

# Mechanism of Gene Environment Interactions in Alzheimers Disease

<https://www.neurodegenerationresearch.eu/survey/mechanism-of-gene-environment-interactions-in-alzheimers-disease/>

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### Country

USA

## Title of project or programme

Mechanism of Gene Environment Interactions in Alzheimers Disease

## Source of funding information

NIH (NIA)

## Total sum awarded (Euro)

€ 2,267,266.97

## Start date of award

01/07/2016

## Total duration of award in years

1

## The project/programme is most relevant to:

Alzheimer's disease & other dementias

## Keywords

Apolipoprotein E, gene environment interaction, Amyloid beta-Protein Precursor, abeta accumulation, amyloid pathology

## Research Abstract

Using well-characterized clinical cohorts, we recently reported that serum levels of DDE, the

metabolite of the organochlorine pesticide DDT is significantly higher in the serum of Alzheimer Disease (AD) cases and is associated with increased risk of AD diagnosis. Further, individuals harboring a polymorphism in APOE and having high serum levels of DDE performed worse on a cognitive task than either those with just the polymorphism or high DDE levels. Finally, we identified that DDT and DDE increase levels of amyloid precursor protein (APP), suggesting a possible mechanism by which DDT exposure may contribute to AD. Based on our initial findings, the goals of this project include: (1) identifying the mechanism by which DDT exposure increases APP levels; (2) determining the effect of APOE genetic status on the effects of DDT on A $\beta$  accumulation and oligomerization; and (3) assessing the effects of DDT exposure on AD pathology and behavioral dysfunction in transgenic mouse models humanized for APOE polymorphisms. We will achieve these goals using a combination of cutting edge techniques including epigenetic analysis, patient-specific stem cells, and transgenic mice harboring human polymorphisms.

### **Lay Summary**

This project will provide a comprehensive analysis of the mechanism by which elevated serum DDE levels are associated with AD diagnosis, cognitive function and AD pathology. Further, valuable information on the role of APOE genotype in this relationship will be determined. In turn, this may aid in identifying potential susceptible populations.

### **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