



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

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PhD student - Early Stage Researcher (ESR13)
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 AD

EuroNeurotrophin Overview

EuroNeurotrophin will be the first European consortium to study small molecule neurotrophin mimetics (synthetic or natural) in depth, use them as molecular probes to interrogate neurotrophins, and emphasise their clinical translation.

Neurodegenerative diseases (ND), like Alzheimer's disease, Parkinson's disease, Multiple Sclerosis and motor neuron disease, are on the rise worldwide. Preclinical studies point to the therapeutic potential of neurotrophins in preventing or slowing the progression of ND. The key idea behind this project is to address the major limitations of neurotrophins by developing novel **small molecule, neurotrophin mimetics** with favourable profiles of stability, tissue penetration and targeted biological actions.

EuroNeurotrophin meets the emerging need for training young researchers in drug discovery and development with a focus on the design, synthesis and isolation of new neuroprotective small molecule neurotrophin mimetics and their assessment using multimodal approaches, as well as their use towards market applications.

Host Institution



VU Amsterdam is a multidisciplinary organisation, with a world ranking of 64 for medical science by CWTS Leiden Ranking (2017). The Neuroproteomics group of VU Amsterdam focuses on two main lines of researches. (1) To decipher the synaptic protein interactome and their neuronal activity-dependent dynamics in the context of memory formation, and the alteration of protein interactomes in neurodevelopmental diseases (autism and schizophrenia) and neurodegenerative diseases (AD, PD and FTD). (2) To reveal alteration of proteome in rodent models of brain disorders, and patient post-mortem brain tissues. These proteomics data generally are hypothesis generating that guide subsequent functional studies aiming at revealing the (novel) mechanistic underpin of the physiological/pathological processes of interest.

Dr Ka Wan Li, Assistant Professor and team leader of Neuroproteomics at VU Amsterdam, has > 25 years of experience in neuroscience research. Dr Li pioneered the use of mass spectrometry and

nano-separation methodologies for neuroscience. Today, he has >160 publications; majority of these articles involved at least in part the use of (quantitative) proteomics/peptidomics for the analysis of brain function and diseases.

Description of tasks for the position

AD is initiated by genetic and environmental stressors that progress through aberrant synapse function and reduction in their number, and lead eventually to neuronal death. As synaptic abnormality is reversal, synapse repair has been targeted as a promising disease modifier strategy. In this study we aim to examine the temporal effect of the new neurotrophin mimetics on synapse proteome in mice models of AD (APP^{swe}/PS1^{dE9} and 5xFAD transgenic mice). State-of-the-art quantitative proteomics, in particular SWATH (data independent analysis), will be applied for the mass spectrometry measurement.

Requirements

- Applicants must hold a MSc or equivalent in the field of biological science, preferable neuroscience or biochemistry.
- Applicants can be of any nationality.
- Applicants must have a very good knowledge (written and oral) of the English language.
- **H2020 MSCA Mobility Rule:** researchers must not have resided or carried out their main activity (work, studies, etc.) in the country of the host organisation for more than 12 months in the 3 years immediately before the recruitment date. Compulsory national service, short stays such as holidays, and time spent as part of a procedure for obtaining refugee status are not taken into account.
- **H2020 MSCA eligibility criteria:** Early Stage Researchers (ESRs) must, at the date of recruitment by the host organisation, be in the first four years (full-time equivalent research experience) of their research careers and have not been awarded a doctoral degree. Full-Time Equivalent Research Experience is measured from the date when the researcher obtained the degree entitling him/her to embark on a doctorate (either in the country in which the degree was obtained or in the country in which the researcher is recruited, even if a doctorate was never started or envisaged).

Benefits

- ✓ The position is full-time with a 12 month duration renewable to 36 months.
- ✓ A very attractive salary plus allowances package according to the allowance amounts defined in the rules for Early Stage Researchers (ESRs) EU Marie Skłodowska-Curie Actions Innovative Training Networks (ITN) (http://ec.europa.eu/research/participants/data/ref/h2020/wp/2016_2017/main/h2020-wp1617-msca_en.pdf)
- ✓ Network-wide specialised training and training in transferable/technical skills.
- ✓ Local specialist training provided by the host institution.
- ✓ Intersectoral and interdisciplinary secondments within the EuroNeurotrophin network.
- ✓ International exposure through participation in scientific conferences.

Application

The application form can be downloaded from our website (www.euroneurotrophin.eu). Interested candidates for the position should submit the completed application form along with their cv, motivation letter, copies of publications and/or thesis (if available) and scans of transcripts to the following emails:

k.w.li@vu.nl and info@euroneurotrophin.eu

IMPORTANT: Please also arrange for two recommendation letters to be submitted directly to

k.w.li@vu.nl and to info@euroneurotrophin.eu

Additional Information

For additional information about the research project and this individual position, please contact:

Dr KaWan Li; Email: k.w.li@vu.nl