

**UNIVERSITÀ DEGLI STUDI DI GENOVA**  
**AREA RICERCA, TRASFERIMENTO TECNOLOGICO E TERZA MISSIONE**  
SERVIZIO PER IL TRASFERIMENTO TECNOLOGICO E DELLE CONOSCENZE  
SETTORE VALORIZZAZIONE DELLA RICERCA, TRASFERIMENTO TECNOLOGICO E RAPPORTI CON LE IMPRESE

**IL RETTORE**

Vista la Legge 9 maggio 1989, n. 168 - Istituzione del Ministero dell'Università e della ricerca scientifica e tecnologica e ss.mm.ii;

Visto lo Statuto dell'Università degli Studi di Genova;

Visto il Regolamento Generale di Ateneo;

Visto il Regolamento di Ateneo per l'Amministrazione, la Finanza e la Contabilità;

VISTA la legge 7 agosto 1990, n. 241 recante "Nuove norme in materia di procedimento amministrativo e di diritto di accesso ai documenti amministrativi" pubblicata sulla Gazzetta Ufficiale n. 192 del 18/08/1990 e s.m.i.;

VISTO il Decreto del Presidente della Repubblica 28 dicembre 2000, n. 445 (Disposizioni legislative in materia di documentazione amministrativa) e s.m.i.;

VISTO il Decreto Direttoriale MUR n. 341 del 15/03/2022 di emanazione di un Avviso pubblico per la presentazione di Proposte di intervento per la creazione di "Partenariati estesi alle università, ai centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base" nell'ambito del Piano Nazionale di Ripresa e Resilienza, Missione 4 "Istruzione e ricerca" – Componente 2 "Dalla ricerca all'impresa" – Investimento 1.3, finanziato dall'Unione europea – NextGenerationEU";

VISTO il Decreto Direttoriale MUR n. 1553 dell'11/10/2022 di concessione del finanziamento del progetto Codice identificativo PE00000006, Acronimo MNESYS, Titolo "*A multiscale integrated approach to the study of the nervous system in health and disease*", registrato alla Corte dei Conti il 23/11/2022 al n. 2948 e relativi allegati;

CONSIDERATO che l'Università degli Studi di Genova è leader dello Spoke 6, dal titolo "*Neurodegeneration, trauma and stroke*";

CONSIDERATO che gli Spoke possono emanare - nell'ambito dei limiti e con le modalità previste dall'Avviso - "bandi a cascata" finalizzati alla concessione di finanziamenti a soggetti esterni per attività coerenti con il progetto approvato;

VISTA la delibera della seduta del 27 settembre 2023 con cui il Consiglio di Amministrazione dell'Università degli Studi di Genova ha approvato l'emanazione del bando a cascata per organismi di ricerca nell'ambito del Progetto MNESYS - "*A multiscale integrated approach to the study of the nervous system in health and disease* - PNRR M4C2 per lo Spoke 6;

VISTO il Decreto del Direttore Generale n. 5418 del 14 novembre 2023 di nomina del Responsabile

del Procedimento;

VISTO il Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023 di emanazione del Bando a cascata per il finanziamento di proposte di intervento per le attività di ricerca svolte da Organismi di Ricerca nell'ambito del programma di ricerca PE MNESYS "A multiscale integrated approach to the study of the nervous system in health and disease", per lo Spoke 6 dal titolo "Neurodegeneration, trauma and stroke", nell'ambito del PNRR, Missione 4, Componente 2, Investimento 1.3 – finanziato dall'Unione europea – NextGenerationEU (CUP D33C22001340002);

CONSIDERATO che alla data di scadenza per la presentazione delle proposte progettuali, fissata entro e non oltre il giorno 14 dicembre 2023, per la **Tematica F – "Molecular profiling early phases of Parkinson's and Alzheimer's diseases: interaction between inflammatory processes and protein misfolding"** era pervenuta a mezzo PEC all'indirizzo [air3@pec.unige.it](mailto:air3@pec.unige.it) la seguente proposta:

**PROPONENTE: Università Cattolica del Sacro Cuore**

**TITOLO PROPOSTA: PROPHECY – Molecular profiling of early phases of Parkinson and Alzheimer's diseases: focus on behavioral and synaptic dysfunctions**

TENUTO CONTO che la Responsabile del procedimento, Ing. Patrizia Cepollina, ha ritenuto ricevibile, ammissibile e conforme la proposta sopra citata;

CONSIDERATO che nel Bando è previsto che la valutazione di merito tecnico-scientifico dei progetti pervenuti sia affidata ad una Commissione composta da almeno tre esperti esterni al Partenariato, indipendenti e competenti dell'Area tematica dello Spoke;

VISTO il Decreto Rettorale n. 6114 del 20 dicembre 2023 con cui è stato emanato l'Avviso di manifestazione di interesse per la costituzione di un albo di esperti indipendenti a supporto della valutazione di merito dei progetti PNRR presentati sui bandi a cascata del progetto MNESYS – A multiscale integrated approach to the study of the nervous system in health and disease;

VISTO l'Estratto del Verbale della Riunione del 12 febbraio 2024 del Comitato Scientifico del programma di ricerca MNESYS "A multiscale integrated approach to the study of the nervous system in health and disease" che ha approvato la "Rosa di Candidati" per le Commissioni di Valutazione dei Bandi a cascata sul Programma MNESYS;

VISTO il Decreto del Rettore n. 855 del 20 febbraio 2024 con cui è costituito l'Albo a supporto delle valutazioni dei progetti presentati in risposta al bando pubblico per la selezione di proposte progettuali da finanziare nell'ambito delle attività di ricerca dello Spoke n. 6 di cui al programma di "A multiscale integrated approach to the study of the nervous system in health and disease" – MNESYS, a valere sulle risorse del Piano Nazionale di Ripresa e Resilienza (PNRR), Missione 4 "Istruzione e Ricerca", Componente 2 "Dalla ricerca all'impresa", linea di Investimento 1.3 "Creazione di Partenariati Estesi alle università, centri di ricerca, alle aziende per il finanziamento di progetti di ricerca di base";

VISTO il Decreto del Rettore n. 1128 del 5 marzo 2024 con cui è stata nominata la Commissione di

valutazione delle proposte pervenute in risposta al bando a cascata di cui al D.R. n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

ACQUISITO il verbale della Commissione di Valutazione della seduta del 16 aprile 2024 (Prot. n. 37982 del 07/05/2024);

VISTO il Decreto del Rettore n. 2289 del 10 maggio 2024 con cui è stata approvata la graduatoria di merito per la Tematica F – “Molecular profiling early phases of Parkinson’s and Alzheimer’s diseases: interaction between inflammatory processes and protein misfolding”, di cui al bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023, indicato nelle premesse del presente decreto;

TENUTO CONTO che in data 15 maggio 2024 è stata inviata all’Università Cattolica del Sacro Cuore la comunicazione con prot. n. 41934 in cui si rendevano noti gli esiti della procedura e si richiedeva la documentazione propedeutica all’adozione del provvedimento di ammissione del finanziamento;

VISTO che in data 20 maggio 2024 con prot. n. 43814 la documentazione richiesta è stata ricevuta dall’Università degli Studi di Genova che l’ha ritenuta conforme a quanto previsto nel bando a cascata di cui al Decreto del Rettore n. 5439 del 14 novembre 2023 e il Decreto Rettorale n. 5474 del 15 novembre 2023, indicato nelle premesse del presente decreto,

## DECRETA

### ART. 1

L’ammissione a finanziamento del progetto PROPHECY – Molecular profiling of early phases of Parkinson and Alzheimer’s diseases: focus on behavioral and synaptic dysfunctions per la **Tematica F – “Molecular profiling early phases of Parkinson’s and Alzheimer’s diseases: interaction between inflammatory processes and protein misfolding”** con Soggetto proponente l’Università Cattolica del Sacro Cuore – come rappresentato negli Allegati B e C alla proposta presentata con domanda di partecipazione prot. n. 74385 del 13 dicembre 2023.

