



Canelif Yilmaz (ESR 8)

Evaluation of small molecule neurotrophin mimetics in models of neurodegeneration and neuroinflammation

Profile

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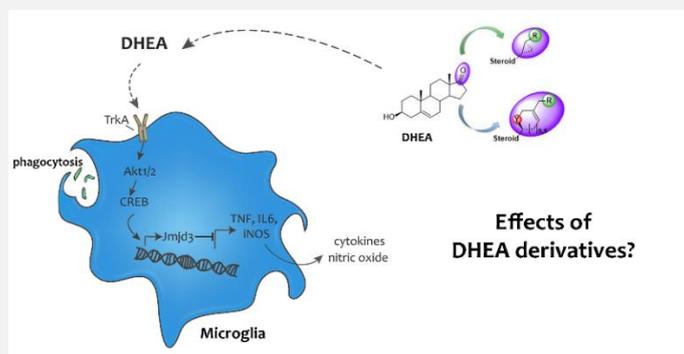


Project: EuroNeurotrophin



My Research

My research project focuses on investigating the anti-inflammatory effects of novel DHEA mimetics, which will be synthesized by fellow ESR's in the consortium. Inflammatory responses of microglia, the innate immune cells of the brain, have previously been shown to be regulated by NGF, the native ligand of TrkA, and also DHEA via TrkA dependent signalling^{1,2}.



Building on that knowledge, I will be testing whether our novel DHEA mimetics will also have a similar effect on regulating neuroinflammation. For this purpose I will use primary microglia, and study the effects of the compounds on the inflammatory responses of microglia, such as cytokine expression and phagocytosis. Furthermore, I will study the brain uptake of labelled DHEA mimetics in spinning disk microscopy. Finally, I will evaluate the efficacy of the DHEA mimetics on Cuprizone model of Multiple Sclerosis, and evaluate if the DHEA mimetics can improve disease pathophysiology.

During my PhD I will also visit our partner AvantiCell Science to receive training in 3D cell culture and bioprinting technologies, FORTH to assess the efficacy of compounds in neuronal cells, and finally UniCaen to assess the druggability of effective compounds.

CV

- 2018-Present, EuroNeurotrophin Early Stage Researcher, PhD student Faculty of Medicine Carl Gustav Carus, TU Dresden, Germany
- 2015-2017, M.Sc. in Neuroscience Bilkent University, Ankara, Turkey
- 2009-2015, B.Sc. in Molecular Biology, with a minor degree in Chemistry, Koç University, İstanbul, Turkey

Publications

- Erol O, Uyan I, Hatip M, Yilmaz C, Tekinay AB, Guler MO. Recent Advances in Bioactive 1D and 2D Carbon Nanomaterials for Biomedical Applications, *Nanomedicine* (2017)
- Okur Z, Senturk OI, Yilmaz C, Gulseren G, Mammadov B, Guler MO, Tekinay AB. Promotion of neurite outgrowth by rationally designed NGF- β binding peptide nanofibers, *Biomater Sci* (2018)
- Yilmaz C, Karali K, Fodelianaki G, Gravanis A, Chavakis T, Charalampopoulos I, Alexaki VI. Neurosteroids as regulators of neuroinflammation, *Front Neuroendocrinol* (2019)





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
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Project Partners



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Introduction

Neurodegenerative diseases like Multiple Sclerosis, Alzheimer's disease or Parkinson's disease are on the rise in developed societies worldwide affecting millions of people. Currently there exists no cure for any of them. 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.

Neuroinflammation is a key component of neurodegenerative diseases³. We investigate how neurotrophins affect neuroinflammatory processes.^{1,2}

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 improve the treatment of neurodegenerative diseases such as Multiple Sclerosis or Alzheimer's disease. Through this work we aim to identify synthetic and natural neurotrophin small molecule mimetics as new candidates in the management of neuroinflammation and neurodegeneration in the context of Multiple Sclerosis and Alzheimer's disease.

References:

1. Alexaki VI, Fodelianaki G, Neuwirth A, Mund C, Kourgiantaki A, Ieronimaki E, et al. DHEA inhibits acute microglia-mediated inflammation through activation of the TrkA-Akt1/2-CREB-Jmjd3 pathway. *Molecular Psychiatry*. 2017
2. Fodelianaki G, Lansing F, Bhattarai P, Troullinaki M, Zeballos MA, Charalampopoulos I, et al. Nerve Growth Factor modulates LPS - induced microglial glycolysis and inflammatory responses. *Exp Cell Res*. 2019
3. Yilmaz C, Karali K, Fodelianaki G, Gravanis A, Chavakis T, Charalampopoulos I, et al. Neurosteroids as regulators of neuroinflammation. *Front Neuroendocrinol*. 2019

