Protein structure and function by hydrogen exchange mass spectrometry analysis

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Contact information of lead PI
Country

USA

Title of project or programme

Protein structure and function by hydrogen exchange mass spectrometry analysis

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,184,029.36

Start date of award

01/12/1983

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

protein structure function, Hydrogen, Mass Spectrum Analysis, Lipid Binding, apolipoprotein E-3

Research Abstract

DESCRIPTION (provided by applicant): The major challenge for the protein chemist is to explain how proteins implement their limited repertoire of structural and biophysical properties to

produce their myriad functions. Unlike any other laboratory method, hydrogen exchange (HX) behavior encodes detailed quantitative information, at amino acid resolution, on the biophysical factors that produce protein function — structure, structure change, interactions, dynamics, and energetics. Previous versions of this NIH grant have been instrumental in developing the HX field by using a variety of NMR methods, but routine NMR analysis is limited to small highly soluble proteins in substantial quantity and high concentration. A developing hydrogen exchange – mass spectrometry technology (HX MS) promises to extend this proven capability to the larger and more complex protein systems that make biology work while requiring only picomoles of protein at sub-micromolar concentrations. This application proposes to perfect the HX MS technology and apply it in studies of important protein systems. They are: 1) apolipoproteins E3 and E4, when lipid- free and lipid-bound, important for cardiovascular and Alzheimer's diseases; 2) the definition of autoimmune antibody epitopes in acquired TTP disease, relevant to antibody therapeutics and to protein interactions more generally; 3) the Hsp104 protein disaggregase, relevant to the control of protein aggregation and amyloid processing. The full development of HX MS and its demonstration with difficult but centrally important protein systems will provide a uniquely powerful methodology that is widely applicable to the study of protein structure – function problems.

Lay Summary

PUBLIC HEALTH RELEVANCE: This proposal is directed at the development and use of a uniquely powerful technology, hydrogen exchange measured by mass spectrometry, for studying the proteins that make biology work. The technology will be used to study three carefully chosen protein systems that are key players in biological function and dysfunction. These are lipid metabolism important in cardiovascular and Alzheimer's disease, antibody interactions important in autoimmunity diseases, and protein aggregation important in amyloid formation and the aging process.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

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