Leibniz Institute on Aging – Fritz Lipmann Institute

Press Release
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Prestigious ERC Consolidator Grant for Jena Researcher

The risk of dementia and other neurodegenerative diseases increases the older we get. One characteristic feature of aging, found also in neurodegeneration, is the loss of protein homeostasis (proteostasis), which leads to an imbalance in cellular processes and also disrupts the function of cell organelles. But how do changes in proteostasis lead to progressive dysfunction of organelles in neurons? Dr. Alessandro Ori from the Jena-based Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) is now investigating this important question in more detail and has been awarded the ERC Consolidator Grant for his research. The ComplexAge project will be funded with 2 million euros over a period of 5 years.

Jena. As people age, the incidence of dementia increases, as does the risk of neurodegenerative diseases. An important hallmark of aging and aging-related neurodegeneration is the loss of protein homeostasis (proteostasis) and the dysfunction of cell organelles. Protein homeostasis refers to those cellular processes that protect the proteome - the ensemble of all proteins in a living organism - by regulating the synthesis, folding, and degradation of proteins within the cell. Disruptions in proteostasis can not only shorten a person's lifespan, but also cause cells to age more rapidly and lead to the development of age-related diseases such as heart disease, diabetes, and neurodegeneration.

Processes in the aging brain

But how do disturbances to proteostasis lead to progressive dysfunction of organelles in neurons in the brain? Deciphering the relationship between the aging-related impairment of proteostasis and the maintenance of protein complexes and organelles in neurons is essential to better understand brain aging and to identify the molecular mechanisms responsible for neurodegeneration. To do this, it is necessary to quantify and comprehensively characterize the proteins in the cells and organelles. This is the only way to determine which chain of molecular processes triggers the loss of proteostasis and how this is mechanistically linked to the impairment of higher cellular functions.

"I hypothesize that defects in protein degradation that occur during aging negatively affect the fitness of neurons, and that protein complexes and organelles also exhibit different susceptibility to the age-related loss of function of protein degradation pathways," reports Dr. Alessandro Ori, research group leader at the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in Jena, Germany. Dr. Ori is an expert in the field of mass spectrometry-based proteomics. In his research, he integrates high-sensitivity mass spectrometry with other omics technologies and biochemical approaches.

From an idea to an innovative research approach

He has now been awarded an ERC Consolidator Grant for his new, innovative research approach. The approved "ComplexAge" project (on the vulnerability of protein complexes and

organelles to protein degradation impairment in aging neurons) will be funded with 2 million euros over the next 5 years.

“To determine whether and which components of the proteome are more susceptible to defects in protein degradation, I plan to develop vertebrate models that allow to selectively inhibit specific protein degradation pathways in vivo in the organism and specifically monitor the effects on the proteome of neurons using quantitative omics approaches,” adds Dr. Ori. This work is being conducted in fish and mouse models as well as using special neurons derived from induced-pluripotent stem cells. Through the systematic quantification of protein localization and assembly status, the researchers aim to derive information about the effects of aging and aging-related impairment of protein degradation on the organization of the proteome - information that could not be determined solely by measuring protein abundance. Furthermore, the identification of assembly intermediates and mislocalized proteins could provide insight into the specific processes that are disrupted in aged neurons.

“The results of my future study may reveal new targets for therapeutic interventions aimed at maintaining neuronal fitness and delaying the onset of dementia in the elderly.”

About the researcher

Alessandro Ori completed his master’s degree in biotechnology at the Università di Bologna in Italy in 2006. During his studies, he completed a research internship at Université Paris Diderot. After receiving his PhD in 2010 from the University of Liverpool, UK, he worked as a postdoctoral researcher in the Structural and Computational Biology Unit research group at the European Molecular Biology Laboratory (EMBL) in Heidelberg, supported by Alexander von Humboldt and Marie Curie fellowships. Since September 2015, he has been a junior group leader at the Leibniz Institute on Aging - Fritz Lipmann Institute (FLI) in Jena. His research group “Aging of Protein Complexes” investigates how aging and environmental factors affect our organs at the molecular level. The group’s goal is to identify, as unbiasedly and objectively as possible, the changes in the proteome that lead to organ deterioration and affect a healthy lifespan.

In 2019, Dr. Ori was awarded the “Life Sciences and Physics” prize of the Beutenberg Campus Jena e.V. for his research results as the best young scientist.

ERC Consolidator Grant

The ERC Consolidator Grant is one of the most highly endowed funding programs of the European Union. With this grant, outstanding scientists receive funding to support them in the further expansion of their own research area and to enable them to carry out visionary basic research. The ERC Consolidator Grant comprises a grant of two million euros over a period of five years.

“I am very proud of this grant because it will dramatically accelerate our efforts to understand the causes of brain aging,” reports Dr. Ori. “I thank my lab members for their hard work, dedication, and creativity, and the FLI for the collaborative and supportive environment I am provided here.”

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Image

FLI researcher Dr. Alessandro Ori receives the ERC Consolidator Grant for his project ComplexAge, which is investigating the impact of protein degradation impairment on aging, especially in neurons. (Photo: FLI / Kerstin Wagner)

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Background information

The **Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)** – upon its inauguration in 2004 – was the first German research organization dedicated to research on the process of aging. More than 350 employees from around 40 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit www.leibniz-fli.de.

The **Leibniz Association** connects 97 independent research institutions that range in focus from natural, engineering and environmental sciences to economics, spatial and social sciences and the humanities. Leibniz Institutes address issues of social, economic and ecological relevance. They conduct basic and applied research, including in the interdisciplinary Leibniz Research Alliances, maintain scientific infrastructure, and provide research-based services. The Leibniz Association identifies focus areas for knowledge transfer, particularly with the Leibniz research museums. It advises and informs policymakers, science, industry and the general public. Leibniz institutions collaborate intensively with universities – including in the form of Leibniz ScienceCampi – as well as with industry and other partners at home and abroad. They are subject to a transparent, independent evaluation procedure. Because of their importance for the country as a whole, the Leibniz Association Institutes are funded jointly by Germany's central and regional governments. The Leibniz Institutes employ around 20,500 people, including 11,500 researchers. The financial volume amounts to 2 billion euros. For more information: www.leibniz-gemeinschaft.de/en/.