Visualizing cell maintenance: Chemical tools to investigate the microenvironments of misfolded proteins

https://www.neurodegenerationresearch.eu/survey/visualizing-cell-maintenance-chemical-tools-to-investigate-the-microenvironments-of-misfolded-proteins/

Principal Investigators
Institution
Contact information of lead PI
Country

European Commission

Title of project or programme

Visualizing cell maintenance: Chemical tools to investigate the microenvironments of misfolded proteins

Source of funding information

European Commission FP7-Seventh Framework Programme

Total sum awarded (Euro)

€ 100,000

Start date of award

01/07/2014

Total duration of award in years

4

Keywords

Research Abstract

The capacity of the cell to maintain protein quality and function diminishes upon aging and disease. Genetic mutations may result in protein malfunction or structural defects due to an alternation of an essential amino acid. The cell has evolved many mechanisms to handle misfolded proteins; some proteins are refolded by molecular chaperones while others are targeted for degradation by the ubiquitin proteasome system and yet others are sequestered in deposits at a specific cellular location. How cells make decisions on a specific protein destination is only hardly understood and progress in this field is slow due to the lack of useful chemical and biological tools.
In this proposal I will address this question by using a methodology that allows visualization of the cellular response towards an unfolded protein of which the physical properties are well

known. The protein is genetically incorporated and correct folding is initially maintained by a small molecule ligand. The proteins are designed to vary in hydrophobicity and stability of the core structure. Unfolding of the protein is induced by depletion of the ligand after which the cellular response can be monitored. With the help of molecular tools it is possible to label interacting proteins that recognize the pool of unfolded proteins at specific stages of the quality control pathway. In addition, current mass spectrometry technologies allow identification of posttranslational modifications which are important for defining the final destination of the unfolded protein. The technology is further elaborated on protein aggregates that play a role in many neurodegenerative diseases.
Information that arises from this study gives novel insights in the cellular dynamics and recognition of misfolded proteins. Understanding these processes will help in the development of novel diagnostics and therapeutics for diseases that are related to misfolded proteins or a defect in the cellular protein quality control machinery.

Further information available at:

Types:
Investments < €500k

Member States:
European Commission

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A