SCREENING AND TREATMENT OF NEUROLOGICAL DISORDERS CHARACTERIZED BY A KIDINS220 DYSFUNCTION

A research group from CIBER, CSIC and Universidad Autónoma de Madrid has identified a new way to treat and prevent disorders related to Kidins220 dysfunction that could improve the development of some neurodegenerative disorders

The Need

Several neurological and psychiatric disorders are characterized by a dysfunction of Kinase D-interacting substrate of 220kDa (Kidins220). There is a strong need to identify molecular signatures involved in Kidins220 dysfunction disorders (stroke, epilepsy, traumatic brain injury, hydrocephalus, iNPH, schizophrenia, SINO syndrome) to design novel screening methods and therapies to improve diagnosis, treatment and prognosis of neurological diseases.

The Solution

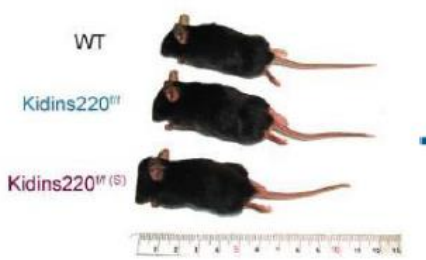
This technology provides a method for prevention and treatment of subjects at risk of suffering from a neurological or psychiatric disorder related to Kidins220 dysfunction. The method is based on the retromer complex and its regulation, and improves the excitotoxicity and ventriculomegaly commonly showed in this disorders.

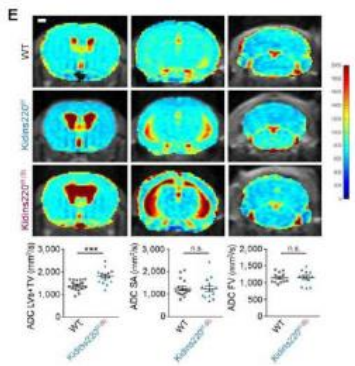
Innovative Aspects

Using Kidins220-deficient mice, the group has discovered the role of KIDINS220 as a regulator of the development of ventriculomegaly and hydrocephalus by regulating AQP4 and the SNX27 retromer (Mol Psychiatry, 2021 and PCT/EP2022/061794). The patent application also proposes the use of R55 (or related compounds) as a highly neuroprotective agent against excitotoxicity to combat **stroke** and other excitotoxicity-related neuropathologies. Retromer stabilizers could also be useful for treating pathologies associated with KIDINS220 dysfunction and pathological variants. The primary objective is to use retromer stabilizers to increase components of the SNX27 complex and the levels of KIDINS220 and AQP4 to improve disorders characterized by KIDINS220 dysfunction and/or ventriculomegaly and/or excitotoxicity.

The use of retromer stabilizers for **stroke** would be completely novel. No one has previously described how excitotoxicity destabilizes retromer, and treatment with retromer stabilizers protects against excitotoxic neuronal death, a discovery contained in the patent. Current stroke treatments are based on completely different pathways unrelated to retromer.Regarding ventriculomegaly and hydrocephalus, as well as SINO syndrome, there are no pharmacological treatments, only surgical ones.

Stage of Development:
In-vivo proof of concept (PoC) in a mouse **ischemia** model.





Intellectual Property:

- Priority European patent application filed (2021).
- National phase: Europe (EP4333833 A1) and USA (US2024/0226062 A1).

Del Puerto, A. *et al.* (2021). Kidins220 deficiency causes ventriculomegaly via SNX27-retromer-dependent AQP4 degradation. *Molecular psychiatry.* DOI: https://doi.org/10.1038/s41380-021-01127-9

Aims

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

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