Biographical Sketch

NAME	POSITION TITLE
MARIAROSA ANNA BEATRICE *NAMED* MARINA MELONE	ASSOCIATE PROFESSOR OF NEUROLOGY, UNIVERSITY OF CAMPANIA LUIGI VANVITELLI DIRECTOR OF INTERUNIVERSITY CENTER FOR RESEARCH IN NEUROSCIENCES (CIRN), NAPLES

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(S)	FIELD OF STUDY
High School liceo-ginnasio "Antonio Genovesi", Naples Italy	High school Diploma	1971	Humanities studies
Department of Pharmacology, School of Medicine, University of Naples "Federico II" Italy	Undergraduate student	1973-77	Neuropharmacology
School of Medicine, University of Naples "Federico II", Italy	MD, Summa cum laude	1977	Medical and surgical studies
School of Medicine, University of Naples "Federico II", Italy	Internal Physician	1977-80	Neurology
School of Neurology University of Naples "Federico II", Italy	Graduate Degree in Neurology	1977-81	Neurology
INSERM UR 523/153 & Institut de Myologie Faculté de Médecine Paris VI (UFR Pitié-Salpêtrière), Paris France	Researcher	1979-80	Neuromuscular Diseases
École Normale Supérieure, Laboratory of Molecular Neurobiology, & Institut L. Pasteur, Paris France	Visiting Scientist	1984, 1986, 1987	Molecular, Cellular and Medical Aspects of cholinergic neurotransmission

RESEARCH AND PROFESSIONAL EXPERIENCE:

A. Personal statement

As a Physician-Neuroscientist, I have been able to move easily from the laboratory to the clinic, and I have been involved in both basic and applied research. My long term research interests involve the development of a comprehensive understanding of key neurodegenerative pathways and how alterations in gene expression contribute to rare neuromuscular and neurological diseases. Furthermore, the study of the cellular and molecular biology of neural or glial phenotype stem cells and their aging mechanisms, as well as the use of animal models, has allowed me to deepen my knowledge of the pathophysiology of the development of the Nervous System and of neurodegenerative and neurometabolic diseases. The latest approach to nanotechnology has allowed me to expand my therapeutic strategies. My academic training and research experience have provided me with an excellent background in multiple biomedical disciplines and areas of specialty, including neurology, neurobiology, neuropathology, cellular and molecular biology, biochemistry, and genetics. Currently, in the field of applied research, I'm involved in research project concerning nutraceutical therapy (i.e. Natural Polyphenolic Compounds) with clinical focus on age related diseases (Neurodegenerative Diseases, cerebral proteinopathies), neglected/rare diseases (Rett syndrome, Huntington disease, Leukodystrophies) and hereditary tumor predisposition syndromes (Neurofibromatosis 1).

In addition, I'm looking for the formulation of nanocarriers containing biomolecules that can greatly improve their efficacy in vivo and/or decrease their toxicity and provide the ability to cross biological barriers (e.g. intestinal, blood-brain barrier, nasal, ocular, pulmonary, skin).

B. Positions and Honors

1978: Internship at Division of Neurology "Antonio Cardarelli" Hospital, Naples Italy
1979-1980 Researcher at INSERM UR 523/153 & Institut de Myologie Faculté de Médecine Paris VI (UFR Pitié-Salpêtrière)
1983-1990 CNR Researcher, ex lege "285/77"
1985-1995 Honorary Fellow in Neurology and Psychopathology at the University of Naples
1984, 1986, and 1987 Visiting Scientist at École Normale Supérieure, Molecular Neurobiology laboratory, Paris
1990-present Neurologist Senior at Second Division of Neurology in University of Campania Luigi Vanvitelli
2002-present Professor's Committee of PhD in Neuroscience, University of Campania "Luigi Vanvitelli"
2011-2013 Research Associated at Institute of Protein Biochemistry National Research Council (CNR), Naples
2013-present Director of InterUniversity Center for Research in Neurosciences (CIRN)
2013-present Research Associated at Institute of Biosciences and BioResources, National Research Council (CNR), Naples
2014 National Scientific Qualification (art.16 of the law 30 December 2010, n.240): Full Professor in Applied Biology (05/F1) and in Human Anatomy (05/H1)
2015-present Scientific Consultant, Museo Corporea Fondazione Idis-Città della Scienza Napoli
2015-present Affiliate Professor at the Sbarro Institute for Cancer Research and Molecular Medicine, Center for Biotechnology, College of Science and Technology, Temple University, Philadelphia, PA, USA
2017 National Scientific Qualification (art.16 of the law 30 December 2010, n.240): Full Professor in Science of Health Professions and Applied Medical Technologies

