PD cohort and must include at least one additional neurodegenerative disease (this can include comparing AD and PD). The study of existing well-annotated and defined cohorts is a requirement and the proposal must demonstrate approved access to utilize the proposed cohorts for the proposed work. Grant proposals could address, but are not limited to, the following areas of study:

1. **Capitalizing on longitudinal data to investigate age-related changes and risk factors across neurodegenerative diseases of aging.** Existing cohorts and datasets may include longitudinal data from age-matched control participants that could be used to better understand the normal distribution of biomarkers in aged populations.

2. **Analysis of existing well-defined neurodegenerative disease cohorts.** A well-defined neurodegenerative disease cohort is defined as a cohort that is ready for use (i.e., no collection of additional data is required, with the exception of longitudinal data) of at least two types of samples (e.g., biologic, clinical, genetics and/or neuroimaging data) in comprehensive (e.g., mild, moderate and severe disease) and/or longitudinal control and disease sample populations. Examples include but are 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. It is also not required that proposals use ADNI or PPMI. Applicants using an alternative, well-defined, neurodegenerative disease cohort must be able to demonstrate written approval or authorization from identified, cohort sponsor organization that proposed data elements are available for analyses to support project aims. Research projects in this category could engage in analyses of control and disease populations that test hypotheses related to aging and neurodegenerative disorders. Well-defined cohorts 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 longitudinal AD and PD datasets already collected and readily available, researchers could investigate CSF and blood-based indicators (e.g. Abeta, phospho-tau, etc.) of disease progression. Robust plans for data analysis, sharing of analysis results, as well as resource sharing for any materials developed through this project (i.e. assay results, intermediate products like gene expression summary data) should be considered.
3. **Standardization and validation 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 or PET methods/data acquisition. The development of novel, innovative models, including mathematical modeling or data mining technologies and their correlation to clinical endpoints is encouraged.

4. **Biomarker cross talk between neurodegenerative diseases.** Research projects in this category could focus on the translation of novel biomarker efforts to identify shared and disparate biochemical biomarkers. Projects may investigate utility of a disease-related biomarker in another disease; for instance, evaluate AD samples for PD-related biomarkers or, conversely, PD samples for AD-related biomarkers, or may suggest new biomarkers for analyses. This is not limited to AD and PD only but must include comparison to one of these two diseases. Data of this nature will be useful in identifying subpopulations within individuals affected by AD, PD or other neurodegenerative diseases.

5. **Investigate common genes, biological mechanisms and signaling/pathways (e.g. GWAS and WGS) across the broader spectrum of neurodegenerative diseases.** Research projects in this category will assess the commonality and potential mechanisms and pathways that may be engaged across the disease spectrum – including AD, PD, FTLD, and other neurodegenerative diseases, and could include analysis across the available platforms for common genes of interest. The value in this area of study is the identification of high-return targets for therapeutic intervention or modification.

**General considerations:** All proposals should be hypothesis-driven and compare either AD and/or PD cohort and/or at least one additional neurodegenerative disease (this can also include comparing AD and PD); each proposal must include two diseases for comparison and must include either AD or PD. Applicants may request support to use the proposed data (e.g. ADNI, PPMI and/or other existing datasets). **Prospective data collection or cohort-building is not appropriate for this RFA but use of data archived (previously banked and analyzed) samples from other existing cohorts is permissible.** Robust plans for comparing or contrasting different diseases, and data analysis and sharing must be considered. Please note: biological samples are not available for use under this RFA. As stated above, the ultimate goal for BAND is to translate the research into strategies to increase understanding of the similarities or differences across and between neurodegenerative diseases to help stratify populations and develop possible diagnostic tools or 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 is strongly encouraged. 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. Applicants should include study personnel (co-investigator or consultant) with significant expertise and familiarity with the identified cohort/database to support scientific oversight of proposed project aims. 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.

**Important Deadlines:**

July 15 2018............................ Website access opens to application materials
August 20 2018............................. Informational conference call*
Sept 10 2018............................. Letters of intent due
October 22, 2018.......................... Full applications invited
December 1, 2018....................... Full applications due
March 2019............................ Anticipated award announcements
April 2019............................. Anticipated funding

*ALZ, ARUK, MJFF, and Weston will hold a 45-minute conference call at 12 p.m. ET on August 20, 2018 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. Compensation for identified consultants with familiarity with the cohort/database is an allowable cost. Budgets must be appropriate and justifiable for the work described. A written budget justification for proposed scope of work is a requirement for all application submissions.

Funds awarded may be used for:
- Data-related 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.
- Publication costs.

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