

Although neurodegenerative diseases including **Parkinson's disease (PD)** represent a major public health issue, because of enormous personal, family, and social costs, therapeutic options for treating neurodegenerative pathologies are still very disappointing. Parkinson's disease is characterized by motor dysfunction associated with a loss of dopaminergic neurons. In addition PD patients suffer from dementia due to severe cholinergic deficits all over the brain. The incidence of the disease ranges from 10–18 per 100 000 people/year but available therapies only treat symptoms of the disease. Therefore, the search for new plant compounds able to slow or protect the underlying neurodegenerative process is becoming a new frontier field of study, showing a high promise of neuroprotection. Our project fits well with the challenge and can contribute to the development of an early intervention - neuroprotective strategy.

It is suggested that some fruits, rich in ellagitannins, including pomegranate, may exert beneficial effects on the brain through metabolic derivatives. **The aim of this project is the search for mechanisms of potential neuroprotective action of a colonic microbiota metabolite of ellagitannins - urolithin A (UA)**, which achieves biologically significant concentrations in plasma and several tissues, after ingestion of pomegranate juice.

In order to search the mechanism of the neuroprotective action of UA we study its impact on the mitochondrial dysfunctions, involved in neurodegeneration associated with Parkinson's disease. Moreover, we assess the effects of UA on processes related to mitochondrial impairment including: oxidative stress, neuroinflammation, degeneration and death of neurons as well as clearance of damaged cellular organelles and macromolecules. For this purpose, an experiment on rats will be performed. We investigate the impact of UA on rotenone-induced neuronal degeneration processes in the brains of rats treated with urolithin A, following the confirmation of its distribution to the central nervous system from the blood. Finally, the effectiveness of neuroprotective activity is validated by microscopic examination of brain tissue and evaluation of activity of dopaminergic and cholinergic system as well as on the basis of motor coordination and cognitive functions in rats.

The obtained results will enable us to enhance our understanding about the distribution of the urolithin into the brain and cellular mechanisms of its neuroprotective activity. This new-found knowledge could be used in the future to develop synthetic derivatives of urolithin-based therapeutics for protection or treatment of neurodegenerative disorders including Parkinson's disease.