B. Other Experience and Professional Memberships:

1986- present Member of the Italian Association of Neuropathology & Clinical Neurobiology, European Confederation of Neuropathological Societies (Euro-CNS) and International Society of Neuropathology
1988- present Member of the Italian Society of Neurology
2000-present Member of the European TREAT-NMD Alliance (www.treat-nmd.eu) and of the European Huntington's Disease Network (EHDN) (www.euro- hd.net),
2009-2011 President of Italian Association of Neuropathology & Clinical Neurobiology (2009-2011)
1990-present Reviewer ad hoc for Lancet, Journal of Cellular Physiology, European Journal of Neurology, Journal of Neuroscience Research, Gene Therapy, Cellular & Molecular Biology Letters, Annals of Neurology, Neurological Science, Genes, Biochemical Pharmacology.
2005-present Reviewer of Public Funding Agencies/Institutions (MIUR SIR (Scientific Independence of Young Researchers) programme and Ministry of Health, Focused Research),
2018-Guest editor of Special Issue in Nutrients: Dietary Curcumin and Human Health

C. Research projects funded (selection, from 2010):

Principal Researcher (PI)/Scientific Director:
-Project "Innovative micro/nanoformulated products for the valorization of bioactive molecules, useful for the health and well-being of the population, obtained from waste products of the ichthyic chain" Project MISE-Fonds for Sustainable Growth - Call "HORIZON2020" PON I&C 2014-2020

-MISSION MEM: Modern Innovative Healthcare Solutions in Improving Outcomes iN MEM (Metabolic Hereditary Diseases). Region Campania Priority objectives and of national importance pursuant to Article 4(1) of the Regulation 1, paragraphs 34 and 34 bis of Law 662/96. Project Line 4: Chronicity Management - 3) PDTA elaboration and implementation for chronic pathologies with high care impact and new structured methods for their Governance in Rare Diseases.
-Nanotechnologies for the Controlled Release of Bio-Active Molecules, Cooperative Technological Transfer Projects and First Industrialisation Projects for Innovative High Potential Enterprises, POR CAMPANIA ERDF 2007/2013
-Neurodegeneration and Neuroprotection: Role of Neuroglobin expression induced by estrogen (Research projects of national interest (PRIN 2010-2011))

D. Research Awards/Grants (selection)

1979 Institut National de la Santé et de la Recherche Médicale (INSERM), France
1980 Association Claude Bernard pour le Développement des Recherches Biologiques et Médicales - Hôpitaux de l'Assistance Publique Paris
1986 European Science Foundation
1987 Association des Myopathes de France (AMF)
2006 Telethon Foundation, France
2004 & 2010-11 Italian Ministry of Universities and Research (MIUR)
2015, 2017 Campania Region, Italy
2017 Italian Ministry of Economy and Development (MISE)-Fonds for Sustainable Growth - Call "HORIZON2020" PON I&C 2014-2020

E. Contribution to Science

Our significant contribution to scientific progress has been to use different methodological approaches to solve an identified problem, or to propose new working hypotheses in both clinical and experimental Neurosciences.

1. On the regulation of the nerve-muscle relationship, the role of the nerve in muscle regeneration and the role of nerve-derived neurotrophins in determining the different molecular forms of AChE, in the 80s we developed new approaches by in vivo and in vitro models.

