NOVEL BIFUNCTIONAL CHEMICAL AGENTS AS THERANOSTIC TOOLS FOR AMYLOID DISEASES

https://neurodegenerationresearch.eu/survey/novel-bifunctional-chemical-agents-as-theranostic-tools-for-amyloid-diseases/

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Country

USA

Title of project or programme

NOVEL BIFUNCTIONAL CHEMICAL AGENTS AS THERANOSTIC TOOLS FOR AMYLOID DISEASES

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,329,128.44

Start date of award

01/08/2015

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

theranostics, Chemical Agents, Amyloidosis, Amyloid, Metals

Research Abstract

?DESCRIPTION (provided by applicant): The aggregation of peptides and proteins plays a key role in many devastating neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and the prion diseases. Although the insoluble amyloid fibrils have long been viewed as the hallmark of these diseases, the soluble oligomers formed by various amyloidogenic peptides have begun to be recognized as the more relevant neurotoxic species involved in these diseases. Among these amyloid disorders, Alzheimer's disease (AD) is the most common neurodegenerative disease. To date there is no treatment for AD and its diagnosis with high accuracy requires a detailed post-mortem examination of the brain. Thus, new insights provided by a detailed investigation at the molecular level of the role o different factors in AD may have a large health-related impact and may allow for the development of novel therapeutics and diagnostic tools for AD. The brains of AD patients are characterized by the deposition of amyloid plaques that contain the amyloid ß (Aß) peptide. In addition, it is known that metal ions can interact with the Aß peptide and dramatically affect its aggregation properties. The long-term goal of this research project is to develop novel therapeutic and diagnostic agents for various amyloid disorders, including Alzheimer's disease. The hypothesis is that transition metal ions, especially copper, increase the toxicity of Aß aggregates by stabilizing the soluble Aß oligomers. The rationale for the proposed research is that the development of bifunctional metal-binding and metal-containing compounds with high affinity for different amyloid aggregates – including soluble Aß oligomers, will result in a novel approach for the development of theranostic agents for AD and possibly other amyloid disorders. The first specific aim is to develop novel bifunctional metal-binding compounds that modulate the metal-mediated stabilization and neurotoxicity of soluble Aß oligomers. Based on our preliminary data, the working hypothesis here is that transition metal ions stabilize the soluble Aß oligomers, with direct implications into how metal ions enhance the neurotoxicity of Aß oligomers. The second specific aim is to develop 64Cu-radiolabeled compounds for positron emission tomography (PET) imaging of amyloid aggregates, including soluble Aß oligomers, as an early diagnostic tool for AD and other amyloid disorders.

Lay Summary

PUBLIC HEALTH RELEVANCE: The proposed research is relevant to public health because it will lead to a better understanding of the molecular mechanisms of aggregation of peptides and proteins related to many devastating neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and the prion diseases. The work proposed herein will generate novel therapeutic agents for controlling the role of transition metal ions in the neurotoxicity of solubl Aß oligomers in Alzheimer's disease, as well as imaging agents for early diagnosis of Alzheimer's disease. This is relevant to the NIH's mission because the proposed bifunctional metal-binding and metal-containing compounds that exhibit high affinity for various amyloid aggregates – including soluble Aß oligomers, hold promise as novel therapeutic agents and diagnostic tools for Alzheimer's disease and other amyloid disorders.

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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