

BIOGRAPHICAL SKETCH

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NAME: **Marcello D'Amelio**

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: **Full Professor, Head Unit of Molecular Neurosciences**

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University of Bari, Italy	M.S.	1994	1999	Medical Genetics
University of Rome, "Tor Vergata"	PhD	2005	2008	Neurosciences
University of Rome, "La Sapienza"	Master	2008	2009	Clinical Research

A. Personal Statement

My research projects are developed within the University Campus Bio-Medico, that is one of the top medical and biomedical research universities in Rome. Additionally, the CERC is home to a set of laboratories bringing together an interdisciplinary team of researchers and clinicians. Each laboratory is directed by a group leader, focusing on the study of the pathology and physiology of the central nervous system, with particular attention to neurodegenerative. This approach facilitates productive collaborations that will be essential for this project. My research group consists of 4 Postdocs (female), 1 research technician (female), 4 PhD students (3 female) and 1 undergraduate student, fully dedicated to the study of different aspects of the brainstem dopaminergic system. Both laboratories headed by me are fully equipped with instruments required for the technological parts of funded research projects, including two fully operating slice electrophysiology rigs, centrifuges and standard equipment for tissue processing, protein and DNA analysis. My team can also take advantage of common research facilities within the University Campus Bio-medico and CERC (confocal microscopy, mass spectrometry, electron microscopy, tissue laser dissector and rooms fully equipped for microsurgery and animal behaviour testing, Astrios Cell Sorter, Cytoflex). Both institutes offer large spaces, cutting-edge technology, and a continuous scientific exchange.

B. Positions, Scientific Appointments and Honors**CURRENT POSITIONS**

2019-present **Full Professor in Human Physiology**
Dept. Medicine and Surgery, University Campus Bio-medico, Rome, Italy

2015-present **Director of Molecular Neuroscience Unit**
Dept. Medicine and Surgery, University Campus Bio-medico, Rome, Italy
Director of Laboratory of Molecular Neuroscience
Dept. Experimental Neuroscience, European Center for Brain Research, IRCCS Santa Lucia Foundation, Rome, Italy

PREVIOUS POSITIONS

2015-2018 **Associate Professor in Human Physiology**
Dept. Medicine and Surgery, University Campus Bio-medico, Rome, Italy

2010-2014 **Assistant Professor**
Dept. Medicine and Surgery, University Campus Bio-medico, Rome, Italy

2008-2010 **Post-doc**

Telethon Fellowship, Dulbecco Telethon Institute, Tor Vergata University, Rome (I);
Dulbecco Telethon Institute recruits brilliant and promising researchers, providing a salary and research funds so that they can work in Italian Institutes of their choosing (see “contribution of science” paragraph for scientific production).

Visiting Scientist

2005 Dept. of Pharmacology, Vanderbilt University Medical Center, Nashville (TN, USA).

2004 Dept. of Genome Sciences, University of Washington School of Medicine,
Seattle (WA, USA).

2004 Laboratory of Biochemistry of the Regional University Hospital of Tours (France).

Fellowships

2004-2007 PhD fellowship, Laboratory of Molecular Psychiatry, University Campus Bio-medico (see “contribution of science” paragraph for scientific production); He was **selected among 120 participants of the Neuroscience PhD course.**

Pre-doctoral Fellowship

2001- 2003 Telethon Fellowship, Telethon Institute of Genetics and Medicine, Napoli, Italy

08-2001-2002 Carrier **Break:** Military Service

SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS

2014 – 2022 Number of Post-docs: 6; Number of PhD: 8; Number of Master Students (medical students): 5 – Dept. Medicine and Surgery at University Campus Bio-medico, Rome, Italy.

One post-doc (Virve Cavallucci), who worked with me for many years, continued her career in research at Catholic University (Rome); Cavallucci has been awarded a competitive grant (for under-40 ys researchers) funded by Italian Ministry of Health; 4 post-doc are currently my collaborators; 2 PhD student (Annalisa Nobili and Livia La Barbera, now post-docs) produced key papers in Alzheimer’s field (including recent Nature Communications, Progress in Neurobiology); They have been awarded by Ghislieri Foundation (Pavia) and Airalzh Foundation, respectively. In 2021, Livia La Barbera, PhD, and Elena Spoletti PhD-student have been selected for two different University Strategic Projects – Young Researcher Scientific Independence in the Alzheimer’s Disease field.

