Potential of Tiny RNAs as a Hope to Detect Parkinson's Disease

Parkinson's disease (PD) is one of the commonest neurological disorders and a leading cause of morbidity. It is very difficult to diagnose its onset during the early stage. This is primarily due to the lack of specific diagnostic biomarkers. Over the years, different groups across the world have worked to characterise different genes as potential markers to diagnose the disorder, with very little consensus. A number of studies have now recognised non-coding RNAs as potential diagnostic tools in neurological disorders, with special emphasis on circulating miRNAs, as they are stable and easily accessible compared to other invasive techniques.

A group of researchers led by Rita Christopher[1] at NIMHANS in Bengaluru have reviewed the efficiency of circulating miRNAs as diagnostic biomarkers in PD. They enumerate the role of various miRNAs as diagnostic and prognostic markers in PD and emphasise that they are better than any protein attribute. Their team has done a thorough analysis of all differentially expressed miRNAs in PD from various studies. Interestingly, they have also classified these studies based on the methodology used for small RNA isolation and measurement.

The authors[1] have focussed on the clinical applications of circulating miRNAs in PD and provide a holistic view of the findings so far. They have summarised the overlap as well as extreme discordance between studies in different groups such as CSF, blood and their derivatives, carried out using different techniques such as microarray, qRT-PCR and next-generation sequencing. The investigations displayed very low consensus and serum candidates had better overlap than biofluids. The review encompasses the limitations and strengths of each of the studies discussed. Apart from that, a number of preanalytical factors that could affect the differential miRNA expression such as the patient cohort, miRNA profiling techniques and certain limitations associated with the same have also been discussed. The authors have scrutinised the prospects of using miRNAs as PD markers. Nevertheless, there is still uncertainty of using miRNAs as true indicators of disease pathogenesis due to the unknown cause-effect mechanism.[2]

MiRNAs are also known to possess transient effects on the mRNA targets due to a short lifespan and have multiple targets.[3] Also, there are multiple miRNAs belonging to a family, which target the same seed sequence, thereby introducing redundancy in the genome.[4] It is interesting to note that despite the presence of numerous studies on miRNAs as biomarkers, there are very few proof of principle studies where modulation of a particular miRNA has been clearly established to lead to disease.

The review highlights the current theoretical and technical limitations to use miRNAs as diagnostic biomarkers in PD. Future prospects would include using other effective candidates as biomarkers such as lncRNAs[5] and circRNAs.[6] These non-coding RNAs are more reliable, have high tissue-specific expression and can provide a higher concordance among studies. Few recent studies have also identified long non-coding RNAs and circular RNAs as finer biomarkers in several neurodegenerative disorders including PD. MiRNA regulation in PD itself is a vicious circle including lncRNAs and circRNAs as key players involved in the pathogenesis of PD. These new classes of non-coding RNAs have been shown to act as sponges and thereby antagonise the role of several miRNAs.[7] We can expect more non-coding RNA-based biomarker studies in the future to diagnose neurological disorders including PD.

Kriti Kaushik, Jayanth Kumar Palanichamy

Department of Biochemistry, AIIMS, New Delhi, India

Address for correspondence: Dr. Jayanth Kumar Palanichamy, Department of Biochemistry, AIIMS, New Delhi - 110 029, India.
E-mail: jayanthaiims@gmail.com

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