

Parkinson's Disease and Mitochondrial Gene Expression

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It is estimated that 6.3 million people suffer from PD worldwide. The World Health Organization gives an estimated crude prevalence of PD as 160 per 100,000 and an estimated incidence per year of 16-19 per 100,000 [1].

Parkinson disease (PD) is associated with progressive loss of dopaminergic neurons in the substantia nigra, as well as with more-widespread neuro muscular changes that cause complex and variable motor and nonmotor symptoms [2]. The loss of dopaminergic neurons is a result of many deregulations caused due to mutations [3]. Both, the high oxidative burden within these cells and defective mt DNA replication could contribute to this selective vulnerability, excitotoxicity and lead into a vicious cycle of cell death. Dopaminergic neurons of the substantia nigra are particularly vulnerable to mt DNA deletions [4].

Mitochondrial DNA polymerase gamma POLG is a nuclear-encoded protein critical for the synthesis, replication and repair of mitochondrial DNA (mt DNA). Abnormal function of this sole mt DNA polymerase leads to defective oxidative phosphorylation and ATP production. Impaired integrity of mt DNA with its depletion causes a broad spectrum of both non-neurological and neurological phenotypes [5]. Patients with mutations in the gene encoding mitochondrial DNA polymerase (POLG) in particular have been known to accumulate multiple mt DNA mutations and develop parkinsonism or related dysmorphic features [6,7].

The products of several PD-associated nuclear genes like Parkin, PINK1, SNCA, DJ-1, LRRK2 and HTR2A show a degree of localization to the mitochondria under certain conditions [8]. Therefore mitochondria represent a highly

promising target for the development of disease biomarkers by use of genetic, biochemical and bioimaging approaches [6,7]. POLG have not been studied yet in correlation with expression of Parkinsons related genes. Although initial studies have been made on these mutations but their role, mechanisms of action but correlation remain yet to be explained [5-9]. The present letter emphasis on the opportunity of new possibilities in diagnosis and treatment of PD.

So far, the diagnosis in PD is primarily based on clinical criteria which suggest the presence of a full-blown PD, while the neurodegenerative process in the PD brain occurs much earlier than the clinical onset. Therefore, the formulation of an early clinical diagnosis is very critical [10]. Mitochondrial genes and their interplay role in PD will also lead to decision of which Genetic test for these gene mutations should be prescribed [11]. Awareness that mitochondrial POLG mutations can underlie Parkinsonism is important for clinicians working in diagnosis and therapeutics of movement disorders, as well as for studies of the genetics of Parkinson's disease. This study is a step forward towards furthering our understanding and research into the etiology of Parkinson's disease especially idiopathic PD, particularly with regard to a possible contribution of mitochondrial dysfunction.

Keywords: DNA; PD; POLG

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