



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 (ESR5)
Production of purified protein targets and x-ray crystal structure determination of target-ligand complexes**

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



The University of Siena is a public research and higher education institution with a strong tradition in chemical, biotechnological and biomedical research, which includes 15 Departments and counts >20,000 students. The laboratory of Protein Crystallography headed by Prof. Stefano Mangani is located in Department of Biotechnology, Chemistry and Pharmacy (DBCP) that offers a highly capable research platform with an excellent track record of scientific publications and research funding.

The research group of Prof. Mangani is focused on the study of protein/enzyme function and of protein-protein interactions. DBCP hosts a Doctorate program in Chemical and Pharmaceutical Sciences coordinated by Prof. Mangani.

Prof. Stefano Mangani is full Professor of Chemistry with over 30 years of academic research and University teaching experience, from undergraduate to post graduate courses, where he teaches Advanced Inorganic Chemistry and Protein Crystallography. He has been involved in the International Doctorate Program in Structural Biology of the University of Florence and in EMBO founded courses in

protein structure, function and interactions; X-ray absorption spectroscopy and x-ray microscopy.

Description of tasks for the position

The ESR will be involved in milligram scale production of pure target proteins (p75NTR, TrkA, TrkB,TrkC) for crystal structure determination of protein-small molecule complexes to drive ligand-based and receptor-based drug design. The procedure will be as follows:

- Protein targets will be cloned, expressed and purified.
- The crystal structures of the adducts between the specified targets and ligands will be obtained and the structural information delivered to partners (e.g.WP1) for help to improve ligand design.
- Other proteins from the downstream signalling cascade found by mechanistic studies of the pathway might be also obtained, crystallised and their tri-dimensional structure determined to better characterise the pathway.

The ESR will have the task to pursue crystal structure determination of the above described systems, assisted by the research team of Prof. Mangani and acquire expertise on protein production, x-ray crystallography and related techniques. Together with experts from the team, he will travel to synchrotron x-ray sources for data collection.

The ESR will be asked to keep updated laboratory notebook and participate to laboratory meetings.

The ESR will participate to the Consortium meetings and will benefit from the training secondments.

Requirements

- Applicants must hold a MSc or equivalent in the field of chemistry, pharmaceutical sciences or biotechnology.
- Applicants should have a strong background in chemistry, biochemistry and, mainly, have the willingness to master structural biology techniques and become experts in protein structure, function and interactions.
- 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:

stefano.mangani@unisi.it and info@euroneurotrophin.eu

IMPORTANT: Please also arrange for two recommendation letters to be submitted directly to stefano.mangani@unisi.it and to info@euroneurotrophin.eu

Additional Information

For additional information about the research project and this individual position, please contact: Professor Stefano Mangani. Email: stefano.mangani@unisi.it