### ART. 2

L’entità dell’agevolazione concessa, a fondo perduto, ammonta a 149.712,50 euro complessivi come rappresentati nell’allegato C alla proposta presentata con domanda di partecipazione prot. n. 74385 del 13 dicembre 2023. L’agevolazione è pari al 100% dei costi di progetto trattandosi di attività di ricerca fondamentale per Organismi di Ricerca. L’agevolazione è concessa a valere sui fondi PNRR - Programma “A multiscale integrated approach to the study of the nervous system in health and disease” – MNESYS Codice PE00000006 a valere sulla Missione 4, Componente 2, Investimento 1.3, ai sensi del Decreto di concessione n. 1553 dell’11 ottobre 2022, registrato alla Corte dei Conti il 23/11/2022 n. 2948, iscritto al Bilancio di Ateneo sul progetto UGOV 100009-2022-TF-PNRR-PE\_MNESYS\_BAC\_DINOGMI.

### ART. 3

Le attività, come indicate dettagliatamente nell’Allegato B alla domanda di finanziamento, dovranno essere avviate a partire dalla data di sottoscrizione del Contratto e concluse entro e non oltre 12 mesi,

affinché siano rendicontate in tempo utile per consentire la chiusura del Programma PE MNESYS, il cui termine è attualmente previsto al 31 ottobre 2025.

Potrà essere valutata e concessa una sola proroga in presenza di ritardi dovuti a circostanze eccezionali e non dipendenti da scelte del Beneficiario esclusivamente nel caso in cui il MUR, a sua volta, proroghi il termine del Programma MNESYS.

#### ART. 4

Il presente atto sarà pubblicato sul sito UniGe <https://unige.it/progetti-finanziati-dal-pnrr> e laddove la normativa vigente lo richiede.

Il documento informatico originale sottoscritto con firma digitale sarà conservato presso l'Area Ricerca, Trasferimento Tecnologico e Terza Missione.

#### ALLEGATI:

Allegato B – Proposta progettuale

Allegato C – Piano economico-finanziario

#### IL RETTORE

Prof. Federico DELFINO

*(documento firmato digitalmente)*

ANNEX B

**PE00000006**

**“A multiscale integrated approach to the study  
of the nervous system in health and disease”**

**MNESYS**

**SPOKE N. 6**

**Research proposal**

Topic addressed by the project  
(with reference to Annex 2)

**Molecular profiling early phases of Parkinson’s and  
Alzheimer’s diseases: interaction between inflammatory  
processes and protein misfolding**

Acronym **PROPHECY** - Molecular profiling of early phases of Parkinson  
and Alzheimer’s diseases: focus on behavioral and synaptic dysfunctions

- Name of the PIs' host institution for the project **Università Cattolica del Sacro Cuore, Roma**
- Name of the Principal Investigators (PIs) **Paolo Calabresi – Claudio Grassi**
- Proposal duration in months: **12**

- Name and qualification of the Principal Investigator (PI)
- Name and qualification of the co-Principal Investigator (PI)
- Name and qualification of the components the research team

ROLE IN THE PROJECT	NAME	SURNAME	DEPARTMENT	QUALIFICATION	YOUNG (under 40 at 31.12.2023)	F/M
Principal Investigator	Paolo	Calabresi	Neuroscience	Full professor	-	M
co- Principal Investigator (PI)	Claudio	Grassi	Neuroscience	Full professor	-	M
Collaborator	Massimiliano	Mirabella	Neuroscience	Associate professor	-	M
Collaborator	Roberto	Piacentini	Neuroscience	Associate professor	-	M
Collaborator	Francesca	Natale	Neuroscience	Assistant Professor	yes	F
Collaborator	Fabiola	Paciello	Neuroscience	Assistant Professor	yes	F
Collaborator	Federica	Campanelli	Neuroscience	Research Assistant	yes	F
Collaborator	Maria	De Carluccio	Neuroscience	PhD student	yes	F
Collaborator	Federica	Servillo	Neuroscience	PhD student	yes	F

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***Please respect the following formatting constraints: Times New Roman, Arial or similar, at least font size 11, margins (2.0 cm side and 1.5 cm top and bottom), single line spacing.***

## ABSTRACT

Parkinson's disease (PD) and Alzheimer's disease (AD) share several features, including misfolded protein aggregation, neuroinflammation, and cognitive dysfunctions. Clinical trials targeting the formation and propagation of pathological aggregates have failed to meet the primary endpoints, and efficient disease-modifying drugs against alpha-synuclein or amyloid beta and tau proteins via active or passive immunization are still an unmet need in the care of PD and AD patients. New findings suggest that early glial activation and consequent neuroinflammation are key factors in initiating pathological processes.

This project aims to identify specific neuroinflammation profiles in the onset of these two diseases, dissecting the mechanisms by which common determinants are involved in early pathological steps.

*In vivo* animal models of synaptic dysfunction characterized by memory impairment will be employed to define neuroinflammatory hallmarks and their contribution to alterations of synaptic plasticity and social interactions. The translational relevance of this project is predicted by the evidence that 1) in the early phases of PD and AD neuroinflammation plays a significant role; 2) a specific alteration of social and cognitive domains, and in particular social interaction, appears to be a major early clinical feature of disease; 3) both aspects can be treated by pharmacological approaches targeting molecular cascades in the meso-cortico-limbic system.

To demonstrate the mechanisms involved, we will target the identified neuroinflammatory factors through *in vivo* and *ex vivo* pharmacological manipulations to protect or recover synaptic and behavioral alterations in experimental animal models.

Our results hold strong translational potential, bringing to the exploitation of efficient disease profiling tools that would be made available at early phases to counteract the first cognitive decline, even before a clinically established diagnosis of PD and AD.



## RESEARCH PROPOSAL

### Section a. State-of-the-art and objectives

Functional and structural alterations of the limbic system often result in a plethora of behavioral symptoms specifically related to the affective domain. However, such symptoms can also represent a warning signal for other types of central nervous system disorders, such as Parkinson's disease (PD) or Alzheimer's disease (AD), two neurodegenerative disorders characterized by high levels of circulating pro-inflammatory molecules and brain accumulation of misfolded proteins which leads, over years, to cognitive and motor impairments. It has been reported that affective alterations, including depressive behaviors, are prodromal in both PD and AD<sup>1</sup>, preceding cognitive and motor symptoms<sup>2,3</sup>. Indeed, affective alterations share different molecular substrates overlapping with PD and AD. For example, depression is associated with a chronic inflammatory state characterized by increased circulating levels of pro-inflammatory cytokines, such as tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) or interleukin- $1\beta$  (IL- $1\beta$ ), and recent evidence suggests that, in both PD<sup>4</sup> and AD<sup>5</sup>, there is an early glial engagement and consequent neuroinflammatory activity before the development of canonical hallmarks of neurodegeneration, such as increased levels of insoluble aggregates of  $\alpha$ -synuclein, tau and A $\beta$ <sub>42</sub>. Preclinical evidence in PD animal models has shown that anxious/depressive symptoms have been observed in the earliest phases of the disease<sup>6</sup>. Similar results have been reported for AD animal models, where even at a young age, there are already alterations in social interaction, social memory, hedonic behavior, and hypothalamus-pituitary-adrenal stress axis response<sup>7</sup>. Furthermore, affective states are modulated by the interaction of different meso-cortico-limbic circuits, which have been shown to be damaged in the early phases of the disease in both PD and AD models. Although these findings suggest that inflammatory responses are associated with limbic behavioral alterations observable in the earliest phases of the disease, the relationships between inflammation, protein misfolding, and limbic system alterations at the molecular and functional levels are poorly understood.

Our published and preliminary data indicate that two different rodent models developed in our labs, mimicking PD and AD pathology, exhibit inflammatory and affective behavioral alterations in the early phases of the disease. Specifically, we previously published that in an animal model of PD, obtained by intracerebral injection of protofibrillary  $\alpha$ -synuclein ( $\alpha$ -syn Pre-Formed Fibrils, PFF), the first signs of dorsal striatal dysfunction appear as early as six weeks after the surgery<sup>8,9</sup>. New preliminary data using the same model, show that four weeks after the surgery, rodents subjected to motor behavioral tasks, such as Walking grid and Rotarod tests, exhibit normal locomotor activity and coordination similar to control animals (Fig. 1A, left panel). At this early time point, the main form of synaptic plasticity in the dorsolateral striatum, the long-term potentiation (LTP), is regularly expressed by spiny projection neurons (SPNs) of PFF-injected rats (Fig. 1A, right panel). Thus, we investigated whether, at this earlier time point, non-motor behaviors were changed, and we observed that  $\alpha$ -syn-PFF rats display a clear deficit in free social approach interactions (Fig. 1B, left panel), leading us to hypothesize that this time point can be considered the beginning of a prodromal phase in which social defects appear before motor impairment. Moreover, in contrast with the intact plasticity in the dorsal striatum, we found that LTP in the SPNs of the Nucleus Accumbens core (NAc) was absent, indicating that at this stage of the disease, plasticity is selectively affected in this limbic area (Fig. 1B, right panel).

