Preclinical Diagnostic Imaging of Amyloid

https://neurodegenerationresearch.eu/survey/preclinical-diagnostic-imaging-of-amyloid/

Principal Investigators

WALL, JONATHAN S

Institution

UNIVERSITY OF TENNESSEE KNOXVILLE

Contact information of lead PI
Country

USA

Title of project or programme

Preclinical Diagnostic Imaging of Amyloid

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,450,282.57

Start date of award

01/09/2007

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Diagnostic Imaging, Amyloid, Amyloidosis, Visceral, pre-clinical

Research Abstract

DESCRIPTION (provided by applicant): Amyloidosis is a devastating pathology associated with a growing number of diseases, including two of the most socio-economically impacting conditions of our time, Alzheimer’s disease (Abeta amyloid) and type 2 diabetes (IAPP amyloid). Furthermore, cardiac amyloidosis in people over the age of 70 and in African American men is now recognized as a significant cause of morbidity. For these patients, there are few treatment

options and no quantitative clinical imaging techniques for whole body detection of disease. Therefore, our long term goals are to develop amyloid-reactive peptides for the clinical detection and therapy of visceral amyloidosis in patients with these devastating conditions. During the first grant period it was shown that certain heparin-reactive small peptides specifically reacted with amyloid deposits but not with healthy tissues. This was demonstrated principally by using radioactively labeled peptides as imaging agents in mice with visceral AA amyloid as well as in mice with Abeta amyloid in the brain vasculature. Binding of peptides with amyloid was evidenced in SPECT images and micro-autoradiographs and was quantified by tissue biodistribution measurements. Recent data has now indicated that these peptides bind not only with highly-charged glycosaminoglycans that are present in all amyloid deposits but also the protein fibrils themselves, regardless of the precursor from which they are formed. We will leverage these novel findings to develop innovative molecular imaging agents and peptide therapeutics. The aims of this 5 year renewal proposal are to: Aim 1: Characterize and develop amyloid-reactive peptides, based on the structure of our lead peptide, p5, by generating variants for the quantitative detection of visceral amyloidosis. Aim 2: Evaluate the therapeutic potential o amyloid-targeting peptides in vitro and in vivo for preventing and removing visceral AA, IAPP, and ApoA2c as well as Abeta-derived amyloid deposits. Aim 3: Examine the fundamental processes underlying the binding of amyloid-reactive peptides with Abeta (1-40) and IAPP synthetic fibrils, as well as AA and ApoA2c fibril extracts. This will enhance our rational design and optimization of amyloid-targeting and therapeutic peptides. To achieve these goals we will combine advanced small animal SPECT/CT imaging, micro- autoradiography and biodistribution measurements for testing new peptides in mice with amyloidosis. Additionally, we will use a battery of in vitro assays that we have established to measure the therapeutic potential of the peptides and investigate the fundamental processes governing the interactions of these reagents with amyloid. These studies will lead to improved and effective molecular imaging radiotracers and companion therapeutics that can be translated and evaluated clinically in patients with these devastating diseases.

Lay Summary
PUBLIC HEALTH RELEVANCE: Peripheral amyloid is a devastating pathology associated with aging and inflammation as well as diseases such as multiple myeloma and type 2 diabetes. PET imaging of amyloid in patients could assist with diagnosis, prognostication, treatment planning, and monitoring response to therapy; however, this capability is not available in the US. We are developing a novel panel of small peptides that have been shown to be effective tracers for PET imaging of amyloid in mice and for detection of amyloid in tissues from patients; additionally, findings indicate that these peptides may also have therapeutic benefit for patients with these devastating 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

Database Tags:
N/A