

# Mechanisms of neurotoxicity of amyloid aggregates.

<https://www.neurodegenerationresearch.eu/survey/mechanisms-of-neurotoxicity-of-amyloid-aggregates/>

## Principal Investigators

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### Country

United Kingdom

## Title of project or programme

Mechanisms of neurotoxicity of amyloid aggregates.

## Source of funding information

The Wellcome Trust

## Total sum awarded (Euro)

€ 8,345,885

## Start date of award

01/03/2010

## Total duration of award in years

6.0

## The project/programme is most relevant to:

Alzheimer's disease & other dementias

## Keywords

### Research Abstract

Some of the most important but unresolved questions about the pathobiology of Alzheimer's disease (AD) are: What are the neurotoxic species of Abeta? How do they injure neurons? How do they induce aggregation of intracellular proteins like tau,  $\alpha$ -synuclein, and TDP-43? Why are the normal mechanisms for removal of these intracellular aggregation-prone proteins overwhelmed in AD? Answers to such questions will provide both insight into the early stages of

disease pathogenesis, and starting points for the discovery of novel diagnostics and therapeutics. We hypothesize that the neurotoxicity of Abeta arises from heterogeneous mixtures of soluble Abeta aggregates, which may have differing toxicities, but which activate complex, interlinked downstream pathways. To deconvolute this complexity we will apply an integrated suite of tools from physics, chemistry, engineering, systems biology and neurobiology to: 1) Investigate Abeta aggregation and its consequences in living cells and animals; 2) Identify its molecular targets; 3) Discover the downstream metabolic and signalling pathways activated by Abeta; 4) Identify the molecular mechanisms by which Abeta induces misprocessing of tau; and 5) Identify the regulators of autophagy (which is an important physiological mechanisms for removal of tau) and determine why autophagy is down-regulated in AD).

### **Lay Summary**

**Further information available at:**

#### **Types:**

Investments > €500k

#### **Member States:**

United Kingdom

#### **Diseases:**

Alzheimer's disease & other dementias

#### **Years:**

2016

#### **Database Categories:**

N/A

#### **Database Tags:**

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