Genetic and Epigenetic Networks in Cognitive Dysfunction (GENCODYS)

https://neurodegenerationresearch.eu/survey/genetic-and-epigenetic-networks-in-cognitive-dysfunction-gencodys/

Title of project or programme

Genetic and Epigenetic Networks in Cognitive Dysfunction (GENCODYS)

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
Professor	Hans	van Bokhoven	STICHTING KATHOLIEKE UNIVERSITEIT	Netherlands

Address of institution of lead PI

Institution STICHTING KATHOLIEKE UNIVERSITEIT
Street Address
City
Postcode

Country

Netherlands

Source of funding information

European Commission

Total sum awarded (Euro)

11647068

Start date of award

01-05-2010

Total duration of award in months

60

The project/programme is most relevant to

Neurodegenerative disease in general

Keywords

Research abstract in English

Mutations in about 400 different genes have been associated with Cognitive Disorders (CD), such as mental retardation, autism, neurodegenerative disorders, and psychiatric disorders. Whereas CD impose a major medical and socio-economical problem, there are no systematic studies that aim to

provide insight into common mechanisms in CD. We propose a systems biology approach to gain insight into common mechanisms leading to cognitive impairment: (1) Identification of genes involved in cognitive disorders. Despite considerable progress in the identification of genes underlying CD, the majority of causative genes in CD remain unidentified. Therefore, our first objective is to identify new genes causative of CD by implementing high-throughput strategies. (2) Elucidation of molecular networks that are commonly disrupted in CD.

Recent genetic and neurobiological research revealed evidence for a number of molecular and cellular pathways that are shared by the various genetic CDs. Prominent examples are Rho GTPase-related genes and genes that regulate chromatin structure/function (epigenetics) associated with mental retardation and autism. Our second objective is to systematically explore this concept by elucidation of molecular networks using functional genomics strategies in genetic models that are the cornerstone of neuroscience, such as mouse and fruit fly. (3) Identify genetic modifiers and small compounds that modulate the disease phenotype. Our third objective is to resolve the molecular underpinnings of the large degree of clinical variability that is typical for all types of CD, even among patients carrying identical gene mutations. Genetic modifier screens in cultured primary neurons as well as in available Drosophila models for CD will be used to reveal phenotypically relevant genetic interactions and molecular networks. Moreover, drug screens shall be conducted in fly and cellular models for CD, which will lead to pharmacological rescue of mouse models.

Lay summary