Paraskevi Krashia, now full-time tenure track in Physiology has been awarded a very competitive post-doc fellowship funded by U. Veronesi Foundation (2018) and Alzheimer’s Association grant (2021); 2 PhD Student (now post-doc) continued their career research at Pharmaceutical Industry and at University of Lausanne, Switzerland (Prof. A. Volterra); All medical students, who I supervised, are currently in the Neurology (3) and Psychiatry (2) Residency training program.

TEACHING ACTIVITIES

2015-present Neurobiology of Aging, Medical School, Tor Vergata University, Rome

2015-present Neurophysiology of feeding, Medical School, University Campus Bio-medico, Rome

2015-present Human Physiology & Neurophysiology, Medical School, University Campus Bio-medico, Rome

2011-2014 Physiology and Physiology of human nutrition, University Campus Bio-medico, Rome

INSTITUTIONAL RESPONSIBILITIES

2019-present Rector's delegate for the Translational Research

2015-present Medicine and Surgery Faculty member, University Campus Bio-medico, Rome

2011-present Graduate medical Student Advisor, University Campus Bio-medico, Rome

2015-present Member of the Master Science Committee, *Integrated diagnosis and treatment of AD and other dementia*, Medical School, Tor Vergata University, Rome

2015-present Member of the Doctoral School Committee, *Bioengineering and Bioscience*, University Campus Bio-medico, Rome

2010-2015 Member of the Doctoral School Committee, *Neuroscience*, Medical School, Tor Vergata University, Rome

COMMISSIONS OF TRUST

2011-present Member of Editorial Board, Neuromolecular Medicine

2012-present Member of Editorial Board, Neuroscience Section, Scientific Reports

2012-present Member of Editorial Board, Molecular Neurobiology

2013 Guest Editor of Current Pharmaceutical Design; Thematic Issue: Targeting Synaptic Dysfunction and Neural Connectivity in Neurological and Psychiatric Disorders

2012-present Evaluator, Alzheimer’s Association, USA

2012-2016 Evaluator, Neurological Foundation of New Zealand

MEMBERSHIPS OF SCIENTIFIC SOCIETIES

2008-present Member, **Society of Neuroscience**
2011-present Member, **Italian Society of Physiology**
2010-2015 Member, **Italian Society of Pharmacology**

PRIZES

2010 Neuroscience Research Prize by Telethon Foundation;
2013 Bioeconomy Rome, International Prize for "outstanding contributions of young Italian scientist in the field of translational research in neurodegeneration"
2014 Raffaele Giuliano Prize for "the quality and originality of the scientific production"
2017 Awarded by Italian Minister of Health Beatrice Lorenzin for scientific merits.

RESEARCH GRANT – ongoing

Modulating synaptic neurotransmission to reactivate the immune reaction against brain tumors. MUR - PRIN 2020 – Role: Unit's PI
Dopamine loss and neuroinflammation in Alzheimer's Disease: two sides of the same coin?" Alzheimer Association, USA - AARG-21-851219; Role: Coordinator

New natural neuroprotective molecules to slow the progression of AD" within the CurAlz Project POR A0375-2020-36665; Role: Co-Pi
Beyond Amyloid Hypothesis: a novel approach to fight Alzheimer's Disease, Fondazione Roma, Role: Coordinator

Pharmacological and non-pharmacological recruitment of dopaminergic mesolimbic pathway in early AD; *Farmindustria*, Italy: Role: Coordinator
Targeting dopamine neuronal loss in a model of Alzheimer's Disease – Alzheimer Association, USA - AARG-18-566270, Role: Coordinator

Ventral Tegmental Area dopaminergic midbrain: new therapeutic target in early Alzheimer's Disease – Italian Ministry of Health RF-2028-1236552; Role: Coordinator

C. Contributions to Science

I obtained my M.Sc. in July 2000, under the supervision of Prof. Ferdinando Palmieri, Dept. of Pharmaco-Biology, University of Bari (Italy);

Between 2000 and 2003 I was awarded a number of fellowships from Telethon Foundation, to work as a junior scientist at Telethon Institute of Genetics and Medicine, Napoli in Prof. Paolo Gasparini Laboratory. There I gain expertise in genetics and developmental embryology.