In the neuroinflammation-AD model of Herpes Simplex Virus-1 infection (HSV-1 AD), obtained by repeated reactivations of HSV-1 replication, triggering brain inflammation and accumulation of misfolded aggregates that lead to the development of an AD-like phenotype<sup>10</sup>, we observed increased anxious behavior in the open field test (Figure 1C). As previously reported<sup>10-12</sup>, the HSV-1 AD animals subjected to thermal stress-inducing HSV-1 reactivation show increased levels of pro-inflammatory cytokines, including IL- $1\beta$  in the hippocampus, accompanied by synaptic plasticity and learning and memory deficits. Notably, during the first rounds of viral reactivations, learning and memory deficits critically depended on neuroinflammation as the IL- $1\beta$  receptor antagonist, anakinra, rescued the AD-like phenotype. After multiple reactivations, there was a substantial increase in the accumulation of tau and A $\beta$ <sub>42</sub>, mimicking AD progression.

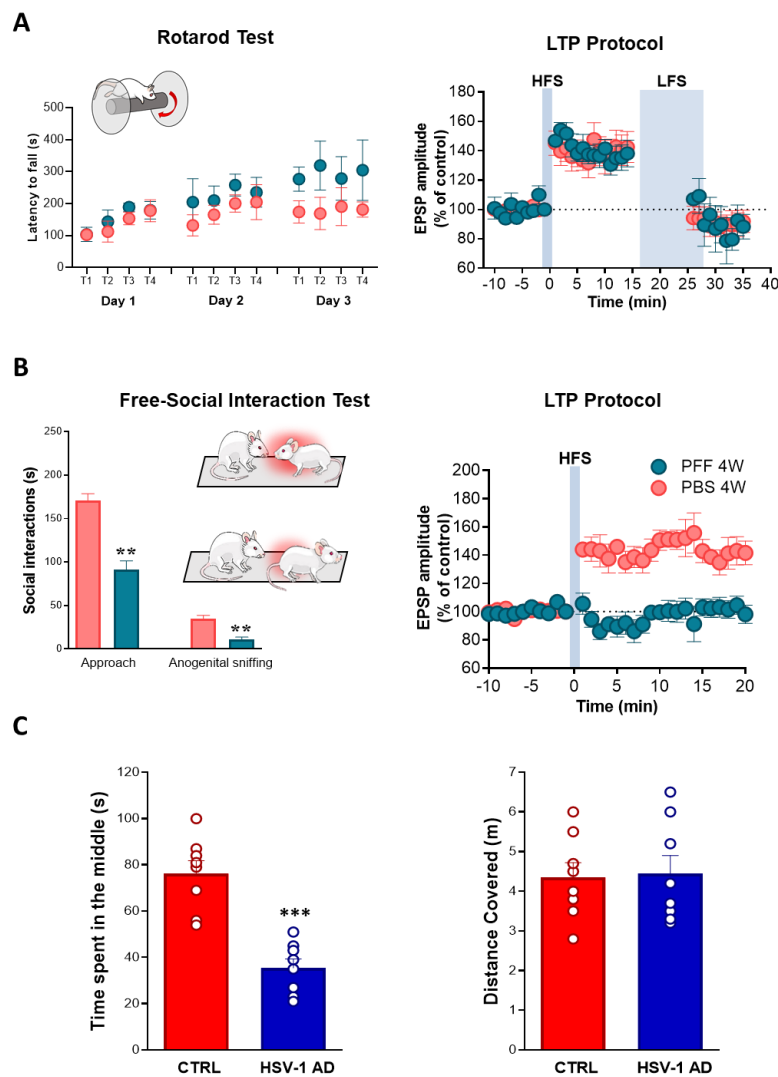


Figure 1. Preliminary data

**A) Modelling premotor stage of PD.** Four weeks post-surgery, PFF-injected rats (PFF, blue) showed no deficit in motor learning compared to the control (PBS, red) group. Ex vivo patch clamp recordings from dorsolateral corticostriatal slices show that  $\alpha$ -syn-PFF-injection did not exert detrimental effects on bidirectional synaptic plasticity of striatal SPNs. **B) Social deficit during pre-motor PD.** During 15-minute free interaction PFF animals interacted less than PBS rats, indicating a deficit in social interaction. Ex vivo patch clamp recordings from nucleus accumbens (core) neurons show that  $\alpha$ -syn-PFF-injection blocks long term potentiation. **C) Anxiety behavior in HSV-1 AD mice.** One week after the second HSV-1 reactivation, animals were subjected to the open field test, for the evaluation of anxious behavior and locomotor activity. HSV-1 AD showed a significant reduction of the time spent in the middle of the open arena (left histogram), independently from locomotor activity. \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

Both rodent models mimic some of the characteristic neuroinflammatory features that guide the progression of PD and AD, respectively and set the ideal conditions for us to study how alterations in the affective domain develop at the early stages of the diseases. The effect of  $\alpha$ -synuclein injection in the dorsal striatum is able to generate progressive parkinsonism. However, whether the early phases are characterized by impairment of social



behavior, which requires an intact ventral striatum, particularly the NAc, has never been investigated. Similarly, the impact of HSV-1 reactivation on affective and social aspects of behavior remains to be investigated.

Based on evidence from the scientific literature and our preliminary data, the main goal of this project is to identify shared inflammatory profiles at pre-prodromic phases of PD and AD, impinging on the function of the limbic system. The specific aims of the project are:

- 1) to characterize meso-cortico-limbic functional alterations at early phases of the pathology in the 2 animal models of PD and AD;
- 2) to identify the relationship between the observed phenotypes and inflammatory signaling in key brain regions of the limbic system.

### **AIM 1: TO CHARACTERIZE MESO-CORTICO-LIMBIC FUNCTIONAL ALTERATIONS AT EARLY PHASES OF THE PATHOLOGY IN THE 2 ANIMAL MODELS OF PD AND AD**

We will perform behavioral and electrophysiological experiments on the previously described animal models: 1) the PD model will be evaluated 4 weeks after the injection of protofibrillary  $\alpha$ -synuclein, when only social deficits are observed; 2) the HSV-1 AD model will be evaluated after two viral reactivations. Aim 1 will be organized into two different tasks.

#### **Task 1.1. Characterization of affective behavior of the HSV-1 AD and PD rodent models.**

Seventy-two hours after the second reactivation, HSV-1 AD animals will be evaluated using multiple behavioral tests to assess social interaction, preference, and memory. The same experimental approach will be used for the PD model 4 weeks after the intracerebral injection of  $\alpha$ -syn. For all tests, data analysis will be performed using commercially available software (i.e., ANY-maze™) and recent open-source software packages such as DeepLabCut or KeyPoint-MoSeq, which leverage the power of artificial intelligence to analyze and classify rodent behavior.

**Task 1.2. Functional and molecular assessment of meso-cortico-limbic alterations.** After behavioral analyses, animals will be sacrificed, and the brain will be collected for further experiments. Specifically, ex-vivo patch-clamp electrophysiology will be performed on the dorsolateral striatum and NAc SPNs to record excitability, synaptic plasticity, transmission, and membrane intrinsic properties. Immunofluorescence and Western blot techniques will be employed to assess molecular alterations. For immunofluorescence analyses, synaptic proteins, such as PSD-95, and markers of activated glial cells (e.g., Iba1/TMEM119, CD68, F4/80, CD86, and GFAP), will be studied. ELISA and Western blot will be employed to quantify the expression of pro-inflammatory cytokines and the levels of aggregated misfolded proteins in samples from the dorsal and ventral striatum and prefrontal cortex.

**Milestone 1. Description of functional and molecular alterations in the meso-cortico-limbic system in early AD and PD mouse models.**

### **AIM 2: TO IDENTIFY THE RELATIONSHIP BETWEEN THE OBSERVED PHENOTYPES AND INFLAMMATORY SIGNALING IN KEY BRAIN REGIONS OF THE LIMBIC SYSTEM.**

Based on results obtained in Aim 1, anti-inflammatory treatment with either the IL-1 $\beta$  receptor anakinra (30 mg/Kg, i.p.) or dexamethasone (5 mg/kg, i.p.) will be used to counteract the detrimental effects of exaggerated inflammatory response in our AD and PD rodent models.

