Evangelia Thanou (ESR 13)

Investigation of the potency of small molecule mimetics of neurotrophins to rescue the reduction in synapse number and the aberrant synapse proteome in mouse models of Alzheimer's Disease

Profile

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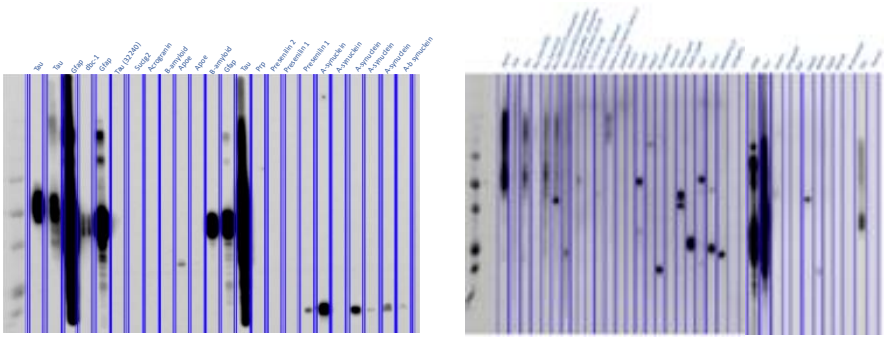
My Research

The main focus of my project is the examination of the temporal effects of neurotrophin mimetics on the brain tissue and on synaptic proteomes in mouse models of neurodegeneration (APPswe/PS1dE9 and 5xFAD transgenic mice for AD; cuprizone mouse model of MS). Firstly, it is expected that the large-scale proteomics data will be hypothesis generating that will guide the subsequent functional studies to explain the mechanistic aspects of the disorders and their rescues by the neurotrophin mimetics. Secondly, our data will provide hints on the neurotrophin mimetics' efficacy on the rescues, which should assist in the design of the future optimal mimetic for the eventual clinical treatment of the disorders. I will use (1) quantitative proteomics to reveal the global changes of proteins in the brain. Around 3000 proteins per sample will be quantified. As current quantitative proteomics are not effective in distinguishing protein isoforms and posttranslational modifications, we use (2) quantitative western blotting to examine these changes. In addition, I will obtain secondments studying signalling pathways in cell culture (FoRTH), compound tracking and brain imaging (TUD) and clinical trial design (Novartis, Athens).



Antibodies against protein isoforms implicated in AD (hippocampus brain region).

Scientific CV

- 2018-recent: EuroNeurotrophin Early Stage Researcher PhD student, Vrije Universiteit Amsterdam, The Netherlands.
- 2016-2018: Master student in Molecular Biomedicine at the Medicine School of National and Kapodistrian University of Athens in collaboration with Alexander Fleming Institute, The role of LRRK2 signaling in resident and infiltrating immune cells in different models of familial and sporadic Parkinson's disease
- 2012-2016: Biology Department School of Sciences and Engineering, University of Crete, Greece.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement no. 765704

EuroNeurotrophin

A European training network for the discovery of neurotrophins small molecule mimetics as candidate therapeutic agents for neurodegeneration and neuroinflammation

Project Coordinator

Dr Theodora Calogeropoulou,
National Hellenic Research Foundation, Greece

Project Partners

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Introduction

Neurodegenerative diseases like Alzheimer's disease or Parkinson's disease are on the rise in developed societies worldwide affecting millions of people. Neurodegenerative diseases primarily affect neurons in the human brain and currently there exists no cure for any of them since most of the available drugs fail to tackle the pathogenesis of neurodegenerative diseases.

Preclinical studies point to the therapeutic potential of neurotrophins, which have been shown to control a number of aspects of survival, development and function of neurons. However, the poor pharmacokinetic properties of neurotrophins render their use as drugs prohibitive.

Objectives

EuroNeurotrophin will address the major limitations of neurotrophins by developing novel small molecule, neurotrophin mimetics with favourable profiles of stability, tissue penetration and targeted biological actions. In the long term, the project will contribute to the further development of small molecule therapeutics for the treatment of neurodegenerative diseases and neuroinflammation, revealing new concepts of neurotrophin receptors signalling and to create a pan-European Neurotrophin Network.

Furthermore, EuroNeurotrophin aims at creating a new generation of young scientists with a broad understanding and skill set in chemical biology with emphasis on the neuroscience field and to educate 14 young researchers regarding the knowledge underpinning the neurotrophin related field as well as on drug and natural products research for neurodegenerative diseases.

Impact

Neurotrophins offer one of the most compelling opportunities to significantly improve the treatment of serious age-related, neurological diseases such as Alzheimer's, Parkinson's, MND/ALS. A major therapeutic advantage of neurotrophic factors is that they tackle both the symptoms of a disease (improving clinical status) as well as its pathogenesis (delaying disease progression) without any prerequisite deep insight into the aetiology or specific pathogenic variables driving the disease process.

We will study neurotrophin small molecule mimetics (synthetic or natural) in depth, and will use them as molecular probes to interrogate the role of neurotrophins and their receptors. It will contribute important new knowledge to the next frontier in biomedical sciences.

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