Then, in 2007 I obtained a PhD in Neuroscience (Department of Neurology, Medical School University of Rome Tor Vergata), working on the association of paraoxonase gene variants with autism in North America, in the laboratory and under the supervision of Prof. Antonio Maria Persico.

During my PhD, I was awarded several short-term fellowships to work as visiting scientist at 1) University of Washington School of Medicine, Seattle (WA, USA): Tutor: Prof. Clement Furlong; 2) Vanderbilt University Medical Center, Nashville (TN, USA): Tutor: Prof. Pat Levitt; 3) Laboratory of Biochemistry of the Regional University Hospital of Tours (France): Tutor Prof. Christian R. Andres. In January 2008, I obtained a Telethon post-doc position in the laboratory directed by Prof. Francesco Cecconi, at the Department of Biology, University of Tor Vergata. My main scientific interest in this period was the link between the apoptosome and cell death, in neurodegeneration.

In January 2010, I was appointed as Director of the Laboratory of Molecular Neuroscience at European Centre for Brain Research, Santa Lucia Foundation, Rome, Italy. Since January 2015, I serve, as Director of the Molecular Neuroscience Unit at Medical School University Campus Bio-medico in Rome, where I was appointed as Associate Professor. In April 2017, I gained the national qualification as full professor in Human Physiology.

In January 2011, I published a Nature Neuroscience paper focusing on the non-apoptotic role of caspase-3 in early AD. This paper has been published few months after the Cell paper by Morgan Sheng (Li et al, Cell. 2010;141:859-71). My paper together with Sheng's work identified a novel role of

caspase-3 in synaptic plasticity, unrelated to classical apoptotic pathway (Full list publications REF.56,57,62,64).

The role of caspase-3 in AD, published on Nature Neuroscience, was the object of a number of News&Views, Commentaries and Interview Articles by prominent scientists in the field of clinical AD, due to its high relevance to the diagnosis and cure of this disease (see excerpts here below). Excerpts:

a) Caspase activation without apoptosis: insight into A β initiation of neurodegeneration by Bradley T Hyman (Nature Neuroscience 14, 5-6, 2011): New work in a mouse model of Alzheimer's disease suggests that early-stage synaptic...

b) Memory-Stealing Caspase by W. Wong (Sci. Signal. 4, ec2, 2011): D'Amelio et al. found that Tg2576 transgenic...

c) Research Highlight: Nature Reviews Drug Discovery 10, 100 (February 2011) | doi:10.1038/nrd3381
After my seminal work on the role of caspase-3 in dendritic spine degeneration in Tg2576 mouse, I produced several parallel key papers on the role played by apoptotic and autophagy molecules in synaptic degeneration and cell death in neurodegeneration diseases and cancer. I also edited a book on apoptosome's functions with Francesco Cecconi. During this period I collaborated with Prof. Guido Kroemer (F), Helene Marie (F), Morgan Sheng (USA), Francesco Cecconi (I), Nicola Mercuri (I), Marco Molinari (I), Martine Ammassari-Teule (I), Stoykova A (D). My last major contribution in AD research is the Nat. Commun. Paper. This work focused on an oft-ignored brain area in early AD: the Ventral Tegmental Area (VTA).

This discovery offers the possibility to reappraise the pathological cascade in AD and reinterpret several previous works, including mine. Almost immediately after publication, I received collaboration requests by neurologists and AD scientists; several neuroimaging papers have been published and other manuscripts are currently under revision.

By using rs-fMRI and SPECT, in collaboration with Prof. Bozzali/Dr.ssa Serra (from IRCCS Santa Lucia, Rome) and Prof.ssa Perani (University San Raffaele, Milan), respectively, we proved that VTA brain region is one of first brain region affected in disease progression: other clinical studies are now ongoing to further prove the role of VTA as biomarker of AD onset).

