

**valapodyn**

Curing Neurodegenerative Disease

[www.valapodyn.eu](http://www.valapodyn.eu)



A European Integrated Project supported through the Sixth Framework Programme for Research and Technological Development

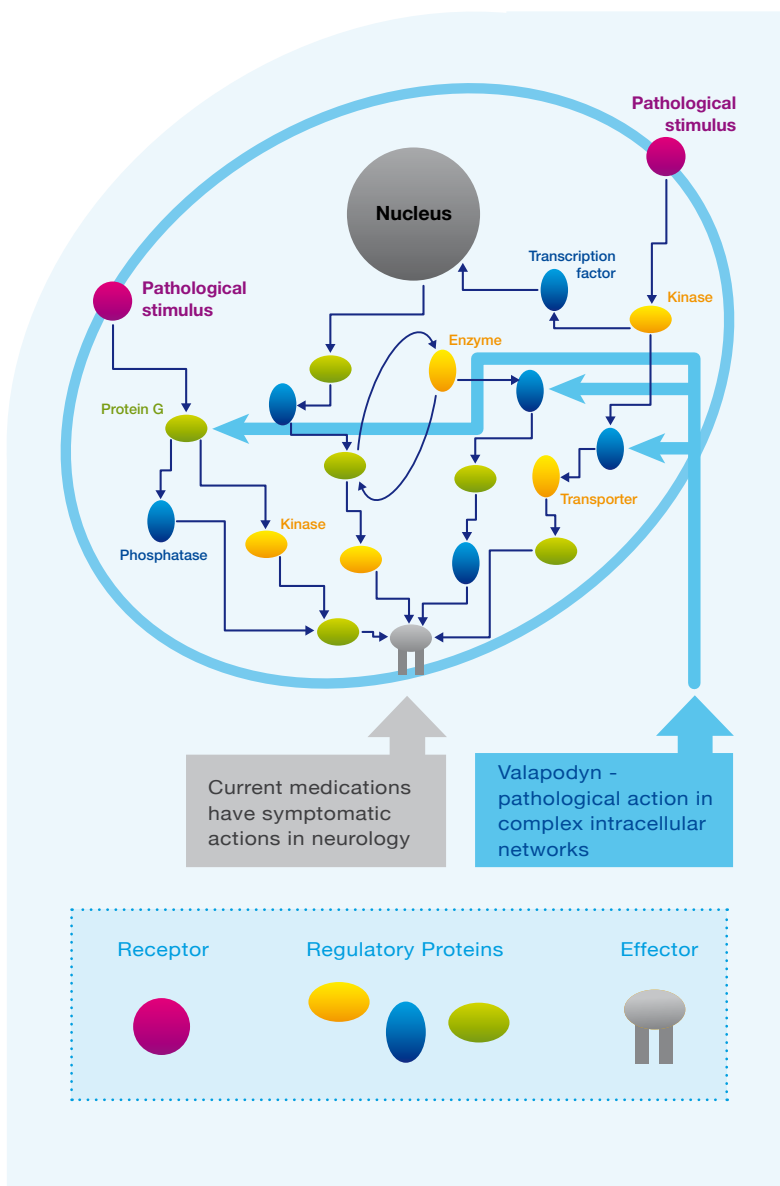




# Context

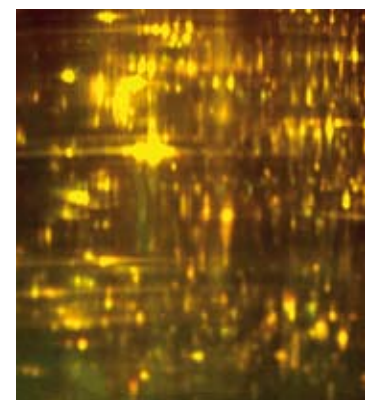
Modern high throughput technologies in biological science, such as genomics, transcriptomics and proteomics, often generate lists of molecules of interest. Yet, this does not necessarily increase our knowledge of biological or pathological processes and leads to the isolation of non relevant therapeutic targets especially when multifactorial diseases are studied. This results in a high failure rate in the development of new drugs and therefore significantly contributes to the high and rising cost of drugs. The challenge, therefore, is to construct a descriptive model from these lists of molecules that reflects the underlying biological mechanisms as accurately as possible, in order to select relevant therapeutic targets.

**Systems Biology** works towards understanding the intricacies of cellular life through the collaborative efforts of biologists, chemists, mathematicians and computer scientists who develop maps of the molecular interaction networks and in some cases dynamic models.



This approach is emerging also in medicine, with **systems pathology** leading to a better understanding of the molecular signature of the disease and **systems pharmacology** providing insight into dynamic system responses upon multiple drug perturbations. Knowledge of the changes of system characteristics during disease progression is absolutely necessary to create a framework for the design of novel combinatorial treatment strategies.

