

METHOD FOR THE TREATMENT OF NEUROLOGICAL DISORDERS

The present invention refers to Heme-Regulated Inhibitor (HRI) Kinase agonists or activators, or pharmaceutical composition comprising thereof, for use in a method for the treatment of a neurological disorder or for use as a neuroprotective agent, including Alzheimer disease and ischemic stroke.

Research goal

The global burden of neurological disorders is increasing yearly worldwide, latest data showing that stroke and Alzheimer disease (AD) are the leading neurological causes of deaths by far: 67.4% and 20.3%, respectively. Although each condition represents a different type of CNS damage (stroke: acute neuronal damage, AD: chronic neuronal damage), all two lead to the same cellular outcome: stress in the endoplasmic reticulum (ER) due to the accumulation of misfolded/unfolded proteins in the organelle. Phosphorylation of the eukaryotic translation initiation factor 2-alpha increases protein-folding and degradative capacities of the ER.

Problem to solve

Unfortunately, there are no current reliable treatments promoting neuroprotection (stroke and AD), therefore, there is an unmet medical need to discover new targets and treatments that provide neuroprotection in damaged neurons after either of this CNS injuries. The HRI kinase belongs to a family of kinases that phosphorylate the eukaryotic initiation factor 2 alpha (eIF2 α), playing a key role in regulating protein synthesis in response to various cellular stresses, and so, it can be a feasible target to promote neuroprotection following acute and chronic CNS damages.

Innovative Aspects

Preliminary in vitro data also show that a temporary-guided activation of HRI by the HRI Kinase agonist or activator BTdCPU allows a longer UPR/ISR-like metabolic state that helps neurons to overcome cellular damage after either oxygen-glucose deprivation (OGD, in vitro stroke model) or A β s exposure. Furthermore, in vivo preliminary studies in a mouse model of ischemic stroke revealed that the BTdCPU dose of 10 mg/kg induced lower lesion volumes and best scores in motor analysis than controls. Overall, these results support a beneficial impact of activating the HRI kinase following acute and chronic CNS damages.

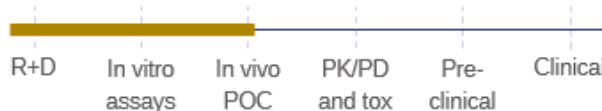
Market opportunity

BTdCPU, or pharmaceutical composition comprising thereof, for use in a method for the treatment of a neurological disorder or for use as a neuroprotective agent, therefore, a new method for the treatment of Alzheimer disease or ischemic stroke.

Intellectual Property:

- Priority European patent application filed (September 19, 2024) **EP24383003.1**
- Suitable for international extension (PCT application)

Development stage:



Available for: *Licensing, co-development*

Aims

Looking for a partner interested in a license and/or a collaboration agreement to develop and exploit this asset.

Contact details

Consorcio Centro de Investigación Biomédica en Red
(CIBER)
otc@ciberisciii.es
<https://www.ciberisciii.es/en>