# Plasticity and formation of lasting memories in health and disease. Genetic modeling of key regulators in adult and aging mammals and in neurodegenerative disease

https://neurodegenerationresearch.eu/survey/plasticity-and-formation-of-lasting-memories-in-health-and-disease-genetic-modeling-of-key-regulators-in-adult-and-aging-mammals-and-in-neurodegenerative-disease/

**Principal Investigators**
**Institution**
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**Country**

European Commission

**Title of project or programme**

Plasticity and formation of lasting memories in health and disease. Genetic modeling of key regulators in adult and aging mammals and in neurodegenerative disease

**Source of funding information**

European Commission FP7-Seventh Framework Programme

**Total sum awarded (Euro)**

€ 2,330,974

**Start date of award**

01/03/2013

**Total duration of award in years**

5.0

**The project/programme is most relevant to:**

Neurodegenerative disease in general

**Keywords**
**Research Abstract**
When an adult mammal acquires new skills and new knowledge, the degree to which transition will occur from temporary to permanent memories of such events is governed by factors such as emotional weight and importance of the experiences for survival. To execute the necessary structural synaptic reorganisations needed to permanently embed novel memories in the brain, a complex and precisely orchestrated molecular machinery is activated. We have found that

rapid down-regulation of Nogo receptor 1 (NgR1) is one key element needed to allow permanent memories to form. Thus, our MemoFlex mice, with inducible overexpression of NgR1 in forebrain neurons, are severely impaired with respect to the ability to form lasting memories. When transgenic NgR1 is turned off in these mice, the ability to form lasting memories is restored. Several other genes are also involved in the process of consolidation of memories, including prompt activity-driven upregulation of BDNF. Very recently, we have discovered that Lotus, a newly identified negative regulator of NgR1, is also upregulated by activity, thus providing additional efficacy to the process of causing nerve endings to become temporarily insensitive to Nogo when plasticity is needed. Based on our experience with neurotrophic factors and the Nogo signaling system, and using additional transgenic mouse models, including the mtDNA Mutator mouse with premature, yet typical aging, NgR1 KO mice and mice modeling neurodegenerative diseases (such as APPSwePSEN mice and our MitoPark mice to model aspects of Alzheimer's and Parkinson's disease, respectively) we will examine the formation of lasting normal and pathological (addiction, posttraumatic stress disorder) memories in adult and aging individuals with and without additional neurodegenerative genotypes known to include cognitive impariment. This research will further the understanding of mechanisms behind memory dysfunction and help the design of memory-improving stratetegies.

**Lay Summary**
**Further information available at:**

**Types:**
Investments > €500k

**Member States:**
European Commission

**Diseases:**
Neurodegenerative disease in general

**Years:**
2016

**Database Categories:**
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