More recently we've taken few steps forward in addressing the question of why DA neurons in the VTA show increased susceptibility to degeneration in AD and how we can rescue VTA function. In particular, we proved that nilotinib, an ABL inhibitor, restores autophagy flux, thus preventing VTA neurodegeneration. Most notably, from a clinical point of view, nilotinib, by preventing DA neuronal loss, preserves dopamine outflow in VTA- projecting areas, improving AD-related behavioral phenotypes. Our findings shed light on the mechanism involved in dopamine neurodegeneration, revealing that autophagy represents a viable therapeutic target in early AD. Interestingly, Nilotinib is now under clinical investigation in a multi-center double blinded, Phase 3 study, that will enroll patients for three years in approximately 50 centers nationwide (ClinicalTrials.gov Identifier: NCT05143528).

Currently, I head the Laboratory of Molecular Neurosciences at the University Campus Bio- medico and the Molecular Neurosciences Unit at the European Centre of Brain Research (CERC), where the Santa Lucia Foundation laboratories are located (Rome, Italy).

Over a span of only a few years, my research unit has been able to acquire research funding equivalent to more than 4.000.000 €.

SELECTED PUBLICATIONS

Spoleti E., Krashia P., La Barbera L., Nobili A., Lupascu C. A., Giacalone E., Keller F., Migliore M., Renzi M., **D'Amelio M.** (2022). Early derailment of firing properties in CA1 pyramidal cells of the ventral hippocampus in an Alzheimer's disease mouse model. EXPERIMENTAL NEUROLOGY, vol. 350, ISSN: 0014-4886, doi: 10.1016/j.expneurol.2021.113969

La Barbera L., Vedele F., Nobili A., Krashia P., Spoleti E., Latagliata EC, Cutuli D, Cauzzi E, Marino R, Viscomi MT, Petrosini L, Puglisi-Allegra S, Melone M, Keller F, Mercuri NB, Conti F, **D'Amelio M** (2021). Nilotinib restores memory function by preventing dopaminergic neuron degeneration in a mouse model of Alzheimer's Disease. PROGRESS IN NEUROBIOLOGY, ISSN: 0301-0082

Nobili A, La Barbera L, **D'Amelio M** (2021). Targeting autophagy as a therapeutic strategy to prevent dopamine neuron loss in early stages of Alzheimer disease. AUTOPHAGY, ISSN: 1554-8635; doi: 10.1080/15548627.2021.1909409.

D'Amelio M, Serra L, Bozzali M. (2018). Ventral Tegmental Area in Prodromal Alzheimer's Disease: Bridging the Gap between Mice and Humans. JOURNAL OF ALZHEIMER'S DISEASE, ISSN: 1875- 8908, doi: 10.3233/JAD-180094

Serra L, **D'Amelio M***, Di Domenico C, Dipasquale O, Marra C, Mercuri NB, Caltagirone C, Cercignani M, Bozzali M. (2018). In vivo mapping of brainstem nuclei functional connectivity disruption in Alzheimer's disease. NEUROBIOLOGY OF AGING, ISSN: 0197-4580, doi: 10.1016/j.neurobiolaging.2018.08.012. ***Co-first**

Serra L., **D'Amelio M.**, Esposito S., Di Domenico C., Koch G., Marra C., Mercuri N. B., Caltagirone C., Artusi C. A., Lopiano L., Cercignani M., Bozzali M. (2021). Ventral tegmental area disconnection contributes two years early

to correctly classify patients converted to alzheimer's disease: Implications for treatment. JOURNAL OF ALZHEIMER'S DISEASE, vol. 82, p. 985-1000, ISSN: 1387-2877, doi: 10.3233/JAD-210171

Sala A., Caminiti S. P., Presotto L., Pilotto A., Liguori C., Chiaravalloti A., Garibotto V., Frisoni G. B., **D'Amelio M.**, Paghera B., Schillaci O., Mercuri N., Padovani A., Perani D. (2021). In vivo human molecular neuroimaging of dopaminergic vulnerability along the Alzheimer's disease phases. ALZHEIMER'S RESEARCH & THERAPY, vol. 13, ISSN: 1758-9193, doi: 10.1186/s13195-021-00925-1

Serra L., **D'Amelio M.**, Esposito S., Di Domenico C., Koch G., Marra C., Mercuri N. B., Caltagirone C., Artusi C. A., Lopiano L., Cercignani M., Bozzali M. (2021). Ventral tegmental area disconnection contributes two years early to correctly classify patients converted to alzheimer's disease: Implications for treatment. JOURNAL OF ALZHEIMER'S DISEASE, vol. 82, p. 985-1000, ISSN: 1387-2877, doi: 10.3233/JAD-210171