-Melone M et al. Regenerated EDL muscle of rats requires innervation to maintain AChE molecular forms. Muscle Nerve. 1990 ; - Koelle GB, et al. Effects of glycyl-L-glutamine in vitro on the molecular forms of acetylcholinesterase in the preganglionically denervated superior cervical ganglion of the cat. Proc Natl Acad Sci U S A. 1988; -Koelle GB.n et al. Distributions of molecular forms of acetylcholinesterase and butyrylcholinesterase in nervous tissue of the cat.Proc Natl Acad SciU S A. 1987

2. Modelling in vitro the Duchenne muscular dystrophy, has allowed us both to identify, the growth factor role and the interplay between muscle and fibroblast cells in determining muscle degeneration.

- Melone M et al. Increased expression of IGF-binding protein-5 in Duchenne muscular dystrophy (DMD) fibroblasts correlates with the fibroblast-induced downregulation of DMD myoblast growth: an in vitro analysis.J Cell Physiol. 2000; - Melone M et al. Defective growth in vitro of DMD myoblasts: the molecular and biochemical basis.J Cell Biochem. 1999

3. We have devoted a great deal of attention to neural and glial differentiation/apoptosis and to physiology, pathology and aging of stem cells.

- Squillaro T et al. Impact of lysosomal storage disorders on biology of mesenchymal stem cells: Evidences from in vitro silencing of glucocerebrosidase and alpha-galactosidase A enzymes.J Cell Physiol 2017 ; -Capasso S et al. Changes in autophagy, proteasome activity and metabolism to determine a specific signature for acute and chronic senescent mesenchymal stromal cells.Oncotarget 2015; -Capasso S et al. Silencing of RB1 and RB2/P130 during adipogenesis of bone marrow stromal cells results in dysregulated differentiation.Cell Cycle 2014; -Galderisi U et al. Efficient cultivation of neural stem cells with controlled delivery of FGF-2. Stem Cell Res 2013

4. Animal and cellular models have become an indispensable tool for us, both to better understand the pathophysiology of neurodegenerative and neurogenetic diseases and, consequently, to develop new therapeutic approaches.

- Alessio N et al. Neural stem cells from a mouse model of Rett syndrome are prone to senescence, show reduced capacity to cope with genotoxic stress, and are impaired in the differentiation process.Exp Mol Med 2018; -Cardinale A et al. Localization of neuroglobin in the brain of R6/2 mouse model of Huntington's disease.Neurol Sci 2018
- Mucerino S et al. Alterations in the carnitine cycle in a mouse model of Rett syndrome. Sci Rep 2017 - Vidoni C et al. Resveratrol protects neuronal-like cells expressing mutant Huntingtin from dopamine toxicity by rescuing ATG4-mediated autophagosome formation. Neurochem Int 2017 -Nuzzo MT et al. Huntingtin polyQ Mutation Impairs the 17β-Estradiol/Neuroglobin Pathway Devoted to Neuron Survival. Mol Neurobiol 2017 -Vidoni C, et al. Dopamine exacerbates mutant Huntingtin toxicity via oxidative-mediated inhibition of autophagy in SH-SY5Y neuroblastoma cells: Beneficial effects of anti-oxidant therapeutics. Neurochem Int 2016 -Melone M et al. Mutant huntingtin regulates EGF receptor fate in non-neuronal cells lacking wild-type protein. BBA 2013

5. We have proposed new models, conceptual frameworks and different pathophysiological hypotheses of rare neuro-muscular diseases, neurogenetic diseases with predominant movement disorders and neurometabolic diseases.

