Genetics Of Parkinson's Disease

Amira Ahmed Gwazi 2385
Supervised By Dr. Aml Elnaili
Libyan International Medical University Faculty Of Applied Medical Science

Introduction

Parkinson's disease (PD) is a neurological disease caused by loss of activity of dopaminergic neurons in substantia nigra and is characterized by presence of lewy bodies in midbrain, Symptoms exhibited as rest tremors, rigidity, bradykinesia, and posture instability. The non motor symptoms include constipation and REM sleep disorder [1,2].
Age is the biggest risk factor, and usually older adults are affected, It is a multifactorial disease with many environmental factors such as head injury well water consumption, and pesticide exposure and genetic mutations. The most important genes will be discussed in the following sections [1].

SNCA

The first causal gene mutation related to familial PD is synuclein alpha (SNCA) gene.
Is a gene localized on chromosome 4 in humans which encodes alpha-synuclein (one of presynaptic protein products) that is responsible for presence of lewy bodies in case of mutation [1].
Many studies showed that there is a strong relationship between SNCA polymorphisms and sporadic PD risk development [2].

PINK1

The mitochondrial protein kinase called PTEN encoded in PTEN-induced kinase 1 (PINK1) gene that located in outer membrane of mitochondria
This protein act to protect the mitochondria from malfunctioning in the course of cellular stress.
Mutation in this gene will prevent the clearance of dysfunctional mitochondria, contributing in developed of PD [2,3].

LRRK2

The most common cause of autosomal dominant PD is the mutation in LRRK2 gene.
The LRRK2 gene is located in chromosome 12p11 and it makes leucine-rich repeat kinase 2 protein.
This plays a role in transmitting signals and assembly of microtubules of cytoskeleton.
The mutation of this gene leads to over activation of kinase causing hyperphosphorelation of other proteins and disassembly of microtubules which lead to neuronal damage [2,3].

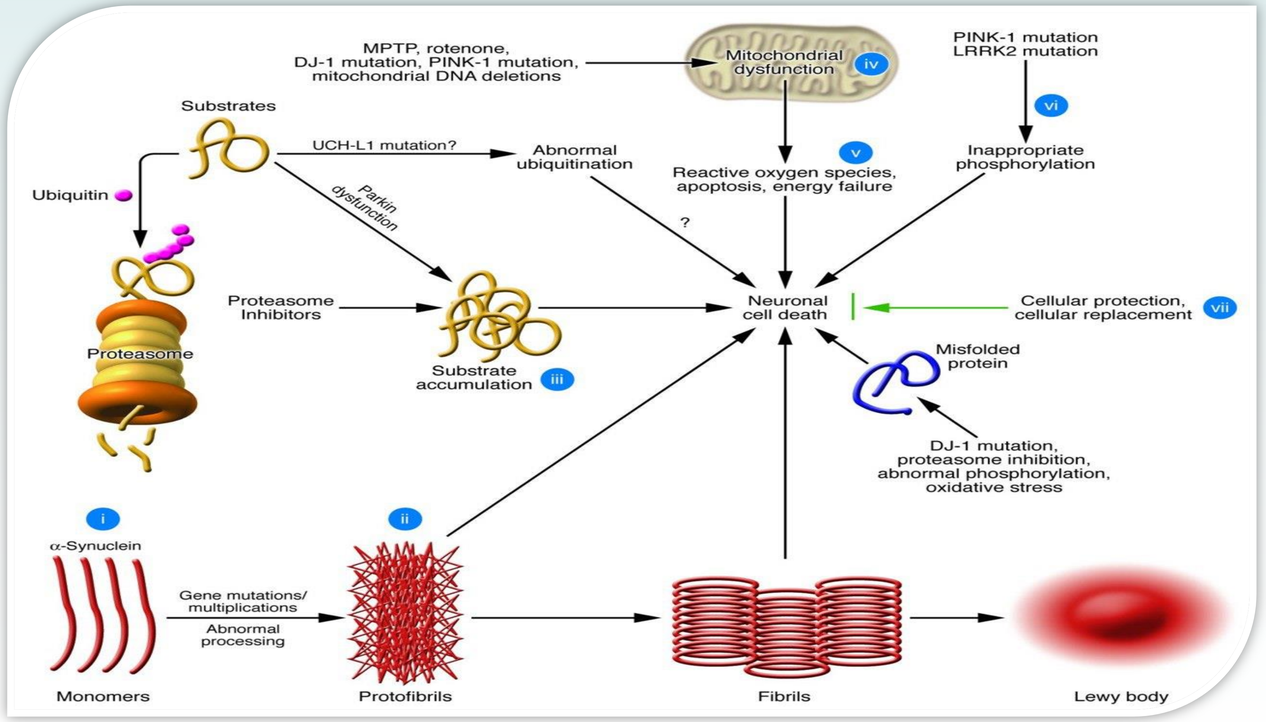

Figure (1) Common Mutations Pathways Of Parkinson's Disease [3] .

Conclusion

Parkinson's disease is a progressive disorder characterized by trembling, slow movement and impaired balance, It is may begin after age 50 (late-onset disease), or before age 50 (early-onset disease), and before age 20 (juvenile-onset disease).
It is a multifactorial disease with causes divided between genetic and environmental factors [1].
Mutations in multiple genes such as PINK1 and LRRK2 cause monogenic form of the disease, while mutations in SNCA, GBA lead to sporadic form.
Other genes (PARK, HLA-DR, NAT2 and GAK) have been associated with an increased risk of developing of PD. and there is a genetic risk including mitochondrial dysfunction associated with PD [3,4].

References

1. Bandres-Ciga S, Diez-Fairen M, Kim J, Singleton A. Genetics of Parkinson's disease: An introspection of its journey towards precision medicine. Neurobiol Dis. 2020;137:104782. doi:10.1016/j.nbd.2020.104782
2. Xiromerisiou G, Dardiotis E, Tsimourtou V et al. Genetic basis of Parkinson disease. Neurosurg Focus. 2010;28(1):E7. doi:10.3171/2009.10.focus09220
3. Savitt J. Diagnosis and treatment of Parkinson disease: molecules to medicine. Journal of Clinical Investigation. 2006;116(7):1744-1754.
4. Parkinson disease. Nature Reviews Disease Primers. 2017;3(1). doi:10.1038/nrdp.2017.14