#### **Task 2.1. Impact of inflammatory responses on social behavior of the HSV-1 AD and of PD rodent models.**

Behavioral analyses described in Task 1.1 will be repeated after anti-inflammatory treatments. Specifically, HSV-1 AD mice will receive 3 injections, one per day, during the first round of virus reactivation and 3 more during the second reactivation procedure. PD mice will receive 8 injections, 2 per week, in the 4 weeks following  $\alpha$ -synuclein intracerebral injection.

**Task 2.2. Evaluation of the inhibition of pro-inflammatory cytokine signaling on meso-cortico-limbic molecular alterations.** At the completion of behavioral analyses, animals will be sacrificed, and the brain will be collected to perform electrophysiological and molecular analyses described in Aim 1, task 1.2.

**Milestone 2. Assessment of the role of neuroinflammation in meso-cortico-limbic alterations observed at early stages of AD and PD.**

The expected results of this project will allow us to identify and characterize the meso-cortico-limbic system alterations occurring at early phases of PD and AD and will shed light on the dependency of such deficits on aberrant inflammatory signaling and misfolded protein accumulation. The current proposal holds a translational solid value, as demonstrating a causal link between inflammation and affective behavior alterations in PD and AD will help develop novel early diagnostic criteria and tailored pharmacological interventions for these two neurodegenerative disorders.

## Section b. Methodology

We propose that at the early stages of PD and AD, altered inflammatory signaling and protein misfolding in brain regions of the limbic system affect emotions and affective behavior. To test our working hypothesis, we will characterize the previously described rodent models of  $\alpha$ -syn PFF rat and HSV-1 AD mouse using molecular, electrophysiological, and behavioral approaches.

### Methods

**Model development:** Wistar adult rats will be bilaterally injected into the dorsomedial striatum with PBS (as the vehicle) or  $\alpha$ -synuclein protofibrils ( $\alpha$ -syn-PFFs), prepared as previously reported<sup>13</sup>. C57/B16 mice will be infected with HSV-1 and subjected to viral reactivation as previously reported<sup>10</sup>.

**Behavioral analyses:** social interaction tests will be performed as described in<sup>14</sup>.

**Electrophysiological recordings:** *ex vivo* patch-clamp and intracellular recordings will be carried out as previously reported<sup>13,15</sup> to measure basal electric membrane properties, synaptic currents, and synaptic plasticity of SPNs in the dorsolateral striatum and NAc in corticostriatal slices.

**Immunofluorescence (IF) and Western blot (WB) analyses.** IF and WB will be performed as previously described in<sup>10</sup>.

**Statistical analyses.** Sample size will be calculated using custom-made Python scripts and will be based on previously published and unpublished data. Specifically, a 5% type I error and 80% power will be considered. For statistical comparisons, parametric or non-parametric tests will be used, as appropriate. The behavioral experiments will be analyzed using two-way ANOVA with treatment, using repeated measures. An appropriate post hoc analysis will be used when necessary. For electrophysiology, a Student's t-test for paired samples will be used to compare the synaptic parameters. Comparisons between the two conditions in terms of synaptic plasticity responses will be made using repeated measures two-way ANOVA at each time point. The significance level will be established at  $p < 0.05$ .

**Ethics statement.** All animal procedures will follow the EU Directive 86/609/EEC, which has been implemented in the Italian national law D.Lgs. 26/2014, art.31. All procedures have already been approved by the ethical committee on animal experimentation of the Catholic University of the Sacred Heart. All experiments have been designed according to the 3Rs principles (refine, replace, reduce).

### Section c. Available instrumentations and resources

All the necessary instruments and resources for the current proposal are already present at the host institution. Specifically, animals will be bred and housed at the Gemelli Science and Technology Park (GSTeP) facility of Experimental models, where all *in vivo* manipulations, behavioral paradigms, and animal model setups will be performed. Electrophysiological recordings will be performed at the GSTeP electrophysiology facility, which is fully equipped to measure neuronal electrical properties, synaptic transmission, and plasticity in *ex vivo* brain slices with patch-clamp and intracellular recordings. Molecular analyses will also be performed using instruments already available at the host institution, such as Uvitec Alliance chemiluminescence for Western blot analysis and the Nikon confocal microscope for immunofluorescence analyses. The research team involved in this project has long-standing experience in stereotaxic surgery, model preparation, behavioral analysis, and patch-clamp or intra/extracellular *ex vivo* recordings. In particular, the lab members have experience in extracellular, intracellular, and patch-clamp recordings on cortico-striatal, NAc, and hippocampal slices to study neuronal membrane properties, synaptic transmission, and plasticity. The PI and Co-PI experience on the previously described animal models is well documented by many papers published in international scientific journals with high impact factors and by several grants awarded. Finally, the ethical committee of the PI and Co-PI institution has already approved the procedures for animal experimentation, and a request for amendment of the experimental protocols can be submitted to the Ministry of Health.

### Section d. GANTT diagram

Milestones	YEAR 1											
	1	2	3	4	5	6	7	8	9	10	11	12
<b>ACTIVITIES</b>												
<b>AIM 1. TO CHARACTERIZE MESO-CORTICO-LIMBIC FUNCTIONAL ALTERATIONS AT EARLY PHASES OF THE PATHOLOGY IN THE 2 ANIMAL MODELS OF PD AND AD</b>												
Task 1.1. Characterization of affective behavior of the HSV-1 AD and PD rodent models.												
Task 1.2. Functional and molecular assessment of meso-cortico-limbic alterations.												
Milestone 1. Description of functional and molecular alterations in the meso-cortico-limbic system in early AD and PD mouse models.												
<b>AIM 2. TO IDENTIFY THE RELATIONSHIP BETWEEN THE OBSERVED PHENOTYPES AND INFLAMMATORY SIGNALLING IN KEY BRAIN REGIONS OF THE LIMBIC SYSTEM.</b>												
Task 2.1. Impact of inflammatory responses on social behavior of the HSV-1 AD and of PD rodent models.												
Task 2.2. Evaluation of the inhibition of pro-inflammatory cytokine signaling on meso-cortico-limbic molecular alterations.												
Milestone 2. Assessment of the role of neuroinflammation in meso-cortico-limbic alterations observed at early stages of AD and PD.												
<b>DISSEMINATION OF RESULTS</b>												
Monitoring project implementation												
Educational seminars												
Dissemination of results (scientific meetings)												
Manuscript preparation												
	1	2	3	4	5	6	7	8	9	10	11	12

## Bibliography

1. Lyketsos CG, Carrillo MC, Ryan JM, et al. Neuropsychiatric symptoms in Alzheimer's disease. *Alzheimers Dement* 2011;7(5):532-539.
2. Citro S, Lazzaro GD, Cimmino AT, Giuffre GM, Marra C, Calabresi P. A multiple hits hypothesis for memory dysfunction in Parkinson disease. *Nat Rev Neurol* 2023.
3. Henry JD, von Hippel W, Molenberghs P, Lee T, Sachdev PS. Clinical assessment of social cognitive function in neurological disorders. *Nat Rev Neurol* 2016;12(1):28-39.
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6. Hayley S, Vahid-Ansari F, Sun H, Albert PR. Mood disturbances in Parkinson's disease: From prodromal origins to application of animal models. *Neurobiol Dis* 2023;181:106115.
7. Varkonyi D, Torok B, Sipos E, et al. Investigation of Anxiety- and Depressive-like Symptoms in 4- and 8-Month-Old Male Triple Transgenic Mouse Models of Alzheimer's Disease. *Int J Mol Sci* 2022;23(18).
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11. De Chiara G, Piacentini R, Fabiani M, et al. Recurrent herpes simplex virus-1 infection induces hallmarks of neurodegeneration and cognitive deficits in mice. *PLoS Pathog* 2019;15(3):e1007617.
12. Marcocci ME, Napoletani G, Protto V, et al. Herpes Simplex Virus-1 in the Brain: The Dark Side of a Sneaky Infection. *Trends Microbiol* 2020;28(10):808-820.
13. Marino G, Campanelli F, Natale G, et al. Intensive exercise ameliorates motor and cognitive symptoms in experimental Parkinson's disease restoring striatal synaptic plasticity. *Sci Adv* 2023;9(28):eadh1403.
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15. Mineo D, Cacace F, Mancini M, et al. Dopamine drives binge-like consumption of a palatable food in experimental Parkinsonism. *Mov Disord* 2019;34(6):821-831.



