Development of small molecule Usp8 inhibitors as therapeutics in Lewy body dementia

https://www.neurodegenerationresearch.eu/survey/development-of-small-molecule-usp8-inhibitors-as-therapeutics-in-lewy-body-dementia/

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Country

United Kingdom

Title of project or programme

Development of small molecule Usp8 inhibitors as therapeutics in Lewy body dementia

Source of funding information

Alzheimer's Research UK

Total sum awarded (Euro)

€ 67,780

Start date of award

01/10/2015

Total duration of award in years

3

Keywords
Research Abstract
Lewy body disease is the second commonest cause of neurodegeneration. Lewy bodies are protein clumps inside brain cells, made of a small protein called ?-synuclein. Their build-up is critically dependent on the amount of ?-synuclein in the brain. Healthy cells remove damaged proteins, principally by attaching on them a tag, which acts as a signal for destruction. This tag (ubiquitin-chain) is regulated by a specialised cleanup crew inside cells. This includes factors that assemble the ubiquitin-chain, shuttle the chain inside cells and eventually disassemble it for

recycling. If we understood this crew that clears ?-synuclein and turn it on or off using small molecules, then we could specifically reduce the accumulation of ?-synuclein and slowdown or stop the disease. Our lab has shown that one such factor, Usp8 is overactive around Lewy bodies trimming off ubiquitin from ?-synuclein, slowing down its breakdown. When Usp8 was blocked genetically it protected against toxicity from the abnormal accumulation of ?-synuclein. We now aim to test whether small molecules that block Usp8 have a beneficial effect without side-effects in brain cells that were derived from skin cells. If successful this study could open the way to novel therapies in this group of diseases.

Further information available at:

Types:
Investments < €500k

Member States:
United Kingdom

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A