Memorandum of Understanding

between

University of Foggia - Department of Clinical and Experimental Medicine - Italy,

and

Collège de France, Université PSL, Center for Interdisciplinary Research in Biology (CIRB) France.

The University of Foggia and the Collège de France, believing the extension and strengthening of exchange and cooperation to be of mutual value to their Institutions and to the development of understanding between peoples, hereby record their intentions to promote academic and scientific collaboration between their institutions.

This Memorandum of Understanding (MoU) sets for the terms and understanding between the Partners, University of Foggia and Collège de France, to collaborate and create a a European network in order to develop research proposals suitable for application to forthcoming calls in the framework of Horizon Europe projects (HorizonEU 2021-2027).

Background

In recent decades, an increasing number of preclinical and clinical studies on gut-brain axis is revealing the impact of the intestinal microbial communities on the development, function and pathophysiology of the central nervous system (CNS) [Cryan et al 2020].
Probiotics are symbiotic live microbes that promote the health of the host [Hill et al. 2014]. Postbiotics are non-viable, inactivated probiotics, i.e. their cellular components and secreted metabolites, that exhibit similar health-promoting properties [Salminen et al. 2021]. The term *psychobiotics* has been recently coined to designate a subgroup of beneficial microorganisms that exert a positive influence specifically on the nervous system and on cognitive functions [Bermúdez-Humarán et al. 2019].
Maturation and function of the microglia, i.e., macrophage cells residing in the CNS, can be regulated by gut microbes [Erny et al. 2015]. Alterations in the immune surveillance and protection of the brain microenvironment, mostly played by microglial cells, contribute to the onset of several CNS diseases, often associated with neuroinflammation, neurodegeneration and aging. Endosymbiotic, probiotic-deriving compounds, such as short-chain fatty acids, can cross the blood-brain barrier, thereby entering the brain parenchyma where they come in contact with

different cell types of the brain tissue, including microglia, possibly modulating neuroinflammation, stress response and other processes connected to relevant phenomena such as neurodegeneration [Dalile et al. 2019]. During the first years of life, i.e., from the late fetal period to infancy, in the so-called window of opportunity, shaping of the infant gut microbiota impacts crucial events of the neurodevelopment, such as myelination, synaptic modelling and maturation of microglia [Borre et al. 2014].

References

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Objectives

-To carry out joint/collaborative research investigating the role of gut microbial metabolites in modulating activity of microglia and their response against neuroinflammation and stress
- To assess the influence of gut microbes on the immune protective function played by microglia in the brain micro-environment
- To investigate the association between dysbiotic gut microbiota and specific neurological disorders

Methods

Through a multidisciplinary approach, research activities will rely on co-colture in vitro systems, ex-vivo experiments, animal models, gene expression, metagenomics and metabolomics studies.

Goals

- Identification of microbial species and/or strains with specific effect on microglia activity and neuroinflammation

- Identification of microbial metabolites (or class of compounds) exerting specific effects on microglia activity and neuroinflammation
- Identification of molecular mechanism underlying gut microbes-brain cross-talk
- Corroborate the relevance of gut-brain communications
- Setting up basis for future microbial-based, gut microbiota-modulating-based treatments of human neurological diseases

Further details on the experimental activities and objectives will be defined in the EU proposal, with wider range of goals and a broader participation of partners.

PARTNERS

The partners involved in this MoU have a solid record of scientific publications related to the topic of interest and potential research within the frame of a forthcoming call in the EU Horizon Programme 2021-2027.

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Both partners are from Academic Institutions that comprise research teams with expertises and laboratories facilities that suit the research area of interest.

Partner I-University of Foggia- Dr. Daniela Fiocco
Expertise in microbiology, host-probiotic interactions, immunomodulation by probiotics and postbiotics, in vitro cell culture systems, culture collection of probiotic strains.

Partner II- Collège de France - Dr. Giampaolo Milior
Expertise in glia- neuron interactions, neuronal and glial cell cultures systems, ex-vivo brain systems, human brain organotypic cultures, animal models of epilepsy.

Purpose of the MoU
The main objective of this MOU is to establish a partnership to co-operate on the study of "Gut microbes-brain connections and related therapeutic perspectives for neurological diseases"

The collaborative work set up through this MoU will allow to prepare a research proposal that could be presented to a forthcoming call of EU Horizon Programme, with the following tentative title "*Gut brain-axis and role of intestinal microbiota in neurophysiology and neuropathology"*

Given its multidisciplinary and crosscutting character, such a topic could suit calls within *Pillar 1-Excellent Science* (European Research Council); as well as *Pillar 2- Global Challenges & European Industrial Competitiveness*- Clusters Health (e.g., Destination 3 "Tackling diseases and reducing disease burden")

Funding
This MoU is not a commitment of funds, but a baseline project for a forthcoming Horizon's projects.

Duration
This MOU may be modified by mutual consent of authorized officials from:
Daniela Fiocco, University of Foggia, Italy
Giampaolo Milior, College de France, France
and come into force from the date of bilateral signature and for a period of two (2) years and may be renewed or terminated at any time upon written notification to the other party.

Contact information

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For the College de France	For the University of Foggia
Name and Title	Name and Title
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Partner signature	Partner signatures