## Curriculum vitae of the PI (max. 2 pages)

### PERSONAL INFORMATION

Family name, First name: Calabresi, Paolo;

Researcher unique identifiers: **ORCID: 0000-0003-0326-5509; Scopus ID 7102418853, 662 articles, H-index 98, citations 34026;**

Date of birth: 20th January 1956;

Nationality: Italian;

URL for website: <https://docenti.unicatt.it/ppd2/en/docenti/78620/paolo-calabresi/profilo>

### • EDUCATION

1988 Postdoc fellow at the Oregon Health Science University-Neuropharmacology, USA

1984-1985 Postdoc fellow at the Max Planck Institute, Neurophysiology, Munich, Germany

1985 Specialization in Neurology cum Laude, University "La Sapienza", Rome

1981 Degree in Medicine and Surgery cum Laude, University "La Sapienza", Rome

### • CURRENT POSITION(S)

2019-present Full Professor of Neurology and Chairman of Neurology, Fondazione IRCCS Policlinico Gemelli, Università Cattolica del Sacro Cuore (UCSC), Rome

2019-present Director of the Post-graduate School of Neurology of Fondazione IRCCS Policlinico Gemelli, UCSC, Rome

2019-present Coordinator of the Neuroscience PhD program of the Dept. Neuroscience Fondazione IRCCS Policlinico Gemelli, UCSC, Rome

### • PREVIOUS POSITIONS

2005-2019 Full Professor of Neurology and Chairman of Neurology, Director of the Post-graduate School of Neurology and Coordinator of the Neuroscience and of the Molecular and Clinical Medicine PhD program, University of Perugia

1999-2004 Associate Professor in Neurology, University Tor Vergata, Rome

1986 -1998 Assistant Professor in Neurology, University Tor Vergata, Rome

### • FELLOWSHIPS AND AWARDS

2020-2022 President of the Italian Society for Neuroscience (SINS)

2008 Award "John B. Penney Memorial Lecture" from the Massachusetts General Hospital, Dept. Neurology and Harvard University

2002 Elected Corresponding Member of the American Neurological Association

1997 Italian Neuroscience Association Prize for Basic and Clinical Research in Neuroscience

1992-1996 Nominated External Reviewer for the *Human Frontier Science Program Organisation*

1987 Farmitalia Prize for Neurology 1987 C.N.R. Grant for Travel Fellowship

1983 European Science Foundation Fellowship

### • SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)

1986-present 37 postdocs and 50 PhD students at Tor Vergata, Perugia and UCSC Universities, most of whom have now independent PI positions as associate and full professors;

2005-present Director of Neurology and Neuroscience specialization courses

### • ORGANISATION OF SCIENTIFIC MEETINGS (if applicable)



I have organized several international meetings on Biomarkers of Neurodegenerative diseases and on preclinical and clinical aspects of Parkinson's disease (e.g.FENS forum 2018, 5th World Parkinson Congress 2019, 18th SINS Congress).

- **INSTITUTIONAL RESPONSIBILITIES**

2020-present Director of the Post-graduate School of Neurology and Coordinator of the Neuroscience PhD program, Catholic University, Rome

2005-2020 Coordinator of the Neuroscience and of the Molecular and Clinical Medicine PhD program, University of Perugia.

- **REVIEWING ACTIVITIES**

External reviewer for ERC 2020 consolidator grant, INSERM (France), ANR, Italian Ministry of Health, Italian Ministry of Education. I am Member of the Editorial Board of Lancet Neurology, Neurobiology of Disease, Journal of Parkinson's Disease, Synapse and Current Neuropharmacology, The Journal of Neuroscience and Movement Disorders Journal.

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES**

I have been part of the governing board of the Italian Neurological Society (SIN) and the Italian Neuroscience Society (SINS). I have been elected a Corresponding Member of the American Neurological Association. I am a member of the Movement Disorders Society, Accademia LIMPE/DisMov, and the European Academy of Neurology.

- **MAJOR COLLABORATIONS (if applicable)**

I coordinate a research group of preclinical and clinical scientists, including about 50 members. I had a long-standing collaboration with Prof. P. Greengard (Nobel Prize in Physiology or Medicine 2000) in the field of DA signaling, and I fostered several clinical and preclinical research collaborations with internationally leading groups (A. Bjorklund, A. Cenci (Lund), E. Bezard (Bordeaux), J. Obeso (Madrid), E. Hirsch (Paris), J. Rothwell (London), A. Graybiel (Boston), M.G. Spillantini (Cambridge), S. Papa (Atlanta).



**Curriculum vitae of the Co-PI (max. 2 pages):**

**PERSONAL INFORMATION**

Family name, First name: Grassi, Claudio;

Researcher unique identifiers: **ORCID: 0000-0001-7253-1685; Scopus Author ID 7101807658, 164 articles, H-index 45, citations 6480;**

Date of birth: 17/12/1956;

Nationality: Italian;

URL for website: <https://docenti.unicatt.it/ppd2/en/docenti/46420/claudio-grassi/profilo>

• **EDUCATION**

1987 PhD in Neuroscience, Università Cattolica Medical School (Rome, Italy)

1986 Post-doctoral specialization in Neurology from Università Cattolica Medical School

1982 MD degree (summa cum laude) from Università Cattolica Medical School

• **CURRENT POSITION(S)**

2019-present Head of the Department of Neuroscience, Università Cattolica Medical School

2018-present Member of the Scientific Committee of “Fondazione A. Gemelli IRCCS”

2014-present Member of the Università Cattolica Board for Research Quality Assessment (PQA)

2005-present Professor of Physiology, Università Cattolica Medical School

• **PREVIOUS POSITIONS**

2018-2022 Deputy Dean of the Medical School, Università Cattolica Medical School

2009-2019 Director of the Institute of Human Physiology, Università Cattolica Medical School

2009-2014 Coordinator of the Bachelor Course in Nursery, Università Cattolica Medical School

2006-2015 Member of the Scientific Committee of the University Hospital “A. Gemelli” in Rome

1998-2005 Associate Professor, Università Cattolica Medical School

1988-1998 Assistant Professor, Università Cattolica Medical School (Rome, Italy)

• **FELLOWSHIPS AND AWARDS**

2021-present President – Italian National Board of Full Professors of Physiology

• **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS**

1988-present More than 15 postdocs and over 25 PhD students at Università Cattolica Medical School.

• **INSTITUTIONAL RESPONSIBILITIES**

2022-present President “Cattolica-TJU Research” s.r.l.

2019-present Head of the Department of Neuroscience, Università Cattolica del Sacro Cuore

2014-present Member of the Università Cattolica Board for Research Quality Assessment (PQA)

2010-2016 Coordinator of the PhD program in Biophysics, Università Cattolica Medical School

2009-present Faculty Member of the PhD program in Neuroscience, Università Cattolica Medical School

• **REVIEWING ACTIVITIES**

Editorial Board Member: *Scientific Reports; Frontiers in Molecular Neuroscience, International Journal of Molecular Sciences, Frontiers in Aging Neuroscience, Frontiers in Synaptic Neuroscience.*

Ad hoc reviewer for numerous scientific journals.

**Reviewer for Research Grant Agencies:** French National Research Agency (ANR); Medical Research Council (UK); FWF (Austrian Science Fund); Alzheimer’s Association (USA); Diabetes (UK); COST (EU); ATIP-Avenir (Francia); Israel Science Foundation (ISF); DFG (German Research Foundation); Flagship ERA-NET (EU); Belgian Alzheimer Foundation (SAO, BE); MIUR: PRIN, Futuro in Ricerca, SIR.

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES**

Society for Neuroscience (SfN); ISTAART; Italian Society of Physiology; Italian Society for Neuroscience (SINS)

- **MAJOR COLLABORATIONS**

Prof. Ottavio Arancio, Dept. of Pathology and Taub Institute for Research on Alzheimer's Disease and Aging Brain, Columbia University - New York, USA; Prof. Yasunori Hayashi, Dept. of Pharmacology, Kyoto University Graduate School of Medicine, Kyoto, Japan; Prof. Fernanda Laezza, Dept. of Pharmacology and Toxicology, University of Texas Medical Branch - Galveston, USA.

