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 (ESR14)

The neuroprotective effects of neurotrophins in novel in vitro and in vivo models of Motor Neurone Disease (ALS/MND)

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

USFD is one of the UK's leading research-led Universities with a high international reputation. A member of the Russell Group (an association of 24 of the UK's leading Universities); 1 of 20 Government funded Biomedical Research Centres (BRC; University-hospital partnership) in the UK, with the unique research theme of Translational Neuroscience for Chronic Neurological Disorders. USFD has close links with industry, commerce and the professions, and achieves consistent success in attracting research grants and funding from regional, national and international organisations. It is ranked in the top 100 World Universities by the Times Higher Education (2016) and top 80 in the QS rankings (2016). In the UK Research Excellence Framework assessment in 2014, 99% of research was rated as internationally recognised or better. USFD's Sheffield Institute for Translational Neuroscience (SITraN) is one of the world leading centres for research into Motor Neurone Disease, Alzheimer's and Parkinson's Disease. It undertakes basic through to applied research and has a proven track record having been awarded orphan drug status for two drugs emerging from its drug screening programme.

Prof. Dame Pamela Shaw, Director of the Sheffield Institute for Translational Neuroscience and the Biomedical Research Centre: Translational Neuroscience for Chronic Neurological Disorders, Faculty Pro-Vice Chancellor for Medicine, Dentistry and Health, Professor of Neurology and Honorary Consultant Neurologist with 430 publications and two patents and >32 years of research experience in the field of neurodegeneration. Prof Dame Shaw contributed to the clinical introduction of the first disease modifying therapy drug for a neurodegenerative disorder (riluzole) and spear-headed other interventions eg non-invasive ventilation which have had a major impact on life expectancy and quality of life for patients with ALS/MND.

Description of tasks for the position

In this project we plan to assess the potential neuroprotective effects of new neurotrophin mimics on:

- *In vitro* cultures of patient and control-derived astrocytes and motor neurones using high throughput screening for UNICAEN library and marine microbial extracts and low throughput for synthetic derivatives.
- Top hits will then be tested on *in vivo* zebrafish models of MND.
- The most promising candidates (1 or 2 compounds) will be taken forward for *in vivo* testing in mouse models of MND.

Requirements

- Applicants must hold an MSc or equivalent in the field of Science
- Applicants can be of any nationality.
- Applicants must have a very good knowledge (written and oral) of the English language. Requirements are detailed here https://www.sheffield.ac.uk/postgraduate/info/englang
- **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 EuroNeutotrophin 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:
neuroscience@sheffield.ac.uk and info@euroneurotrophin.eu
IMPORTANT: Please also arrange for two recommendation letters to be submitted directly to neuroscience@sheffield.ac.uk and to **info@euroneurotrophin.eu**

Additional Information

For additional information about the research project and this individual position, please contact:
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Prof. Dame Pamela Shaw Email: pamela.shaw@sheffield.ac.uk