Algorithms for Glyco-Proteoform Detection

https://neurodegenerationresearch.eu/survey/algorithms-for-glyco-proteoform-detection/

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Country

USA

Title of project or programme

Algorithms for Glyco-Proteoform Detection

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,671,588.07

Start date of award

01/04/2016

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Cerebral meninges, Cerebrospinal Fluid, abeta deposition, Mass Spectrum Analysis, Algorithms

Research Abstract

? DESCRIPTION (provided by applicant): Our proposal seeks to create and apply new top-down glyco-proteomics procedures that permit unbiased discovery of alterations in protein glycosylation. This includes the creation of algorithms that assemble glycoproteoform networks from multi-dimensional mass spectrometry (MS) datasets, the application of cross-correlation analysis to link glycoproteoform networks with MS spectral information and the creation of an

evidence feedback strategy to permit statistical scoring with unique glycoproteoform informatics tools. An innovative aspect of the proposed technologies is that they are intended to permit evaluation of glycoproteins that present with glycosylation at more than one amino acid residue, a well-recognized bottleneck in the top-down field. Our aims also include the application of the top-down algorithms to enable unsupervised “”discovery”” of glycoprotein biomarkers in biofluids. We will use these new tools to monitor the cerebrospinal fluid (CSF) of brain insulin resistance (BIR) rodent models with the intent to discover biomarkers that correlate with development of pathologies or clinical symptoms that are associated with Alzheimer’s disease (AD) spectrum disorders. In particular, we seek to establish rodent models to determine if brain metabolic dysfunction early in life contributes to amyloid-beta (A?) peptide deposition in cerebral vasculature and meninges (MG), a common occurrence in dementia patients. A? deposits occur sporadically in the elderly but have a high prevalence in AD and Down syndrome patients. Such deposits are difficult to diagnose without sampling of the brain, and are often not caught until after the occurrence of multiple cerebral hemorrhages and onset of cognitive impairment. Here, we will determine if BIR induces A? deposition in cerebral vasculature and meninges of the rodent models and correlate changes to novel proteins in CSF. These experiments are expected to provide a list of candidate markers for evaluation in CSF human subjects. If our project aims are successful, we will not only have developed innovative new basic science tools for glycoscientists, but also, established innovative clinical proteomics procedures for the discovery and development of glycoprotein-based biomarkers.

Lay Summary
PUBLIC HEALTH RELEVANCE: Top-down mass spectrometry pays homage to the chemistry of biology. Chemical reactions in eukaryotes are programmed in both time and space; however, external stimuli (environment and disease) continually highjack these processes. The goal of this research is to develop next generation proteomics tools that rapidly quantify hard to predict chemistry on translated genes in the secretory pathway in the context of normal eukaryote physiology as well as pathobiology associated with Alzheimer’s disease spectrum disorders.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

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N/A

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