

# Understanding death-receptor signaling and physiology in the nervous system: A roadmap for the development of new treatments to neurodegenerative diseases and neurotrauma

<https://neurodegenerationresearch.eu/survey/understanding-death-receptor-signaling-and-physiology-in-the-nervous-system-a-roadmap-for-the-development-of-new-treatments-to-neurodegenerative-diseases-and-neurotrauma/>

## Principal Investigators

### Institution

### Contact information of lead PI

### Country

European Commission

## Title of project or programme

Understanding death-receptor signaling and physiology in the nervous system: A roadmap for the development of new treatments to neurodegenerative diseases and neurotrauma

## Source of funding information

European Commission FP7-Seventh Framework Programme

## Total sum awarded (Euro)

€ 2,500,000

## Start date of award

01/06/2014

## Total duration of award in years

5.0

## The project/programme is most relevant to:

Neurodegenerative disease in general

## Keywords

### Research Abstract

The aim of this proposal is to elucidate the molecular mechanisms and physiological relevance of death-receptor signaling in the nervous system and to harness this knowledge for the development of novel treatments to neurodegenerative diseases and neurotrauma. The main focus is on the p75 neurotrophin receptor (p75NTR), which is predominantly expressed in the

developing nervous system and is highly induced upon different types of adult neural injury. Additional studies on other death receptors, such as DR6, are also described. p75NTR signaling can induce neuronal death, reduce axonal growth and decrease synaptic function, hence there is a good rationale for inhibiting p75NTR in neural injury and neurodegeneration. Recent discoveries from my laboratory have clarified the mechanism of p75NTR activation and provided new insights into the underlying logic of p75NTR signaling, paving the way for a genetic dissection of p75NTR function and physiology. These discoveries have open new avenues to elucidate the molecular mechanisms underlying ligand-specific responses and downstream signal propagation by death-receptors, unravel the physiological relevance of death-receptor signaling pathways in health and disease, and develop new strategies to block death-receptor activity in neural injury and neurodegeneration.

To drive progress in this research area it is proposed to: i) Elucidate the mechanisms by which p75NTR and other death receptors become activated by different ligands and elicit distinct, ligand-specific cellular responses; ii) Elucidate the mechanisms underlying the specificity and diversity of p75NTR signaling and decipher their underlying logic; iii) Elucidate the physiological significance of distinct p75NTR signaling pathways through genetic dissection in knock-in mice; iv) Harness this knowledge to identify and characterize novel p75NTR inhibitors.

This is research of a high-gain/high-risk nature, posed to open unique opportunities in research & development.

### **Lay Summary**

**Further information available at:**

#### **Types:**

Investments > €500k

#### **Member States:**

European Commission

#### **Diseases:**

Neurodegenerative disease in general

#### **Years:**

2016

#### **Database Categories:**

N/A

#### **Database Tags:**

N/A