Human genetic studies of Alzheimer disease and other dementias

https://neurodegenerationresearch.eu/survey/human-genetic-studies-of-alzheimer-disease-and-other-dementias/

Principal Investigators

Caroline Graff

Institution

Karolinska Institutet

Contact information of lead PI
Country

Sweden

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Human genetic studies of Alzheimer disease and other dementias

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Swedish Research Council

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€ 228,509

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Total duration of award in years

3

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Research Abstract
Using a sample-collection of familial dementias we will identify genetic causes of Alzheimer disease and of frontotemporal dementia. In total 4800 DNA samples including more than 700 families have been recruited through our geriatrics clinic. Based on the family histories and ages at onset we have identified 100 families/individuals where whole-genome sequencing is expected to reveal causal mutations. These families are also selected to enable follow-up studies in additional bio-samples such as serum, cerebrospinal fluid, fibroblasts, RNA and brain-tissue. A major part of this project is the discovery of healthy family members who surprisingly have passed the age of disease onset by several years without any sign of disease but who are confirmed mutation carriers. That is, these very rare individuals represent what is known as

reduced penetrance and must carry protective mechanisms (modifying molecules such as RNA and proteins or epigenomic marks) which prevent them from developing disease. Using –omic technologies we will explore the mechanisms of reduced penetrance in patient-derived cell models. The group, Translational Genetics, has experience of next-generation sequencing, both whole-exome sequencing, and sequencing of gene-panels, and have workflows for variant prediction that can be applied. The group has proven experience also of functional studies and particularly in neuropathology, being responsible for the Brain Bank. Finally, the discoveries can be directly applied in our genetic counseling practice and in follow-up studies for pre-symptomatic clinical characterization similar to ongoing projects in the group. Finding additional genetic factors in dementias will be important for understanding the underlying mechanisms, developing diagnostic tools and new treatment strategies which are desperate needed for these untreatable, common diseases of the human brain.

Further information available at:

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Investments < €500k

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Sweden

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N/A

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2016

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