APP as a common denominator for Alzheimers disease and osteoporosis

https://neurodegenerationresearch.eu/survey/app-as-a-common-denominator-for-alzheimers-disease-and-osteoporosis/

Principal Investigators

XIONG, WEN-CHENG

Institution

GEORGIA REGENTS UNIVERSITY

Contact information of lead PI
Country

USA

Title of project or programme

APP as a common denominator for Alzheimers disease and osteoporosis

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,743,119.27

Start date of award

15/08/2016

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Musculoskeletal System... Neurodegenerative... Neurosciences... Osteoporosis... Skeletal System... Women's Health for IC Use

Research Abstract

? DESCRIPTION (provided by applicant): Osteoporosis, a common skeletal degenerative disorder, is characterized by decrease of bone- mass and micro-architectural deterioration of bone tissue. Alzheimer’s disease (AD) is a most common neurodegenerative disorder with cognitive dementia. Intriguingly, AD patients frequently have lower bone mineral density and higher rate of hip fracture, compared with the same age normal population. Several newly identified AD risk genes/loci encode proteins critical for osteoclastic activation and/or bone-mass homeostasis. Increasing evidence from clinical and genetic studies thus supports a degree of co-morbidity of both disorders. However, very few studies are available to address their relationship. The goal of this proposal is to determine if and how the Swedish mutant amyloid precursor protein (APPswe) acts as a common denominator for AD and osteoporosis/osteopenia. APP is a ubiquitously expressed transmembrane protein. Its cleavage product, A?, is believed to be a major culprit for both early- and late-onset AD. We thus speculate that APP/A? may contribute to the AD-associated skeletal deficits. By use of Tg2576 mice, a well-characterized AD animal model that ubiquitously expresses APPswe under the control of prion promoter, we observed age-dependent osteoporotic bone deficits in this animal model. By use of newly generated conditional/cell type specific APPswe transgenic mouse models, we found that APPswe plays important roles in regulating osteoblast (OB)-mediated bone formation and osteoclast (OC)-mediated bone resorption. However, the underlying mechanisms are unclear. In this proposal, we will address this issue. It is our hope that the results from this research may not only provide a potential link between AD and osteoporosis/osteopenia, but also identify unrecognized functions of APP and reveal new pathological mechanisms underlying both disorders.

Lay Summary

PUBLIC HEALTH RELEVANCE: The goal of this proposal is to investigate mechanisms of APPswe in regulating osteoblastic bone formation and osteoclastic bone resorption.

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