To address these needs and to develop new tools for therapeutic research, the participants of the VALAPODYN (Validated Predictive Dynamic Model of Complex Intracellular Pathways Related to Cell Death and Survival) project have created a network composed of leading authorities in the fields of dynamic systems biology, genomics, proteomics, bioinformatics and neuroscience.



Proteomics Facility



# Objectives

The objective of the VALAPODYN project is to develop a new innovative Systems Biology approach to model **the dynamics of Molecular Interaction Networks (MIN)** related to cell death and survival in the organism. The future dynamic model will be dedicated to the selection of **drug targets for human brain pathologies** such as epilepsy, ischemia, Parkinson and Alzheimer.

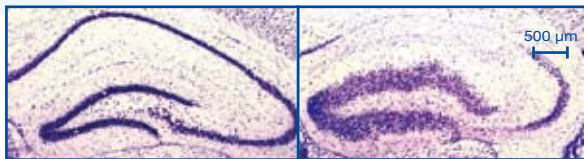
The project validates **dynamic models for neuro-**

**degeneration** through the characterisation of (new) drug targets in an animal model for **epilepsy** where neuronal death is the initial step in the pathological process.

Changing the paradigm of current biological data analysis methods, VALAPODYN develops a dynamic and quantitative analysis method to select new therapeutic targets through MIN dynamic models.



Increase of expression of a variant of acetylcholinesterase in the hippocampus of mice subjected to acute stress (right) compared to controls (left).



Cell loss and neuroplasticity observed in the hippocampus of a mouse model of mesiotemporal lobe epilepsy (right) compared to controls (left).

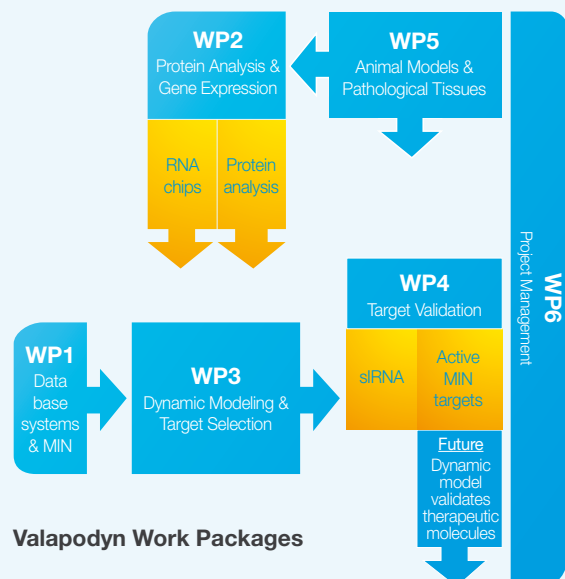


# Strategy

To develop a large-scale MIN modelling method that will allow to rationally address the physiopathology of several diseases, the VALAPODYN project is structured into **five interacting modules** :

1. A 'static' representation of the biological system to be modelled (WP1).
2. Experimental measures of the components of the system (WP2).
3. A mathematical modelling method (WP3).
4. Molecular testing and validation of the mathematical models (WP4).
5. Development of high quality cellular and animal models (WP5).

The new tools developed to build the dynamic models of neurodegeneration processes will constitute the basis for future therapeutic research in several other diseases including cancer, ischaemia, Alzheimer disease and neuromuscular disorders and more generally for multifactorial diseases.



# Consortium

The VALAPODYN consortium consists of 7 partners, coming from 5 European countries. It gathers many years of research in different fields such as genomics (FBRAA), proteomics (ULG), molecular

interactions (HELIOS, BIOBASE), RNA interference (HUJI), neuroscience (INSERM), and management expertise (ALMA).

Institut National de la Santé et de la Recherche Médicale, Grenoble, France / [www.inserm.fr](http://www.inserm.fr)

BIOBASE, GmbH, Wolfenbuettel, Germany / [www.biobase-international.com](http://www.biobase-international.com)

