Precision Medicine for Alzheimer Disease and Related Disorders

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This application seeks to initiate a precision medicine program in Alzheimer disease (AD), a clinical area for which there is great need and broad expertise and resources at BU. We hypothesize that the reason current drugs used to treat AD are ineffective and clinical trial studies have largely failed is the assumption that AD is a single disease, when in fact, it has been well documented by clinical, imaging, neuropathological and genetic studies that AD is a heterogeneous disease. The primary aims of this ARC are to identify subtypes of AD within the Framingham Heart Study (FHS) dataset, validate these subtypes using other available data from the national AD Centers database and other public databases, investigate the biological underpinnings of these subtypes, and identify new therapeutic targets specific for these subtypes. As a first step, we will employ multiple computational strategies including “Big Data” analytics in collaboration with Thomson Reuters for identifying AD subtypes or risk factor profiles that are defined by profiles based on deep phenotyping (e.g., cognitive testing, medical history, brain imaging, biomarker, lifestyle) and ‘Omic (e.g., genetic, genomic, methylomic, proteomic, and metabolomic) data. In subsequent funding periods, we propose to validate these subtypes in other datasets, derive stratification model(s) for assigning prospectively studied persons along the disease spectrum to disease subtypes for testing drug response and predicting prognosis, and evaluate experimentally the biological underpinnings of one or more subtypes and identify new therapeutic targets. This project introduces a very novel approach for extracting key information from very large and complex datasets that will define subtypes and risk profiles for AD. This program is uniquely suited at BU because of the availability of and experience working with the FHS dataset, world class clinical and basic science experts in AD, and opportunity to replicate and validate findings using local resources including the BU AD Center.