Optical imaging of small bio-molecules in living cells and tissues by nonlinear Raman microscopy coupled with vibrational tags

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Contact information of lead PI
Country

USA

Title of project or programme

Optical imaging of small bio-molecules in living cells and tissues by nonlinear Raman microscopy coupled with vibrational tags

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,178,303.67

Start date of award

01/06/2015

Total duration of award in years

3

The project/programme is most relevant to:

Huntington's disease

Keywords

Alkynes, Huntington gene, Deuterium, optic imaging, Isotopes

Research Abstract

? DESCRIPTION (provided by applicant): The goal of the project is to develop a general optical imaging technology for studying vital small bio-molecules (e.g., amino acids, nucleic acids, fatty acids, glucose, neurotransmitters and drugs) inside live cells and tissues, an important but otherwise intractable goal. To do so, we propose to couple the emerging stimulated Raman scattering (SRS) microscopy, which is capable of producing concentration maps of chemical bonds in biological samples, with three distinct classes of small vibrational tags with characteristic Raman transitions, including alkyne moieties (i.e., C¿C triple bond), deuterium isotope and 13C isotope. While alkyne tags are generally applicable to any small biomolecules, deuterium isotope and 13C isotope will be particularly useful for labeling amino acids. When spectrally targeting these vibrational tags labeled to small bio-molecules, SRS microscopy is ideally suited for probing functional metabolism of living systems at microscopic level, as proved in our recent publications. We have laid out systematic plans as to how to crystallize this concept into a mature and general technical platform. Accompanied by the technical development, several biomedical applications are being proposed (some with exciting preliminary data) including imaging neurogenesis in living brain tissues by monitoring the metabolic incorporation of alkyne-tagged deoxyribonucleoside into newly born neurons, multicolor chemical imaging by developing a color palette of metabolite library, monitoring protein synthesis in nervous systems with deuterium-labeled amino acids, and probing intracellular protein degradation during Huntingtin aggregation with 13C-labeled phenylalanine. If successfully implemented, we will establish a new imaging platform of bioorthogonal nonlinear Raman microscopy that could allow us to interrogate a broad spectrum of small bio-molecules with superb sensitivity, specificity, biocompatibility and multiplex ability. The resulting bioorthogonal nonlinear Raman microscopy might do for small bio-molecules what fluorescence imaging of organic dyes and fluorescent proteins has done for larger molecular species, bringing small bio-molecules under the illumination of modern light microscopy.

Lay Summary

PUBLIC HEALTH RELEVANCE: The unprecedented ability to visualize protein synthesis and protein degradation inside health and disease brain tissues should be able to offer important insights regarding the misregulation of protein metabolism in neurodegenerative diseases such as Alzheimer’s disease, Parkinson disease and Huntington disease. In addition, tumors are known to exhibit drastically aberrant metabolic activities compared to healthy tissues. Thus, our unique technique to image small metabolites could also be adopted to probe the microenvironment of abnormal tumor metabolism.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Huntington's disease

Years:
2016

Database Categories:

N/A

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