# Protease Systems Biology in Tumorigenesis and Neurodegeneration

https://neurodegenerationresearch.eu/survey/protease-systems-biology-in-tumorigenesis-and-neurodegeneration/

**Principal Investigators**
**Institution**
**Contact information of lead PI**
**Country**

European Commission

**Title of project or programme**

Protease Systems Biology in Tumorigenesis and Neurodegeneration

**Source of funding information**

European Commission FP7-Seventh Framework Programme

**Total sum awarded (Euro)**

€ 1,499,760

**Start date of award**

01/02/2012

**Total duration of award in years**

5.0

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

Neurodegenerative disease in general

**Keywords**
**Research Abstract**

Proteolysis affects every protein through limited processing or degradation. Unlike other post?translational modifications, proteolysis is irreversible and occurs intra? and extracellularly. The large number of genetically encoded proteases in man (> 560) illustrates the importance of proteolysis. However, the in vivo substrate profiles of most proteases have remained elusive; presenting a major hurdle to understanding protease function in health and disease.

System?wide identification of protease substrates is now enabled by novel proteomic strategies for the quantitative determination of neo N? and C?termini. In this project, proteolytic events and cleavage products are identified and validated in cellular model systems in order to understand how proteolysis contributes to tumor aggressiveness and neurodegeneration.

In the area of tumor biology, the paracrine loop between cancer and stroma cells is dissected. Both cell types secrete cytokines and cytokine?modifying proteases; thereby potentiating tumor proliferation and invasiveness. Identification of key cleavage events and key proteases in tumor?stroma interaction unravels the role of proteolysis in cellular communication. In addition, the substrate profile of the stroma?specific, cell?surface protease “Fibroblast activation protein” is determined.

In the area of neurodegeneration, this project identifies and validates substrates of the orphan, neuroprotective protease DJ?1. Mutants of DJ?1 are associated with early?onset Parkinsonism. In addition a novel dual?label approach for the monitoring protein?specific degradation rates on a proteome?wide scale is established. This unique strategy examines the relation between a–synuclein aggregation (a hallmark of Parkinson’s disease) and impaired proteome turnover.

The combination of novel proteomic techniques with state?of?the?art cell biological approaches is uniquely suited to determine how proteases control cellular fate in tumorigenesis and neurodegeneration.

**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:**
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