AD-PLCG2

Towards druggable targets in Alzheimer's disease through characterization of PLCG2-related path-ways in neurons and microglia

Alzheimer's disease (AD) has an important genetic component and among the genetic factors characterized, the PLCG2 gene is of major therapeutic interest, because it harbours a reported protective variant with a hypermorphic effect on enzyme function. The pathways and interaction partners of this gene/protein may therefore provide promising candidates for the discovery of new drug targets for AD. However, It may be more relevant to target a factor upstream or downstream in the pathophysiological pathways dependent on PLCG2, rather than PLCG2 itself. In addition, this gene has been studied mainly in microglia due to its reported specific expression in only this cell type. However, this gene is also expressed in other cell types, especially in glutamatergic neurons, and we were able to show that PLCG2 is present in synapses and involved in synaptic connectivity. Thus, our preliminary results point out multiples functions of PLCG2 in the brain.

In this context, our consortium proposes a project to characterize PLCG2-related pathways in human induced neurons/microglia and animal models and the selection of the most promising drug targets within these pathways through comprehensive omics analyses, integrated experimental and computational systems biology approaches, and access to large population-based cohorts to facilitate the translation of genetic findings into dis-ease modulation approaches.

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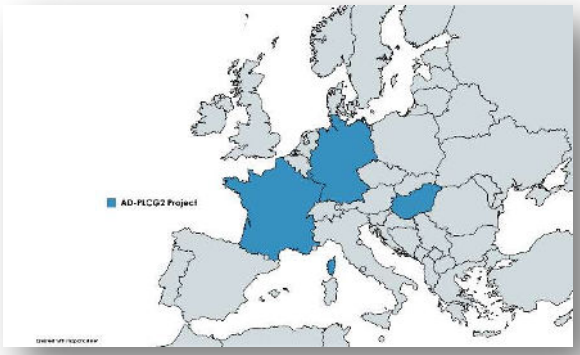

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