

## InCure

### Innate Immune Activation in Neurodegenerative Disease

The mammalian central nervous system is an intricate and fragile structure which on one hand is open to change in order to store information, but at the same time is vulnerable to damage from injury, pathogen invasion or neurodegenerative diseases (NDs). Microglia, representing the brain's innate immune system, execute a number of physiological functions important for the maintenance of tissue homeostasis, synapse remodelling and neurotrophic factor secretion. In NDs and more particular upon chronic exposure to aberrant proteins or RNA, microglia mount a persistent sterile and proinflammatory immune response and neglect their physiological and beneficial functions. This chronic innate immune activation contributes to disease development and progression.

The central aim of InCure is to study this innate immune activation by combining a systems biological approach and functional analysis of the three most frequent NDs: Alzheimer's disease (AD), Parkinson's disease (PD) and Fronto-Temporal-Dementia (FTD), all of which have been described to harbour an inflammatory disease component.

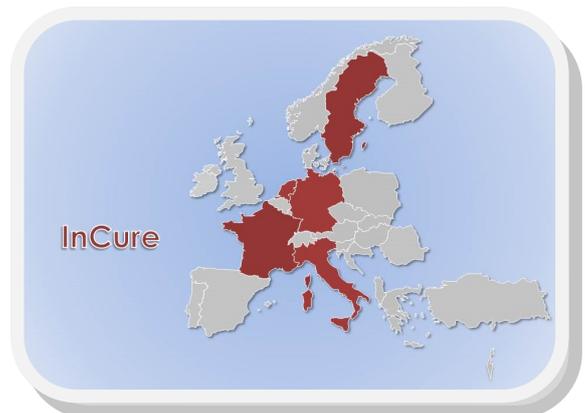
Microglial and neuronal gene network hubs, modules and checkpoints will first be analyzed on a cellular level using disease relevant immunostimulants. Next, these findings will be replicated using state-of-the-art animal models of AD, PD and FTD. Our goal is to identify shared and overlapping networks and compare those to changes of functional readouts. Importantly, we will valorize our findings by analysing human microglial cells and brain tissue derived from AD/PD/FTD patients. Furthermore we will assess whether identified network changes correlate to disease phenotypes and progression using CSF samples from AD, PD and FTD patients. The unique strength of our research consortium is that it combines different expertise from the field of neurology, experimental neuroscience, neuropathology and systems biology. It is essential to reveal these common network hubs and checkpoints to identify new diagnostic biomarkers but also to gain insights into prevention and early treatment of these NDs.

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