JPND
research
EU Joint Programme – Neurodegenerative Disease Research

DAMNDPATHS

Elucidation of common transcriptional targets in vulnerable DopAmine, MotorNeuron and frontotemporal Dementia disease PATHwayS

Our goal is to identify shared molecular pathways leading to selective neuronal cell death in a group of clinically distinct neurodegenerative diseases. We will start with three devastating motor neuron diseases: amyotrophic lateral sclerosis (ALS), spinal muscular atrophy and spinobulbar muscular atrophy - all characterized by the loss of neurons that control voluntary muscles. Genetic causes of these diseases are different, but the patterns of neuronal degeneration are similar.

We will use RNA sequencing technology to identify genes that are activated in either vulnerable or degeneration-resistant neurons during disease progression. Targets will be verified in post mortem tissues from ALS patients, as well as Fronto-temporal dementia and Parkinson's Disease patients, to evaluate cross-disease relevance of the genes. We will then use cellular disease models based on patient-specific neurons from induced pluripotent stem cells, to examine the function of candidate genes in neuronal vulnerability or resistance. Finally, we will examine the ability of selected genes to modify disease progression in vivo in mouse models.
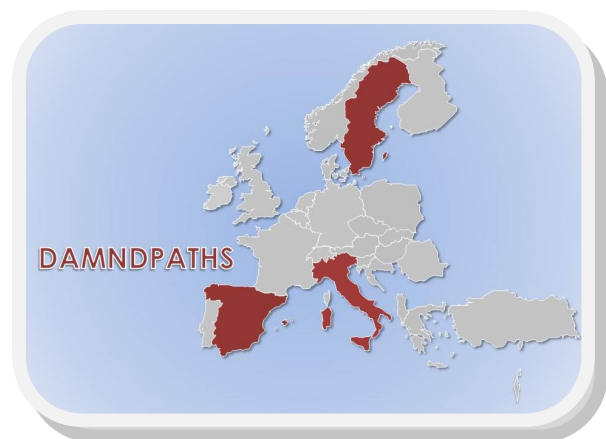
We are confident that these complementary approaches will lead us to discover key pathways at a stage of disease that may still be reversible, thus opening new avenues for the development of disease-modifying agents that can alleviate the burden of these devastating diseases.
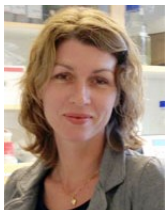
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* Contributions from participating JPND Member Countries are currently being finalised for this project