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. PD present with tremors, muscle rigidity, 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. On the other hand, alpha-synuclein (α-Syn) protein aggregates in dopaminergic neurons form Lewy bodies that may impair the function of these neurons, as observed in Figure 1.

MicroRNAs
MicroRNAs (miRNA) are small, non-coding RNA molecules that regulate many biological processes, including gene expression. 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 more effective treatment plans. Expression of miRNA-34b and 34c may reflect α-Syn level and potentially serve as disease progression biomarkers for PD.

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

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.

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References