TAGCNINE

TArGeting C9ORF72 function in ALS/FTD

Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) are fatal adult-onset neurodegenerative diseases characterized by the degeneration of neurons in motor and frontal cortices with a comparably high cumulative lifetime risk (1 in 400 for ALS, 1 in 740 for FTD) and substantial patient-to-patient phenotypic variability. Socio-economic needs for advances in the treatment of these diseases in aging societies are therefore more pressing than ever. While in the past decade we have witnessed enormous progress in defining molecular alterations associated with ALS and FTD, many uncertainties and inconsistencies remain that have so far limited the development of therapies to cure these devastating diseases.

Our transnational team proposes a multidisciplinary approach to test the central hypothesis that C9ORF72 mutation causes ALS/FTD via combined loss of physiological and gain-of-toxic functions that converge on the endolysosome system and the generation of extracellular vesicles. TAGCNINE comprises a multi-national group of experts in complementary fields ranging from neuroscience, biochemistry and cell biology to in vitro modelling, and neurology/epidemiology. By integrating molecular analyses in human models of increasing complexity with information derived from epidemiological and biochemical data from ALS/FTD patients, we aim to unravel the cascade of events by which loss of C9ORF72 and C9ORF72 mutations in motoneurons and in glia cause neurodegeneration.

Our results will predict nodes and reveal novel targets in C9-ALS/FTD and lay the foundations of a pre-clinical drug testing platform for ALS/FTD. Given the phenotypic similarities and clinical overlap between ALS, FTD, and ALS-FTD we expect our studies to be of general importance for the treatment of these devastating diseases.

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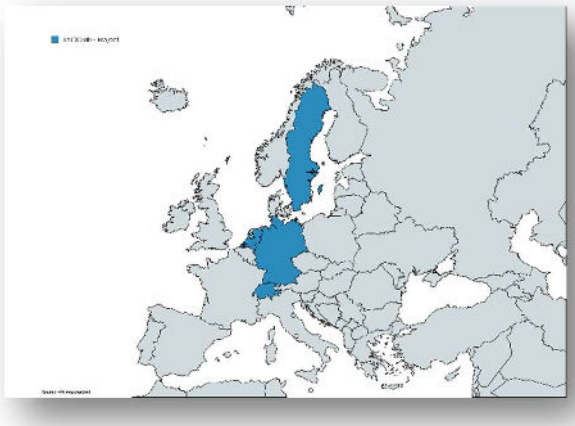

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