

# LODE

## Loss of neurotrophic factors in neurodegenerative Dementias: Back to the crossroads of proteins

Neurodegenerative dementias are characterised by a continuous loss of neurons that are not replaced. Why neurons die in disease-affected brain regions is still a matter of discussion. This project explores a key common pathological mechanism across the three major neurodegenerative diseases leading to dementia: Alzheimer's disease, Frontotemporal dementia, and Lewy body dementia. Specifically, our project aims at deciphering the link between neurotrophic factors and exosomes in neurodegenerative dementias. Exosomes are part of the family of "bioactive vesicles". Their role in the bloodstream, where the distal communication between cells is crucial, has been extensively described in particular related to the immune system. Exosomes secretion can be used by cells – including neurons – to discard molecules or to exchange molecules.

We imagine that, in a "rarefied" neuronal network, occurring invariably during ageing, exosomes could be the key player of neuronal communication: accordingly, survival of neurons could be easily affected by factors modulating exosomes release and/or composition. If successful, the project may open new perspectives in the dementia field, help to translate recent advances in exosome research into the clinical context for a more accurate and early diagnosis of dementia, foster nanotechnology approaches for brain drug delivery in neurodegenerative dementias and foster the development of tailored assays.

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**Coordinator:** Roberta Ghidoni  
 E: [rgidoni@fatebenefratelli.eu](mailto:rgidoni@fatebenefratelli.eu)  
 T: +39-030-3501725




### Project Partners:



COORDINATOR | ROBERTA GHIDONI

 **Roberta Ghidoni**, IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia, Italy

**Giuseppe Di Fede**, Foundation IRCCS Carlo Besta Neurological Institute, Milan, Italy

 **Katharina Landfester**, Max Planck Institute for Polymer Research, Mainz, Germany

 **Maria Grazia Spillantini**, University of Cambridge, Cambridge, UK

#### External collaborators (no funding):

 **Christine Van Broeckhoven/Julie van der Zee**, VIB-UAntwerp Center for Molecular Neurology, University of Antwerp, Belgium

 **Efrat Levy**, NYU Langone Medical Center, Nathan S. Kline Institute for Psychiatric Research, Orangeburg, NY, USA