Small vessel diseases in a mechanistic perspective: Targets for InterventionAffected pathways and mechanistic exploitation for prevention of stroke and dementia

https://www.neurodegenerationresearch.eu/survey/small-vessel-diseases-in-a-mechanistic-perspective-targets-for-interventionaffected-pathways-and-mechanistic-exploitation-for-prevention-of-stroke-and-dementia/

Principal Investigators
Institution
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Country

European Commission

Title of project or programme

Small vessel diseases in a mechanistic perspective: Targets for InterventionAffected pathways and mechanistic exploitation for prevention of stroke and dementia

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European Commission Horizon 2020

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€ 5,998,300

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01/01/2016

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5.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract
Stroke and dementia rank among the most pressing health issues in Europe. Cerebral small vessel diseases (SVDs) have emerged as a central link between these two major co-morbidities. SVDs account for more than 30% of strokes and at least 40% of dementia cases. They encounter multiple distinct diseases that can be separated based on their underlying genetic defects, risk factors, and clinical presentations. Despite this profound impact on human

health, there are no treatments with proven efficacy against SVDs. The applicants have made major progress in identifying key mechanisms involved in SVDs and their co-morbidities. We recently identified blood pressure variability as a major independent risk factor for multiple SVDs, stroke, and dementia and illuminated the roles of the blood brain barrier and the extracellular matrix in small vessel function. We further identified novel molecular pathways (TIMP3, LTBP1, TGFß) that are shared between different SVDs and thus point towards common mechanisms. This EU network, which brings together basic scientists and academic clinicians, will make use of novel animal models and expertly phenotyped patient cohorts to identify key mechanisms common to multiple SVDs and determine how these mechanisms contribute to individual SVDs. We will: i) identify common molecular, cellular, and physiological mechanisms that compromise the function of microvessels in different SVDs; ii) determine how these common mechanistic defects intersect to drive brain damage; and iii) validate the relevance of mechanisms through interventions in experimental systems (isolated microvessels and in vivo) and in patients (exploratory proof of concept trials). Our resources including novel animal models and state-of-the art technologies (e.g. proteomics & ultra-high field MRI) as well as expertise in clinical trials support the feasibility of the approach. In fact, studies by the applicants already revealed novel attractive targets for therapeutic intervention.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
European Commission

Diseases:
Alzheimer's disease & other dementias

Years:
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N/A

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