PS36

MOLECULAR TRIGGER MECHANISMS FOR NEURODEGENERATION PROCESS VIA MITOPHAGY IN PARKINSON'S DISEASE.

Alexandra Sochirca[1], Ludmila Sidorenko[1], Svetlana Sidorenko[2]
[1]State University of Medicine and Pharmacy Nicolae Testimitanu, Chișinău, Republic of Moldova
[2]Rehabilitation Clinic Valens, Bad Ragaz, Switzerland

Introduction. Parkinson's disease (PD) is a chronically progressing neurodegenerative disorder, which is associated with the following clinical core features bradykinesia, tremor, and rigidity. It is considered the second most common central nervous system degenerative disorder, which occupies the second place after Alzheimer's disease. Its molecular mechanism lies in the process of mitophagy, which is involved in the development of a range of neurodegenerative diseases, and the mutation of PINK1 and Parkin genes. Goal: The evaluation of the molecular background of PD's pathogenesis. Methods and materials: A bibliographic study of scientific literature specialized in molecular mechanisms of pathogenesis of Parkinson's disease. The number of researched scientific articles has counted 15 essays on the subject, analyzed using PubMed, Google Scholar, Oxford Academic, and Medline, published from 2014 to 2024, filtered out by the keywords. Results: Scientific data analysis has shown that the fundamental process of Parkinson's disease lies in mitochondrial dysfunction, which is why the removal of the damaged organelles exerts significant influence over the disease. Parkin and PINK1 proteins create together the so-called Pink1-Parkin signaling pathway, which plays the core role in mitochondrial degradation because Pink1 encodes the PTEN-induced putative kinase with mitochondrial targeting sequence and Parkin is an E3 ubiquitin ligase. PINK1 forms a unique translocase complex on the outer membrane of the mitochondria, by which this organelle can regulate the level of PINK1 and Parkin. Thus, mutations of Parkin and PINK1 lead to the translocation of both of the proteins, which causes the incorrect regulation of mitochondrial autophagy and the accumulation of defective mitochondria as a consequence, starting the neurodegenerative process of Parkinson's disease. Conclusion: Thus, the main molecular mechanism for PD emergence is the accumulation of defective mitochondria, caused by the mutations of PINK1 and Parkin genes, the expression of which dysregulates the mitochondrial activity, leading to the accumulation of the defected mitochondria and disruption of the mitophagy.

References:

1. M.I. Shadrina, P.A. Slominsky, S.A. Limborska, Chapter 6 - Molecular Mechanisms of Pathogenesis of Parkinson's Disease, Editor(s): Kwang W. Jeon, International Review of Cell and Molecular Biology, Academic Press, Volume 281, 2010.
2. Sonia Gandhi, Nicholas W. Wood, Molecular pathogenesis of Parkinson's disease, *Human Molecular Genetics*, Volume 14, Issue 18, 15 September 2005, Pages 2749–2755.
3. Srinivasan E, Chandrasekhar G, Chandrasekar P, Anbarasu K, Vickram AS, Karunakaran R, Rajasekaran R, Srikumar PS. Alpha-Synuclein Aggregation in Parkinson's Disease. Front Med (Lausanne). 2021 Oct 18;8:736978.
DOI: 10.3389/fmed.2021.736978. PMID: 34733860; PMCID: PMC8558257.

4. Sidorenco A., Klenov N., Soloviev I., Bakurskiy S., Boian V., Sidorenko L., Vakhrushev A., Morari R., Savva Y., Sidorenko I. Base Elements for Artificial Neural Network: Structure Modeling, Production, Properties; Circuits, Systems and Signal Processing; 2023; vol. 17, p. 177-183, E-ISSN: 1998-4464, DOI: 10.46300/9106.2023.17.21.

Corresponding author: Sochirca Alexandra
State University of Medicine and Pharmacy Nicolae Testimitanu, Faculty of General Medicine, Bulevardul Ștefan cel Mare și Sfânt 165. MD-2004, Chișinău.
E-mail: sochirca.alecsandra@gmail.com
ORCID: 0009-0008-0237-5558