**Appendix: All current grants and on-going and submitted grant applications of the PI (Funding ID)**

**Current grants (Please indicate "No funding" when applicable):**

<i>Project Title</i>	<i>Funding source</i>	<i>Amount (Euros)</i>	<i>Period</i>	<i>Role of the PI</i>	<i>Relation to current proposal</i>
<b>Clinical, molecular and electrophysiological profiling of Parkinson's Disease: the role of non-pharmacological therapies</b>	Ministero Salute	985,000.00	20/05/2023-20/05/2025	Coordinator	The same experimental PD model with a focus on different areas
<b>Mechanisms underlying therapeutic approaches in an alpha-synuclein-based model of Parkinson's disease: from pharmacological to non-pharmacological strategies</b>	MUR	200,000.00	01/10/2023-01/10/2025	Coordinator	Similar experimental model with different hypotheses and focus on different areas and therapeutic approaches
<b>Motor activity and PD</b>	Jefferson University	200,000.00	02/04/2022 – 02/04/2024	Head of RU	not related
<b>Clinical and preclinical PD</b>	Rete Italiana Neuroscienze	450,000.00	01/01/2021-31/12/2023	Head of RU	not related
<b>Markers in neurodegeneration</b>	Consiglio Nazionale Ricerca	140,000.00	01/01/2021-31/12/2023	Head of RU	not related
<b>Motor function in PD</b>	National Institute of Health	211,600.00	01/01/2019-31/12/2023	Head of RU	not related
<b>Device in neurology</b>	Ministero della Salute	1,000,000.00	25/10/2021-26/10/2024	Coordinator	not related



## Curriculum vitae of each component of the research team:

### (1) PERSONAL INFORMATION

Family name, First name: Mirabella, Massimiliano

Researcher unique identifier: **ORCID: 0000-0002-7783-114X; Scopus Author ID 7003525518, 219 articles, H-index 44, citations 7126;**

Date of birth: 19<sup>th</sup> May 1963;

Nationality: Italian;

### • EDUCATION

2009 PhD in Neuroscience, Catholic University Medical School

1993 Specialization in Neurology Summa cum Laude, Catholic University of the Sacred Heart, School of Medicine, Rome

1989 Degree in Medicine and Surgery, Catholic University of the Sacred Heart, School of Medicine, Rome

### • CURRENT POSITION(S)

2017-present Associate Professor of Neurology, Medicine and Surgery, School of Medicine, Catholic University

### • PREVIOUS POSITIONS

2008-2018 Appointed Professor of Diseases of the central and peripheral nervous system in the residency training program of Emergency Medicine

1999-2009 Appointed Professor of Clinical Neurophysiology, Neurology and Neuroanatomy. School of Neurophysiology, Catholic University, Rome

1999-2003 - Catholic University, Institute of Neurology, Rome - Neurologist 1997-1999 - Catholic University, Institute of Neurology, Rome - Research Assistant

1989-2012- Catholic University, Neuromuscular Pathology and Biochemistry Laboratory, Rome (immunohistochemical, immunopathological and ultrastructural analysis of muscle biopsies; morphological and molecular biology studies, in situ-hybridization, immuno-EM, cell cultures and confocal microscopy)

1989-2004 Center for Neuromuscular Diseases, Unione Italiana Lotta alla Distrofia Muscolare (U.I.L.D.M.), Rome Section - consultant neurologist

### • FELLOWSHIPS AND AWARDS

1998-1999: fellowship from Telethon-Italy for the project "Apoptosis and mitochondrial encephalomyopathies: exploring pathogenic mechanisms".

1996-1998: fellowship from Telethon-Italy for the project "Does apoptosis play a role in inflammatory myopathies?"

1993-1995 and 1996: research fellowship at the Neuromuscular Center del Department of Neurology (University of Southern California, USC) directed by Prof. Valerie Askanas and W.K. Engel.

2010 fellowship from AFM (Association Française contre les Myopathies): "Development of mesoangioblast-based muscle regenerative therapy for inclusion-body myositis"

### • SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)

2011-present Prof. Mirabella trained and supervised more than 40 MD students, more than 25 residents in Neurology and more than 10 PhD student in Neurosciences

### • INSTITUTIONAL RESPONSIBILITIES

2013-present Director of U.O.S. Sclerosi Multipla, Policlinico Universitario "A. Gemelli" IRCCS

2011-present Head of DH of Neurology- Coordinator of Center for Multiple Sclerosis- Policlinico "A. Gemelli"



2008-present Appointed Professor of Neurology in the residency training program of Legal Medicine and Ophthalmology  
2005-present Coordinator of Inflammatory Myopathies outpatients clinic  
2006-present Chief of the Laboratory for diagnosis and research on inflammatory myopathies, stem cells and muscle regeneration (Institute of Neurology, Catholic University)  
2003-present Appointed Professor of Clinical Pathology in the Neurology, and Neurophysiopathology residency training programs, Catholic University, Rome.  
2000-present Coordinator of Multiple Sclerosis outpatient clinic  
2000-present Dirigente medico I livello, Clinica Neurologica, Institute of Neurology, Catholic University, Rome

#### • **REVIEWING ACTIVITIES**

Prof. Mirabella is ad hoc reviewer of many neuroscience and clinical neurology journals (Neurology, Brain, Journal of Clinical Investigation, Nature Medicine, FEBS letters, Cell death and differentiation, Eur J Neurol, Gene, Clinical Immunology, Muscle&Nerve, Neuromuscular Disorders, BMC Neurology, and others) and collaborates as invited reviewer of research applications with several international granting agencies. Member of Editorial Board of Frontiers in Aging Neuroscience as Review Editor; Guest editor for Journal of personalized medicine (Special issue on personalized medicine for Multiple Sclerosis). Member of the Editorial Board of the newly established annual issue of Clinical and Experimental Rheumatology entirely devoted to idiopathic inflammatory myopathies (the official organ of the International Myositis Society committed to host the recommendations and guidelines officially endorsed by the Society)

#### • **MEMBERSHIPS OF SCIENTIFIC SOCIETIES**

Member of the Italian Society of Neurology (SIN) and of the MS study group  
Member of European Society of Microscopy  
Member of Società Italiana di Scienze Microscopiche (Italian Society of Microscopic Sciences)  
Member of the International Myositis Assessment and Clinical Studies Group (IMACS)  
Founder member of Associazione Italiana di Miologia (Italian Association of Myology)  
Member of the World Muscle Society  
Corresponding Associate of American Academy of Neurology  
Member of the steering committee of "Istituto Virtuale Sclerosi Multipla e Disordini Neuroimmunologici" (IVSM), Neurosciences and neurorhabilitation IRCCS network (RIN)  
Member of the panel of experts for Regione Lazio: "a working table to define a regional network model of Multiple Sclerosis Centers"

#### • **MAJOR COLLABORATIONS:**

Giorgio Tasca, John Walton Muscular Dystrophy Research Centre Newcastle University Translational and Clinical Research Institute, UK  
Renato Mantegazza and Lorenzo Maggi, Istituto Neurologico Besta, Milano, Italy  
Claudio Gasperini and MAGNIMS Study Group  
Olga Ciccarelli, UCL Queen Square Institute of Neurology, UK  
Edmondo Campisi and Rashid Rumah, The Rockefeller University, New York, USA

#### **(2) PERSONAL INFORMATION**

Family name, First name: Piacentini, Roberto;  
Researcher unique identifier: **ORCID: 0000-0003-4215-1643; Scopus Author ID 12767233800, 49 articles, H-index 30, citations 2894;**  
Date of birth: 23<sup>rd</sup> November 1973;  
Nationality: Italian;



### • EDUCATION

2009 PhD in Neuroscience, Catholic University Medical School  
2004 PhD in Biophysics, University "Sapienza", Rome  
2000 Degree in Physics, University "Sapienza", Rome

### • CURRENT POSITION(S)

2018-present Associate Professor of Physiology, Università Cattolica Medical School

### • PREVIOUS POSITIONS

2011-2017 Assistant Professor of Physiology, Università Cattolica Medical School  
2009-2011 Postdoctoral fellow at the Institute of Human Physiology, Università Cattolica Medical School  
2004-2006 Fellowship at the the Institute of Human Physiology, Università Cattolica Medical School  
2001-2004 Fellowship at the Department of Human Physiology and Pharmacology, "Sapienza" University

### • FELLOWSHIPS AND AWARDS

2017: high-quality publication award from Università Cattolica del Sacro Cuore.  
2013-2015: Three Awards for the best research at Università Cattolica del Sacro Cuore.

### • SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)

2011-present Prof. Piacentini supervised more than 3 PhD students and several Post-Docs.

### • INSTITUTIONAL RESPONSIBILITIES

2018-present: Faculty Member of the PhD program in "Neuroscience" at Università Cattolica.

### • REVIEWING ACTIVITIES

Prof. Piacentini is a member of the Editorial Board of the peer reviewed international journal "Neural Regeneration Research" and is Associate Editor for the journal "Frontiers in Molecular Neuroscience". Furthermore, he is reviewer for multiple peer-reviewed international journals, such as: Journal of Alzheimer's Disease, European Journal of Pharmacology, Scientific Reports and many more. Finally, Prof. Piacentini is a reviewer for the Italian Ministry of University and Research for the evaluation of multiple grants and also for the Alzheimer's Association.

### • MEMBERSHIPS OF SCIENTIFIC SOCIETIES

2013- Present – member of the Italian Society of Physiology (SIF)  
2009- Present – member of the Society for Neuroscience (SfN)

### • MAJOR COLLABORATIONS (if applicable)

Prof. Piacentini actively collaborates with national and international researchers from different countries, such as: i) Prof. Ottavio Arancio, from Columbia University, New York, USA; ii) Prof. Gal Bitan, UCLA, Los Angeles, USA; iii) Prof. Anna Teresa Palamara, from University "Sapienza", Rome, Italy; iv) Prof. Alfonso Grassi, from Salerno University, Salerno, Italy; v) Prof. Daniela Puzzo, from Catana University, Catania, Italy.

### (3) PERSONAL INFORMATION

Family name, First name: Paciello, Fabiola;

Researcher unique identifier: **ORCID: 0000-0002-8473-8074; Scopus Author ID 12767233800, 42 articles, H-index 19, citations 1212;**

Date of birth: 14<sup>th</sup> June 1987;

Nationality: Italian.





- **EDUCATION**

2016 Professional master's degree in clinical Neuroscience and neuropsychology, LUMSA University, Rome

2014 PhD in Neuroscience, Catholic University Medical School, Rome

2010 Master's Degree in Cognitive neuroscience and psychological rehabilitation, University "Sapienza", Rome

2008 Bachelor's degree in psychology, University "Sapienza", Rome

- **CURRENT POSITION(S)**

2019-present Assistant Professor of Physiology, Università Cattolica Medical School

- **PREVIOUS POSITIONS**

2020 Visiting research at the Italian Institute of Technology, Genova, Italy

2018-2019 Postdoctoral fellow at the Institute of Human Physiology, Università Cattolica Medical School

2016-2018 Postdoctoral fellow at the the Institute of Cellular Biology and Neurobiology, Consiglio Nazionale delle Ricerche, Rome, Italy

2015-2016 Postdoctoral fellow at the Institute of Human Physiology, Università Cattolica Medical School

- **FELLOWSHIPS AND AWARDS**

2021-2022-2023: high-quality publication award from Università Cattolica del Sacro Cuore.

- **SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS (if applicable)**

2019-present Dr. Paciello supervised 2 PhD students.

- **INSTITUTIONAL RESPONSIBILITIES**

2023-present Member of the "Rising Stars" commission, Università Cattolica Medical School

- **REVIEWING ACTIVITIES**

Dr. Paciello is scientific reviewer for multiple peer-reviewed international journals, such as Neurobiology of Disease, frontiers in Cellular Neuroscience and many more. Dr. Paciello is a reviewer for the research grant section of the Royal National Institute for Deaf People – National hearing loss charity.

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES**

Italian Society of Physiology (SIF)

Society for Neuroscience (SfN)

Italian Society of Neuroscience (SINS)

#### **(4) PERSONAL INFORMATION**

Family name, First name: Francesca, Natale;

Researcher unique identifier: **ORCID: 0000-0001-7856-930X; Scopus Author ID 12767233800, 12 articles, H-index 7, citations 349;**

Date of birth: 13th September 1988;

Nationality: Italian.

- **EDUCATION**

2020 PhD in Neuroscience, Catholic University Medical School, Rome

2013 Master's Degree in Neurobiology, University "Sapienza", Rome

2011 Bachelor's Degree in Biological Sciences, University "Sapienza", Rome

- **CURRENT POSITION(S)**

2023-present Assistant Professor of Physiology, Università Cattolica Medical School

- **PREVIOUS POSITIONS**

2020-2023 Postdoctoral fellow at the Department of Neuroscience, Università Cattolica Medical School

2016-2020 PhD student at the Institute of Human Physiology, Università Cattolica Medical School

2014-2015 Internship at the Institut Pasteur, Paris, in the laboratory of Prof. Uwe Maskos

2012-2013 Internship at the European Brain Research Institute

- **FELLOWSHIPS AND AWARDS**

2021 Winner of “Best Presentation Award”, Young Researchers in Physiology meeting

2015 Winner of a scholarship at the Scuola Internazionale Superiore di Studi avanzati (SISSA), Trieste

2014 Winner of a scholarship at the Institut Pasteur, Paris

**REVIEWING ACTIVITIES**

Dr. Natale is scientific reviewer for multiple peer-reviewed international journals, such as Scientific Reports, BMC Neuroscience, Brain Sciences, Journal of Translational Medicine, Journal of Extracellular Vesicles and many more. Furthermore, Dr. Natale is also a member of the Editorial Board, section Neurodegeneration for the scientific journal Frontiers in Neuroscience. Finally, Dr. Natale is a grant reviewer for the Italian Ministry of University and Research.

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES**

Italian Society of Physiology (SIF)

Society for Neuroscience (SfN)

Brainstorming Research Assembly for Young Neuroscientists (BraYn)

**(5) PERSONAL INFORMATION**

Family Name, First Name: Campanelli Federica

Researcher unique identifiers: **ORCID ID: 0000-0002-6731-7067; SCOPUS: 57204126911; Research ID:**

**AAB-2485-2019; 18 articles, H-index 8, citations 313;**

Date and place of birth: February 26, 1991 - Rome (Italy)

Nationality: Italian

- **EDUCATION**

2021 PhD in Clinical and Molecular Medicine, curriculum Neuroscience (SSD Med/26, XXXIII), University of Perugia, Department of Medicine, Perugia, Italy

2020 Course of Systematic Reviews of animal studies (SYRCLE-team)

2018 Master in Criminology, Forensic Sciences, Investigative Criminology, and Criminal

2018 Training Course FELASA- Federation of Laboratory Animal Science Associations- Accredited course F023/09

2017 Course of advanced biostatistics - Use of statistics in biomedical research: Software R

2017 Course “Neural Stem Cells: Development and Brain Repair”

2016 MSc in Pharmaceutical Chemistry and Technology (Industrial Pharmacy), University “La Sapienza” of Rome, Italy, 110/110 cum laude

2010 High School Diploma, Liceo Scientifico Statale L. Pasteur, Rome, Italy



- **CURRENT POSITION(S)**

October 2020 – present: Postdoctoral Research fellow (Assegno di ricerca) at the Università Cattolica del Sacro Cuore, Department of Physiology, Rome, Italy (Lab Chief: Prof Paolo Calabresi).

Study of behavioral and electrophysiological alterations of the basal ganglia in early experimental models of Parkinson's disease. Pharmacological and non-pharmacological approaches. Study of functional (electrophysiological and behavioral) and structural (morphological) alterations induced by a different treatment (i.e., transcranial magnetic stimulation, exercise) on the corticostriatal pathway in a model of Parkinson's disease.

- **PREVIOUS POSITIONS**

October 2019 – June 2020: Visiting PhD student at the University of Genève, Switzerland, Department of Neuroscience, Laboratory of Synaptic Brain Dysfunction (Lab Chief: Prof Camilla Bellone).

November 2017 – 2020: PhD student at the University of Perugia, internship at Fondazione Santa Lucia, Laboratory of Neurophysiology (Lab Chief: Prof Paolo Calabresi).

November 2016 – October 2017: Fellowship grant at the Santa Lucia Foundation, Laboratory of Neurophysiology (Lab Chief: Prof Paolo Calabresi).

