microRNA-34b and 34c as disease progression biomarkers for Parkinson's Disease

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Introduction

Parkinson's Disease

Parkinson's Disease (PD) is a neurodegenerative disorder that affects the motor abilities of individuals over the age of 60.[1] PD present with tremors, muscle rigidness, bradykinesia (slow body movements), poor balance and posture, and loss of coordination. Non-motor symptoms include impairments in cognitive ability, sleep disorders, swallowing problems, emotional changes and/or depression, and difficulty controlling bladder and bowel movements. PD is characterized by decreased levels of dopamine, a neurotransmitter that is responsible for coordinating movement.[2] On the other hand, alpha-synuclein (α-Syn) protein aggregates in dopaminergic neurons form Lewy bodies that may impair the function of these neurons[3] , as observed in Figure 1.

MicroRNAs

MicroRNAs (miRNA) are small, non-coding RNA molecules that regulate many biological processes, including gene expression.[4] They consist of 18-22 nucleotides and inhibit protein expression by complementary binding to the 3'-UTR region of messenger RNA (mRNA), as seen in Figure 2.[5,6] miRNA-34b and 34c can bind to 3' UTR of α-Syn and are downregulated in patients with PD.[7] Without a cure for PD, it is important to monitor disease progression in order to gauge treatment efficacy and to develop better and more effective treatment plans. **Expression of miRNA-34b and 34c may reflect α-Syn level and potentially serve as disease progression biomarkers for PD.**

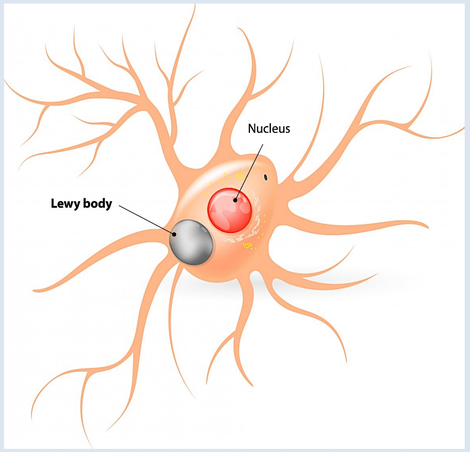

Figure 1. Lewy body inclusion on a dopamine producing neuron.[7]

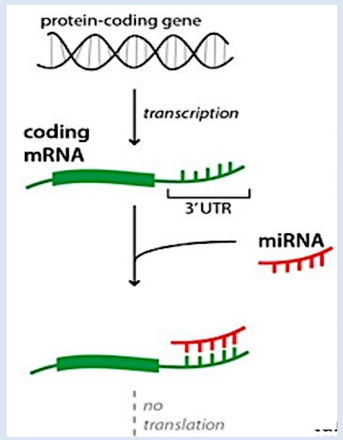

Figure 2. miRNA binding to repress translation.[8]

Methods

Samples

- 30 total human serum samples (15 fast progression PD, 15 slow progression PD)

miRNA Extraction

- Qiagen miRNeasy Serum/Plasma Kit for isolation and purification of total miRNA

Preamplification and Quantitative Real-Time PCR

- Taqman Assay

Results

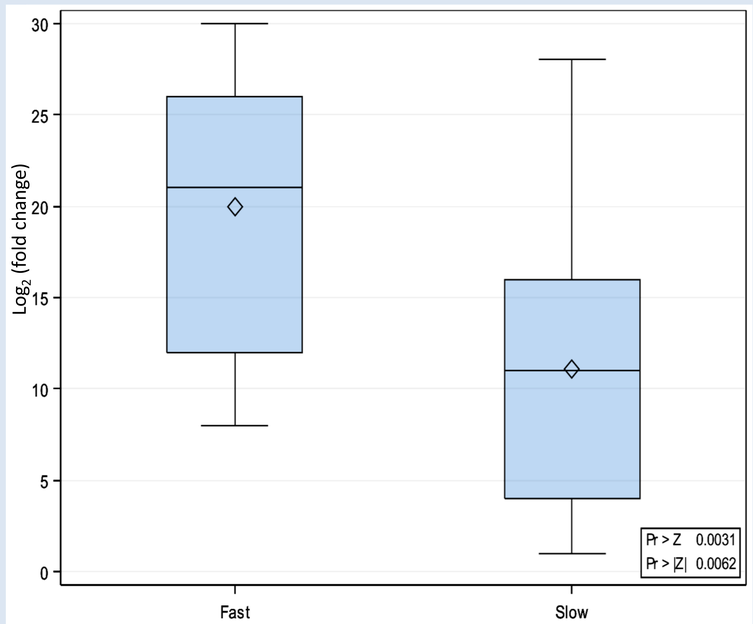

Figure 3. miR-34b expression in fast vs. slow PD progressors

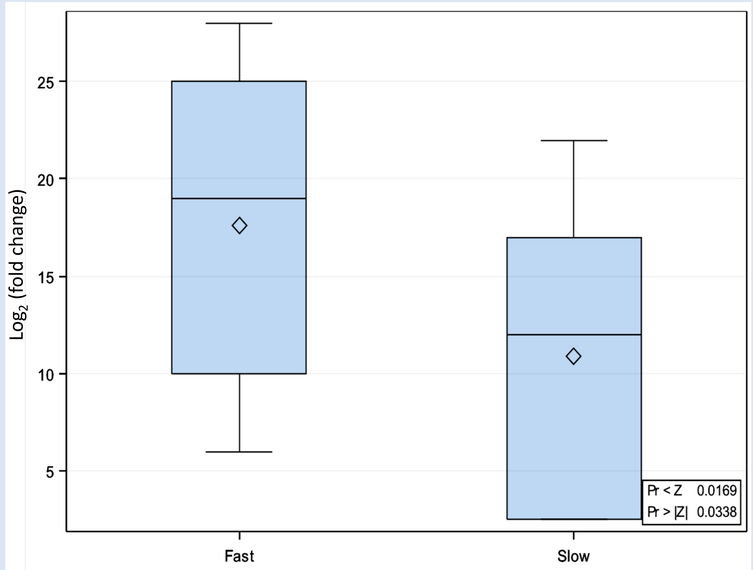

Figure 4. miR-34c expression in fast vs. slow PD progressors

MicroRNAs-34b and 34c are significantly upregulated in fast progressors compared with slow progressors

We hypothesize that fast progressors will have higher levels of α-Syn compared with slow progressors, thus we anticipate lower miR-34b and 34c expression in fast progressing patients. However, this was not observed in our preliminary data; expression of both miR-34b and 34c were significantly higher in fast progressors compared with slow progressors (p-values of 0.0025 and 0.0156). The reason behind this observation is unclear. One possible explanation is that α-Syn protein aggregates make miRNA-34b/c less accessible to the 3'UTR regions for binding, causing more "free" miRNA-34b/c in the serum, especially in fast progressors that we hypothesized having higher levels of α-Syn.

Conclusions

Due the significant different in expression of miR-34b and 34c in fast progressors compared with slow progressors, these miRNAs can serve as biomarkers to distinguish these 2 groups of PD patients. These miRNAs also have the potential to monitor disease progression and improve management and treatments of PD.

Future Work

We plan to repeat this study with a larger sample size to confirm our findings. Additionally, we are investigating miRNA 34b and 34c expression levels in the same cohort of patients, at 1-2 years after diagnosis to assess accuracy of these biomarkers for disease progression monitoring.

Acknowledgments

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