

# Functions of human and mouse Trem2 in vivo

<https://www.neurodegenerationresearch.eu/survey/functions-of-human-and-mouse-trem2-in-vivo/>

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### Country

USA

## Title of project or programme

Functions of human and mouse Trem2 in vivo

## Source of funding information

NIH (NIA)

## Total sum awarded (Euro)

394839.4495

## Start date of award

01/04/2016

## Total duration of award in years

1

## Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Genetics... Neurodegenerative... Neurosciences

## Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer disease (AD) is the most common cause of dementia and is characterized by extracellular plaques formed by the deposition of amyloid-? (A?) peptide and intracellular tangles comprised of hyperphosphorylated forms of the tau protein. Gliosis and inflammation are associated with areas of heavy pathology and likely play a key role in shaping disease progression. Microglia, the immune cells of the central nervous system (CNS), are increasingly recognized for their critical roles in the pathogenesis of AD and

other neurodegenerative diseases such as frontotemporal dementia (FTD) and Parkinson disease (PD). The strongest genetic risk factor for both AD and CAA is  $\epsilon 4$  allele of the apolipoprotein E (APOE) gene, but recently the TREM2 locus was identified as a risk factor for AD with the most significantly associated coding variant as rs75932628 (encoding R47H) with an odds ratio rivaling that of APOE. Because human and mouse Trem2 differ by ~25% at the amino acid level, we aim to create novel knock-in mouse lines that express normal human TREM2 or the TREM2-R47H variant in place of the endogenous mouse Trem2 locus. Characterizing these novel lines along with our existing Trem2<sup>-/-</sup> mouse line either at baseline or upon immune stimulation will allow us to fundamentally answer whether the TREM2-R47H variant functions as a loss of function or gain of function. Additionally, we have recently found that TREM2 can serve as a receptor for lipoproteins. These mice will be critical in developing new therapeutics that target TREM2 in the context of neurodegeneration and in testing the functional effects of lipoprotein binding to normal vs R47H variant of TREM2.

**Further information available at:**

**Types:**

Investments < €500k

**Member States:**

United States of America

**Diseases:**

N/A

**Years:**

2016

**Database Categories:**

N/A

**Database Tags:**

N/A