March 2016 - September 2016: Unipharma Graduates Erasmus+ scholarship winner (2016) Internship scholarship at Université Descartes, Paris, France.

January 2015 - January 2016: Dissertation internship, Antidoping Laboratory of Rome, Rome.

November 2013 – January 2014: Pharmacy undergraduate training, Policlinico A. Gemelli, Hospital Pharmacy, Rome.

- **FELLOWSHIPS AND AWARDS:**

2020 Travel Grant SINS for FENS Virtual Forum 2020.

2019 EMBO Short-Term Fellowship 2019.

2019 Travel Grant SINS for 18th National Congress of the SINS 2019.

2019 The Best Poster Award: National Meeting of PhD Students in Neuroscience 2019, Naples, Italy.

2017 PhD Fellowship grant at the University of Perugia, Perugia, Italy

2016 Fellowship grant at the Fondazione Santa Lucia, Rome, Italy

2016 Unipharma Graduates Erasmus+ Scholarship Winner for research activity in the Laboratory of Pharmacokinetics and Pharmacology, Paris Descartes University, Paris, France

- **SUPERVISION OF GRADUATE STUDENTS; PhD POSTDOC STUDENTS:**

2016-2018: Supervision of 3 graduate Master students at the Fondazione Santa Lucia, Laboratory of Neurophysiology, Rome, Italy.

2021-present: Supervision of 2 PhD students, Università Cattolica del Sacro Cuore, Rome, Italy.

- **TEACHING ACTIVITIES:**

2022-present: Subject expert in Physiology (Degree Course in Sciences and Techniques of Preventive and Adaptive Motor Activities) at San Raffaele University, Pisana, Rome, Italy. Tutoring and teaching activity of undergraduate students and thesis reviewer.

- **ORGANISATION OF SCIENTIFIC MEETINGS:**

2023 Organizer of the NATIONAL MEETING OF PHD STUDENTS IN NEUROSCIENCE 2023, Turin, Italy, as a Member of the first Youth Committee of the Italian Society of Neuroscience (SINS).

2023 Organizer of the Department seminar in Neuroscience in "Alpha-synuclein nella malattia di Parkinson: il ruolo terapeutico dell'esercizio fisico" - Università Cattolica del Sacro Cuore, Rome, Italy.

- **INSTITUTIONAL RESPONSIBILITIES:**

2023 Organizer of the Department seminar in Neuroscience in "Alpha-synuclein nella malattia di Parkinson: il ruolo terapeutico dell'esercizio fisico" - Università Cattolica del Sacro Cuore, Rome, Italy.

2022-present Member of the first Youth Committee of the Italian Society of Neuroscience (SINS).  
2022-present Subject expert in Physiology; Faculty: Sciences and Techniques of Preventive and Adaptive Motor Activities; San Raffaele University, Pisana, Rome, Italy.

- **REVIEWING ACTIVITIES:**

September 2023-present: Editor for the Special Issue: "Neurobiological underpinnings of neurodegenerative and neuropsychiatric disorders: from models to therapy", Frontiers in Neuroscience.

2021-present: Peer-review Reviewer for Neuropharmacology, Neuropsychopharmacology, Pharmaceutical Biology, Parkinson's disease, Biology journals.

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES:**

2022\_Member of the first Youth Committee of the Italian Society of Neuroscience (SINS)

2018\_Member of the Italian Society of Neuroscience (SINS)

2020\_Member of the Federation of European Neuroscience Societies (FENS)

- **MAJOR COLLABORATIONS:**

Collaborations in the field of pharmacological and non-pharmacological treatments for PD: B. Picconi (Rome); F. Gardoni (Milan); E. De Leonibus (Naples); A. Usiello (Naples); N. Mercuri (Rome);

International collaborations:

S. Cisternino (Paris), mechanisms involved in the regulation of exchanges molecules across the BBB;

C. Bellone (Geneve), neuronal network in social behavior related to autism;

S. Papa (Atlanta), PD and movement disorders;

R. Smeyne (Jefferson University), a-syn and non-pharmacological treatments.

## (6) PERSONAL INFORMATION

Family name, First name: De Carluccio Maria

Researcher unique identifiers: **ORCID: 0000-0003-3623-5904, Scopus Author ID 58074381500, 3 articles, H-index 2, citations 15**

Date of birth: 13/05/1997

Nationality: Italian

- **EDUCATION**

2019 Bachelor's degree in biotechnology from Università La Tuscia (Viterbo)

2021 Master's degree in Biotechnology for Personalized Medicine from Università Cattolica del Sacro Cuore (Rome)

2021 National qualification to Biological Practice (Section A, Università La Tuscia Viterbo)

2021 Neuroscience PhD student at Università Cattolica del Sacro Cuore (Rome)

2023 Training course for the protection and handling of animals in scientific research Carried out with CENRIS, Università Cattolica S.Cuore

- **CURRENT POSITION(S)**

2021-present PhD student in Neuroscience at the Università Cattolica del Sacro Cuore (Rome)

- **MEMBERSHIPS OF SCIENTIFIC SOCIETIES**

2023 Member of SINS, Italian Society of Neuroscience

2023 Member of Brayn, Brainstorming Research Assembly for Young Neuroscientists

- **MAJOR COLLABORATIONS**

Prof. M.T. Viscomi (Rome, Università Cattolica del Sacro Cuore)

## (7) PERSONAL INFORMATION

Family name, First name: Servillo, Federica;

Researcher unique identifiers: **ORCID: 0000-0003-2615-6129; Scopus Author ID 58487039200, 2 articles, H-index 1, citations 2;**

Date of birth: 10th May 1995; Perugia – Italy

Nationality: Italian

### • EDUCATION

2023: Training course for the protection and handling of animals in scientific research, Università Cattolica del Sacro Cuore Rome – Italy

2021/11/01-Present: Neuroscience PhD program, Università Cattolica del Sacro Cuore – Rome - Italy

2021: National qualification to biological practice (section A), University of Tuscia – Viterbo – Italy

2021/04/21: Master's degree in Medical, Veterinary or Forensic Biotechnological Sciences, University of Perugia – Italy – Final Grade: 110/110 *cum laude*

2018/04/17: Three-year Degree in Biotechnology, University of Perugia – Italy Final Grade: 108/110

### • CURRENT POSITION

PhD Student in Neuroscience at Università Cattolica del Sacro Cuore - Rome – Italy

### • FELLOWSHIPS AND AWARDS

2023\_ Marlene and Paolo Fresco Basic Science Pre-Doctoral Fellowship at the Neuroscience Institute at NYU Langone Health – New York – USA – Supervisor: Prof. Richard W. Tsien

2021\_ PhD Fellowship at Università Cattolica del Sacro Cuore – Rome – Italy – Mentor: Prof. Paolo Calabresi

2018\_ Erasmus+ Traineeships in Barcelona Biomedical Research Park (PRBB) – University Pompeu Fabra (UPF) – Barcelona – Spain – Supervisors: Prof. Rafael Maldonado Lopez and Dr. Elena Martin Garcia

### • MEMBERSHIPS OF SCIENTIFIC SOCIETIES

2023\_ Member of BraYn Association

2023\_ Member of the Italian Society of Neuroscience (SINS)

### • MAJOR COLLABORATIONS (if applicable)

Prof. Alessandro Usiello, CEINGE – Biotecnologie Avanzate Franco Salvatore – Naples – Italy

Prof. Maria Teresa Viscomi, Università Cattolica del Sacro Cuore – Rome – Italy



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## STANDARD PERSONNEL COST TABLE

## PERSONNEL COST

COST RANGE/LEVEL	NUMBER OF SUBJECTS	HOURLY COST. see note	HOURS AMOUNT	
Low	2	31 €	500	15.500 €
Medium	2	48 €	750	36.000 €
High	2	73 €	250	18.250 €
TOTALS	6		1500	69.750 €

HOURLY COST: reference should be made to the Interministerial Decree n. 116 of January 24, 2018





PROJECT BUDGET	PERSONNEL COST	OVERHEAD	Costs for Specialist Consulting Services	License costs directly attributable to the project	Costs for materials and equipment directly attributable to the project	Costs for other types of expenses directly attributable to the project	TOTAL COST
	69.750,00 €	10.462,50 €			50.000,00 €	19.500,00 €	149.712,50 €