Instructions for Proposal Form:

* Provide a brief bio and picture for use on the APDA website and APDA publications

* Provide a description in donor terms of the aims of the grant/fellowship for the 12 month period

* Submit this form electronically, no later than July 1, 2015, to hgray@apdaparkinson.org

USE YOUR INDIVIDUAL FORM, FOLLOWING THE OUTLINE BELOW:

Name of Institution: Boston University School of Medicine

Project Title: Comparison of microRNAs across Parkinson's brains and biofluids

Investigators/Authors Bio/Pictures:

Dr. Latourelle is a genetic epidemiologist who has been involved in the study of the genetics of Parkinson’s disease since 2002. Upon appointment to the Department of Neurology at the Boston University School of Medicine in 2009 she has worked in affiliation with the Neurogenetics laboratory on the development and implementation of novel methods for in-depth analysis of large-scale datasets generated in genome-wide association studies (GWAS), microarray, and sequencing studies of DNA, RNA and microRNAs. Particular emphasis includes studies of alternate phenotypes such as age of onset, dementia, disease penetrance and gene expression, including recent work relating genetic variation with gene expression data to assess potential functionality of observed genetic associations to Parkinson’s disease. In addition to her recent research into the effects of miRNA on neurodegenerative disease, she is currently leading a project using functional linkage networks to allow efficient analysis of the potential impact of gene-by-gene interaction on Parkinson’s disease risk.

Objective: The objective of this study is a comprehensively compare the miRNA profile observed in PD brain samples to that observed in cerebrospinal fluid (CSF) and serum, allowing the identification of neuro-pathologically relevant, yet clinically accessible miRNA for potential use as biomarkers.

Background:

miRNAs are small non-coding mRNA molecules that regulate gene expression and due to their small size may cross the blood-brain barrier and circulate in peripheral fluids such as CSF or blood serum. Because of this unique property, miRNAs show clinical promise as biomarkers for neurodegenerative diseases. Recent attempts to identify miRNA biomarkers for PD in circulating plasma using a microarray-based assay produced encouraging results, but have not been successfully validated. We suggest that using primarily affected tissues from postmortem patient samples as an initial miRNA screening approach may
enhance subsequent analysis of miRNA alterations found in CSF or blood by decreasing noise and irrelevant signals and ultimately lead to more effective detection of PD biomarkers. A comprehensive evaluation of the correspondence of brain miRNA and miRNA detectible in biofluids is the logical first step to drive forward these projects.

**Methods/Design:** Burgos et al. (2014) recently completed a high throughput sequencing study of miRNA (miRNA-Seq) in a large cohort of CSF and blood serum PD and control samples. We will capitalize on this previous work by sequencing the frontal cortex of 42 brain samples (31 PD and 11 control) from the same subjects contributing CSF and serum samples to that project, allowing direct comparison of brain and peripheral miRNA profiles within the same subject. This unique dataset will provide opportunity to greatly expand our understanding of the inter-tissue relationships and circulating properties of miRNA in neurological diseases.

**Relevance to Diagnosis/Treatment of Parkinson’s disease:** The completion of this project will provide the first step in translating neuro-pathologically derived miRNA profiles into accessible biomarkers. These biomarkers will have potential clinical utility in monitoring the efficacy of therapeutic interventions or for categorizing PD cases at increased risk for rapid progression or dementia, which is also of relevance to clinical trials.