JPND research
EU Joint Programme – Neurodegenerative Disease Research

# CrossSeeds

## Mechanisms of pathogenic protein cross-seeding in neurodegenerative disorders

As the acronym "CrossSeeds" implies, this project is based on the hypothesis that a number of brain disorders including Alzheimer's disease (AD), Parkinson's disease (PD) and Huntington's disease (HD) share common pathogenic mechanisms leading to neurodegeneration.

A traditional view on these devastating disorders focuses on individual, disease-specific enzymes and/or aggregating proteins contributing to aspects of neuropathology.

This consortium combines experimental approaches from fundamental, pre-clinical and clinical neuroscience with computational approaches to identify cross-disease pathways leading to pathogenic protein aggregation.

All three diseases have at least one feature in common: aggregation of pathogenic proteins associated with neurodegeneration. For example, Abeta peptides modified by glutaminyl cyclase (QC) to form pyroglutamate (pGlu) act as seed for protein aggregation and provoke neurodegeneration in AD. As shown in preliminary experiments the AD-specific peptide pGlu-Abeta is also present in Lewy bodies of substantia nigra dopaminergic neurons of PD subjects and induces cross-seeding of a-synuclein.

Our research expects to substantiate the hypothesis that post-translational modifications such as QC-catalysed pGlu-formation induce or enhance the amyloidogenic properties of Abeta, alpha-synuclein and huntingtin.

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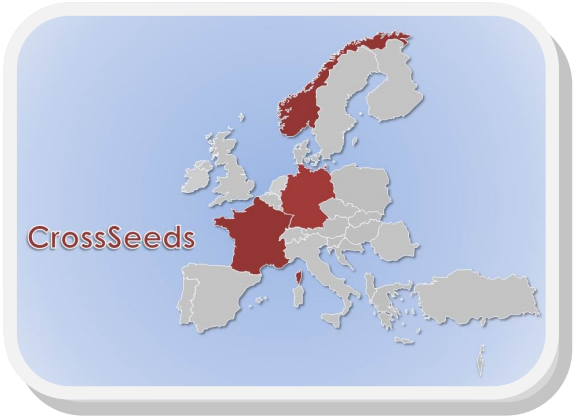


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* Contributions from participating JPND Member Countries are currently being finalised for this project