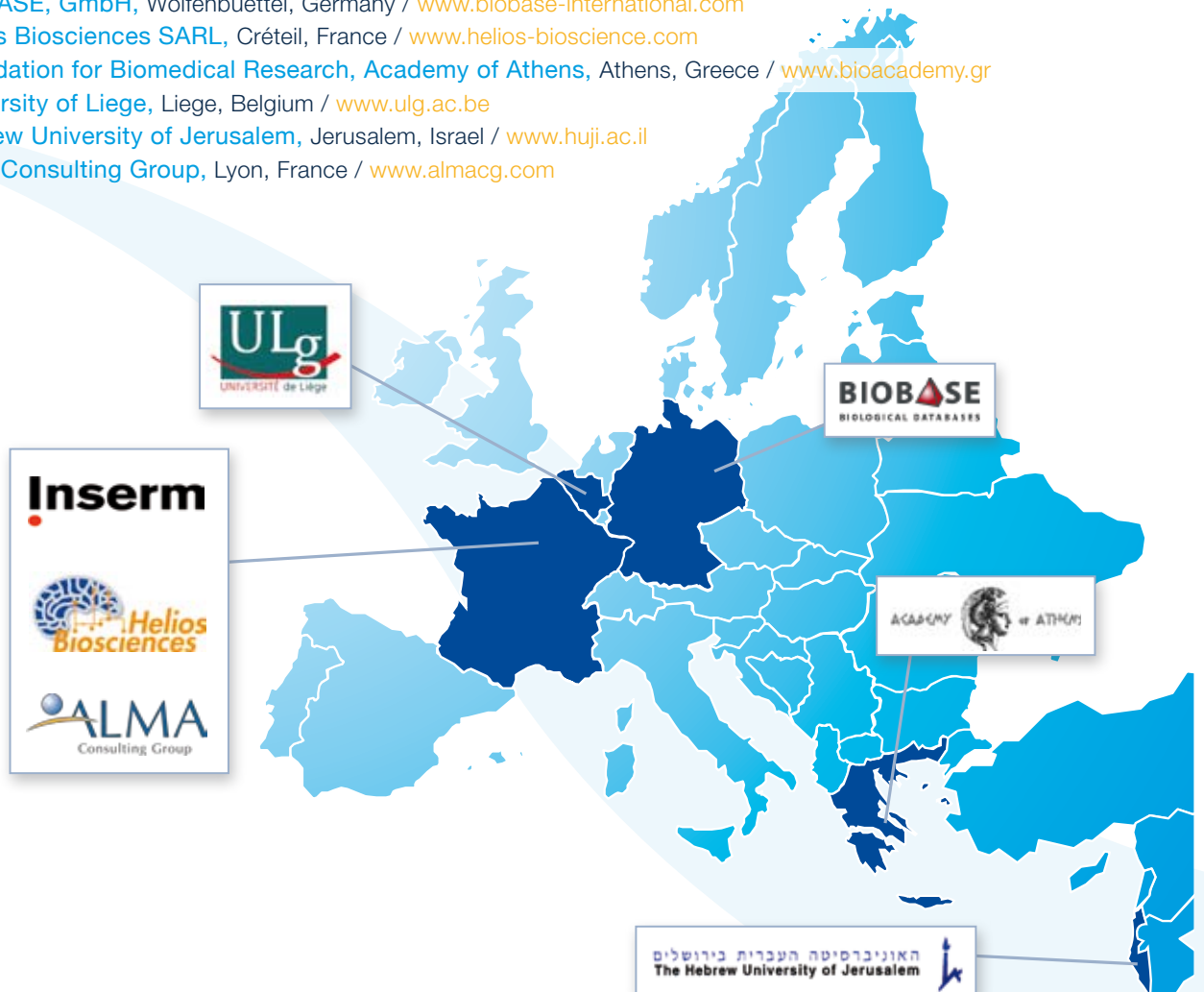
Hélios Biosciences SARL, Créteil, France / [www.helios-bioscience.com](http://www.helios-bioscience.com)

Foundation for Biomedical Research, Academy of Athens, Athens, Greece / [www.bioacademy.gr](http://www.bioacademy.gr)

University of Liege, Liege, Belgium / [www.ulg.ac.be](http://www.ulg.ac.be)

Hebrew University of Jerusalem, Jerusalem, Israel / [www.huji.ac.il](http://www.huji.ac.il)

Alma Consulting Group, Lyon, France / [www.almacg.com](http://www.almacg.com)



# Acknowledgments

The VALAPODYN project is supported by the European Commission through the Sixth Research Framework Programme for Research and Technological Development (FP6, 2002-2006) at a level of 1,488,649 € (for a total budget of 2,145,354 €).

The VALAPODYN project addresses the thematic area “Life sciences, genomics and biotechnology for health”. The project has been started on 1st October 2006 and will last 36 months.



[www.valapodyn.eu](http://www.valapodyn.eu)

#### Project Coordinator:

INSERM - Dr Antoine Depaulis: [antoine.depaulis@ujf-grenoble.fr](mailto:antoine.depaulis@ujf-grenoble.fr), +33 4 76 63 54 14

#### Dissemination Manager:

The Foundation for Biomedical Research of the Academy of Athens (FBRAA) - Dr Despina Sanoudou: [dsanoudou@bioacademy.gr](mailto:dsanoudou@bioacademy.gr), +30 2 1 06 59 74 53

#### With the support of ALMA Consulting Group:

Dr Raffaella Catena: [rcatena@almacg.com](mailto:rcatena@almacg.com), +33 (0)4 72 35 80 30