



Editorial

Biofluid-based Biomarkers for Parkinson’s Disease: A New Paradigm

Sok Kean Khoo *

Department of Cell and Molecular Biology, Grand Valley State University, Grand Rapids, MI 49503, USA

* **Correspondence:** E-mail: khoos@gvsu.edu; Tel: +1-616-331-5916

Parkinson’s disease (PD) is a neurodegenerative disorder that affects more than 6 million people worldwide. There is neither a cure nor a laboratory blood test to diagnose or monitor this progressive disease. The current gold-standard for clinical diagnosis based primarily on motor features is “too little, too late”: initial misdiagnosis can be as high as 30% and patients are usually in moderate to advanced disease stages when first diagnosed. Thus, development of translatable biomarkers that can accurately diagnose PD at its earliest stage are essential for earlier therapeutic intervention to impact clinical outcomes.

Overview of the “Biofluid Biomarkers for Parkinson’s Disease” Special Issue

This special issue focuses on current developments of biofluid-based biomarkers for PD. Biofluids such as cerebrospinal fluid (CSF), blood, serum, and plasma are attractive resources for biomarker studies as they are relatively easy to obtain at lower costs compared with neuroimaging. Protein or gene expression changes in these biomarker candidates can reflect disease status and can be measured objectively with standard laboratory equipment.

The first research study [1] asks whether previously identified PD biomarkers of circulating microRNAs (miRNAs) in blood plasma can be validated in a new cohort of patients. Petillo *et al.* previously screened miRNAs using microarray technology to identify and replicate a panel of four

plasma miRNA biomarkers that can distinguish PD from healthy controls [2]. In this validation study, a new, independent cohort of PD patients and healthy controls was obtained and different quantitative real-time PCR (qRT-PCR) equipment was used to assess the biomarker performance. They found their results reproducible and that qRT-PCR is a robust diagnostic assay. These results highlight the importance of detection assay optimization and biomarker validation as essential stages in biomarker development prior translating into clinical settings.

The second research study [3] examines central nervous system (CNS) debris-loaded phagocytes in peripheral blood mononuclear cells (PBMC) as potential PD biomarkers. Neuromelanin plays both protective and toxic roles in the dopaminergic neurons. In normal physiology, it binds to iron and provides neuroprotection from oxidative stress, but degenerating or dying neurons may release neuromelanin as a source of chronic inflammation [4]. First, the authors showed that fungal melanin-binding decapeptide (4B4) can bind to neuromelanin in human substantia nigra. Assuming that neuromelanin is one of the phagocytosed neuronal debris that is re-circulated into the peripheral blood, it can later be detected in a significantly higher level in PBMC of PD patients. These results propose a potential new approach to evaluate various CNS-debris laden phagocytes in PBMC as PD biomarkers.

Three review articles were also presented. Conti and Alessio [5] described various proteomics approaches, including emerging studies of protein post-translational modification, to identify PD biomarkers from CSF. Several limitations on protein analyses and using CSF as a source for biomarker research were highlighted. Recent reports on differential biomarkers for PD in CFS also reaffirm the challenge of limited validation studies and various biological confounding factors that need to be addressed [6,7]. Shinde *et al.* [8] provided an up-to-date and comprehensive list of biofluid-based miRNA biomarkers for PD. Several miRNA biomarkers can be replicated in various tissue types, research groups, and detection platforms, showing the robustness of miRNA-based biomarkers for diagnostic purposes. However, lack of validation studies and small sample sizes remain a challenge as well to enable these biomarkers to move forward into clinical practice. The final review by DeMarshall *et al.* [9] focused on using autoantibodies in serum as diagnostic biomarkers for PD. Neuronal damage may generate cell type-specific debris that can enter the blood circulating system, activate a specific immune response, and trigger specific autoantibodies for debris clearance. Recent studies have identified PD-specific autoantibodies as potential biomarkers for PD diagnostics.

Conflict of Interest

The author declares no conflict of interest.

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