Therapeutic targeting of impaired lysosomal flux in Alzheimer’s disease

https://neurodegenerationresearch.eu/survey/therapeutic-targeting-of-impaired-lysosomal-flux-in-alzheimer%c2%92s-disease-2/

Question
Principal Investigators

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Related
Institution

Multiple

Contact information of lead PI
Country

Ireland|United Kingdom

Title of project or programme

Therapeutic targeting of impaired lysosomal flux in Alzheimer's disease

Source of funding information

CoEN

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€ 379,112

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01/06/2018

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2

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Research Abstract

There are currently no effective treatments for Alzheimer’s disease (AD). Novel approaches are urgently needed.
Innovative systems that increase the clearance of disease-associated proteins in and around brain cells are one such approach. Increased clearance of these proteins via lysosomal flux show extremely encouraging results in AD animal models, clearing the two hallmark brain changes that define AD, deposition of amyloid-beta-protein (Abeta) and tau.

However, therapeutic targets which will selectively modify lysosomal flux to prevent these brain changes are lacking. Our previous research indicates that the lysosomal Ca2+ release channel protein, TRPML1, has major potential as such a target.
This proposal will use our multidisciplinary expertise to determine the therapeutic potential of TRPML1 in AD. TRPML1 is easily targetable and selectively activated/inactivated by lipid molecules called the phosphoinositides (PI), specifically PI(3,5)P2 and PI(4,5)P2, respectively. Many previously identified AD risk genes bind to PI(4,5)P2 (including ApoE4, PICALM, BIN1, CD2AP). Another AD risk gene can alter PI(4,5)P2 metabolism (INN5PD). We will test the hypothesis that these previously identified risk genes regulate phosphinositide activity to contribute to AD pathology by altering TRPML-1 mediated lysosomal flux, and determine whether targeting this TRPML1 defect offers therapeutic potential for AD. Combining a multi-disciplined approach involving our expertise in AD neuropathology, TRPML1 function, lysosomal flux and AD genetics, this research presents an exciting opportunity to develop novel disease-modifying therapeutic/diagnostic platforms with selective innovative targeting of lysosomal flux defects to combat AD pathogenesis in populations worldwide.

Further information available at:

Types:
Investments < €500k

Member States:
Ireland, United Kingdom

Diseases:
N/A

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2016

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