Molecular Imaging of Biomaterials – Single Cells

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Country

USA

Title of project or programme

Molecular Imaging of Biomaterials - Single Cells

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,578,681.65

Start date of award

30/09/1992

Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Spectrometry, Mass, Secondary Ion, molecular imaging, Biocompatible Materials, Ions, Liposomes

Research Abstract

DESCRIPTION (provided by applicant): This research is aimed to push the boundaries of imaging mass spectrometry with unique biological applications directed toward the chemical

characterization of single biological cells. A special emphasis is placed upon probing the lipid distributions and the role of small molecule neurotransmitters embedded in neurotransmitter vesicles primed for exocytosis and brain lipids in Alzheimer’s disease. Model systems include liposome cell mimics, mast cells, PC12 cells and brain tissue where membrane structure is changing. The central approach is to utilize an advanced bio-analytical mass spectrometry-based protocol to acquire two and three dimensional molecule-specific image information at the nano-scale level. Transformational mass spectrometry instrumentation for secondary ion mass spectrometry (SIMS) is proposed to complete this mission. Special emphasis is placed upon implementing a novel gas cluster ion beam (GCIB), consisting of an Ar4000+ projectile, which has been shown to desorb molecules without breaking bonds and without chemical damage buildup on the sample. There are four specific aims for this proposal. First, we propose to combine 3- dimensional imaging with a tightly focused C60+ ion source and a GCIB source especially tuned by chemistry to dramatically enhance spatial resolution and ionization efficiency in imaging. This will increase sensitivity and therefore spatial resolution as we push t the limits obtained by dynamic SIMS. Second, the effectiveness of these protocols will be verified using well-characterized liposome particles as stand-ins for biological cells. Third, developments in the first two aims will be implemented to image the substructure of vesicles in single cells in order to gain a better understanding of what regulates chemical communication via exocytosis. These studies will provide fundamentally important information about how neurotransmitter release is regulated for plasticity and pharmacology. Fourth, metabolic labeling with stable isotope-encoded lipid and protein species will be used to elucidate spatial and temporal changes in the molecular architecture of single nerve cells. We will then use this imaging methodology to study protein aggregation in single nerve cells and a model for Alzheimer’s disease. The overarching objective is to establish the unique imaging strategy proposed here as a valuable new tool for use by the larger biological community.

Lay Summary

PUBLIC HEALTH RELEVANCE: We propose to make significant advances in imaging mass spectrometry in three dimensions which are needed to test dynamical theories of biological function at the single cell level. Special emphasis is placed upon probing the lipid distributions and the role of small molecule neurotransmitters embedded in fused vesicles which might play a role in influencing, for example, Alzheimer’s disease states. An overarching objective is to provide a unique capability to the larger biological and public health research community.

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

Database Tags:
N/A