Identification of new sustainable biomolecules with neuroprotective effects: a multifaceted screening of the Mediterranean biodiversity

Giorgia Spandri[1], Alessia Lambiase[1,2], Hind Moukham[1], Elisa Toini[1,2], Fabrizio Grassi[1,2], Giovanni Zecca[1,2], Massimo Labra[1,2], Farida Tripodi[1,2] and Paola Coccetti[1,2]
g.spandri@campus.unimib.it
[1] University of Milano Bicocca, Department of Biotechnology and Biosciences, Milano, Italy
[2] National Biodiversity Future Center (NBFC), Palermo, Italy

Keywords: *S. cerevisiae*, human neuroblastoma cells, Parkinson's disease, bioactive molecules, vegetal biodiversity, age-related diseases, protein aggregation, α-synuclein

Abstract:

Aging is a multifactorial physiological condition mediated by different biological pathways, which influence lifespan and play an essential role in the pathogenesis and evolution of several diseases. The development of age-related diseases is also influenced by environmental factors and, according to the One Health concept, human health is closely connected with animal and environmental health. Indeed, following the bioprospecting research approach, the biodiversity well-being allows to identify a variety of compounds with bioactivities and beneficial effects for the prevention or treatment of human diseases. Among these, Parkinson's disease (PD) is a neurodegenerative disorder that affects 10 million people worldwide and is associated with α-synuclein misfolding and aggregation. Here, we screened 63 Italian plant extracts with the help of a phylogenetic analysis, which investigates plants relationship based on their bioactivities, and through a high-throughput screening using yeast cells expressing human α-synuclein (PD model). The combination of these two approaches led to the selection of four extracts from *S. pratensis, V. Thapsus, A. lusitanicum* and *G. flavum* plant species with strong anti-aging and antioxidant activities.
Then, extracts were tested for their capacity to prevent α-synuclein self-assembly, one of the most promising approaches for the treatment of Parkinson's disease. α -synuclein aggregation *in vitro*, detected by thioflavin T (ThT) fluorescence, was strongly decreased in the presence of the four selected extracts, suggesting that *S. pratensis, V. thapsus, A. lusitanicum and G. flavum*extracts could prevent α-synuclein aggregation and toxicity at least *in vitro*. Consistently, this antiaggregation properties were confirmed in yeast PD model and also in neuroblastoma cells where α-synuclein oligomers strongly decreased.
Further experiment are now underway to identify which compounds, isolated or in combination, are responsible for the observed effects.
In conclusion, our promising results can lead to develop new strategies for the prevention of protein aggregation in neurodegenerative diseases.
This project is part of the National Biodiversity Future Center – NBFC, funded under the National Recovery and Resilience Plan (https://www.nbfc.it/).