Small molecules mimicking GDNF for regeneration of dopaminergic neurons in vivo

https://neurodegenerationresearch.eu/survey/small-molecules-mimicking-gdnf-for-regeneration-of-dopaminergic-neurons-in-vivo/

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Country

United Kingdom

Title of project or programme

Small molecules mimicking GDNF for regeneration of dopaminergic neurons in vivo

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Parkinson's UK

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1

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Research Abstract

Parkinson’s disease (PD) is caused by degeneration and progressive loss of neurons in the brain. In particular, dopaminergic (DA) neurons of the substantia nigra pars compacta (SNpc) gradually degenerate and die. It is estimated that in Western countries more than 6 million people live with PD and the number of suffering people will raise with general aging of the population. Glial cell line-derived neurotrophic factor (GDNF) protects and repairs distinct neuronal populations, including DA neurons. GDNF protein and the related factor neurturin were intracranially delivered to parkinsonian patients in five clinical trials, but the results have been inconclusive. The pharmacokinetic properties of these proteins complicate their therapeutic use,

since they have to be delivered directly into the brain. This proposal deals with the development of small molecule GDNF mimetics that can efficiently protect and repair DA neurons in vivo. We earlier discovered several chemical compounds that activate GDNF receptors in immortalized cells and support the survival and regeneration of GDNF-dependent neurons in vitro. In particular, one of these compounds was shown to positively influence DA neurons. In proposed project we first plan to test the second available molecules for the ability to support cultured DA neurons. Afterwards we will test these compounds in animal model of PD. In the future (out of the scope of this project) resulting lead compounds will be further optimized to improve their efficacy, pharmacokinetic properties and safety in vivo.

Further information available at:

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