Serra L., **D'Amelio M***, Di Domenico C., Dipasquale O., Marra C., Mercuri NB, Caltagirone C, Cercignani M, Bozzali M. (2018). In vivo mapping of brainstem nuclei functional connectivity disruption in Alzheimer's disease. NEUROBIOLOGY OF AGING, ISSN: 0197-4580, doi: 10.1016/j.neurobiolaging.2018.08.012. ***Co-first**

Caligiore D, Silveti M, **D'Amelio M**, Puglisi-Allegra S, Baldassarre G. (2020). Computational Modeling of Catecholamines Dysfunction in Alzheimer's Disease at Pre-Plaque Stage.. JOURNAL OF ALZHEIMER'S DISEASE, ISSN: 1387-2877, doi: 10.3233/JAD-200276

Krashia P, Nobili A, **D'Amelio M** (2019). Unifying Hypothesis of Dopamine Neuron Loss in Neurodegenerative Diseases: Focusing on Alzheimer's Disease.. FRONTIERS IN MOLECULAR NEUROSCIENCE, ISSN: 1662-5099, doi: 10.3389/fnmol.2019.00123.

Cordella A, Krashia P, Nobili A, Pignataro A, La Barbera L, Viscomi MT, Valzania A, Keller F, Ammassari-Teule M, Mercuri NB, Berretta N, **D'Amelio M** (2018). Dopamine loss alters the hippocampus-nucleus accumbens synaptic transmission in the Tg2576 mouse model of Alzheimer's disease. NEUROBIOLOGY OF DISEASE, vol. 116, p. 142-154, ISSN: 0969-9961, doi: 10.1016/j.nbd.2018.05.006

D'Amelio M, Puglisi-Allegra S, Mercuri N. (2018). The role of dopaminergic midbrain in Alzheimer's disease: Translating basic science into clinical practice.. PHARMACOLOGICAL RESEARCH, ISSN: 1043-6618, doi: 10.1016/j.phrs.2018.01.016

D'Amelio M, Nisticò R. (2018). Unlocking the secrets of dopamine in Alzheimer's Disease.. PHARMACOLOGICAL RESEARCH, ISSN: 1043-6618, doi: 10.1016/j.phrs.2017.06.018

Nobili A, Latagliata EC, Viscomi MT, Cavallucci V, Cutuli D, Giacobozzo G, Krashia P, Rizzo FR, Marino R, Federici M, De Bartolo P, Aversa D, Dell'Acqua MC, Cordella A, Sancandi M, Keller F, Petrosini L, Puglisi-Allegra S, Mercuri NB, Coccurello R, Berretta N, **D'Amelio M** (2017). Dopamine neuronal loss contributes to memory and reward dysfunction in a model of Alzheimer's disease. NATURE COMMUNICATIONS, vol. 8, ISSN: 2041-1723, doi: 10.1038/ncomms14727

Cavallucci V, Berretta N, Nobili A, Nisticò R, Mercuri NB, **D'Amelio M** (2013). Calcineurin inhibition rescues early synaptic plasticity deficits in a mouse model of Alzheimer's disease.. NEUROMOLECULAR MEDICINE, ISSN: 1535-1084

D'Amelio M, Rossini PM (2012). Brain excitability and connectivity of neuronal assemblies in Alzheimer's disease: From animal models to human findings.. PROGRESS IN NEUROBIOLOGY, vol. 99, p. 42-60, ISSN: 0301-0082

D'Amelio M, Sheng M, Cecconi F (2012). Caspase-3 in the central nervous system: beyond apoptosis. TRENDS IN NEUROSCIENCES, vol. 35, p. 700-709, ISSN: 0166-2236

D'Amelio M, Cavallucci V, Middei S, Marchetti C, Pacioni S, Ferri A, Diamantini A, De Zio D, Carrara P, Battistini L, Moreno S, Bacci A, Ammassari-Teule M, Marie H, Cecconi F (2011). Caspase-3 triggers early synaptic dysfunction in a mouse model of Alzheimer's disease.. NATURE NEUROSCIENCE, vol. 14, p. 69-76, ISSN: 1097-6256