- Caterino M et al. Huntingtin protein: A new option for fixing the Huntington disease countdown clock.Neuropharmacology 2018 -Pascarella A et al. Vacuolated PAS-positive lymphocytes as an hallmark of Pompe disease and other myopathies related to impaired autophagy. J Cell Physiol 2018 - Napolitano F, et al.. Autosomal-dominant myopia associated to a novel P4HA2 missense variant and defective collagen hydroxylation.Clin Genet 2018
-Sampaolo S et al. Identification of the first dominant mutation of LAMA5 gene causing a complex multisystem syndrome due to dysfunction of the extracellular matrix. J Med Genet. 2017 -Melone M et al. Unusual Stüve-Wiedemann syndrome with complete maternal chromosome 5 isodisomy. Ann Clin Transl Neurol 2014

6. Humanity living in developed countries is experiencing an increase in life expectancy; however, this positive outcome seems to be at the cost of a greater incidence of lifestyle- and age-associated diseases. We have therefore shifted the focus from cure to prevention and we have extended the focus of our research, adding food, and therefore diet, to drugs.

-Melone M et al.The carnitine system and cancer metabolic plasticity. Cell Death Dis2018
- Squillaro T. et al. Adult-onset brain tumors and neurodegeneration: Are polyphenols protective?J Cell Physiol 2018 - Esposito T., et al. Synergistic Interplay between Curcumin and Polyphenol-Rich Foods in the Mediterranean Diet: Therapeutic Prospects for Neurofibromatosis 1 Patients.Nutrients2017
-Gentile M. et al. Ruta graveolens L. induces death of glioblastoma cells and neural progenitors, but not of neurons, via ERK 1/2 and AKT activation.PLoS One 2015

Selected Peer-reviewed Publications in the last three years (from 2015 to 2018)

1. Di Cristo F, Finicelli M, Digilio FA, Paladino S, Valentino A, Scialò F, D'Apolito M, Saturnino C, Galderisi U, Giordano A, **Melone MAB**, Peluso G. Meldonium improves Huntington's disease mitochondrial dysfunction by restoring peroxisome proliferator-activated receptor γ coactivator 1α expression.J Cell Physiol. 2018 Oct 26.
2.Alessio N, Pipino C, Mandatori D, Di Tomo P, Ferone A, Marchiso M, **Melone MAB**, Peluso G, Pandolfi A, Galderisi U. Mesenchymal stromal cells from amniotic fluid are less prone to senescence compared to those obtained from bone marrow: An in vitro study. J Cell Physiol. 2018 Nov;233(11):8996-9006
3. Squillaro T, Cimini A, Peluso G, Giordano A, **Melone MAB**. Nano-delivery systems for encapsulation of dietary polyphenols: An experimental approach for neurodegenerative diseases and brain tumors. Biochem Pharmacol. 2018 Aug;154:303-317.
4. Alessio N, Squillaro T, Özcan S, Di Bernardo G, Venditti M, **Melone M**, Peluso G, Galderisi U. Stress and stem cells: adult Muse cells tolerate extensive genotoxic stimuli better than mesenchymal stromal cells. Oncotarget. 2018 Apr 10;9(27):19328-19341.
5. Terracciano C, Pachatz C, Rastelli E, Pastore FS, **Melone MAB**, Massa R. Neurofibromatous neuropathy: An ultrastructural study. Ultrastruct Pathol. 2018 May-Jun;42(3):312-316.
6. Alessio N, Riccitiello F, Squillaro T, Capasso S, Del Gaudio S, Di Bernardo G, Cipollaro M, **Melone MAB**, Peluso G, Galderisi U. Neural stem cells from a mouse model of Rett syndrome are prone to senescence, show reduced capacity to cope with genotoxic stress, and are impaired in the differentiation process. Exp Mol Med. 2018 Mar 22;50(3):1.
7. Caterino M, Squillaro T, Montesarchio D, Giordano A, Giancola C, **Melone MAB**. Huntingtin protein: A new option for fixing the Huntington's disease countdown clock. Neuropharmacology. 2018 Jun;135:126-138.
8. Terracciano C, Farina O, Esposito T, Lombardi L, Napolitano F, De Blasiis P, Ciccone G, Todisco V, Tuccillo F, Bernardini S, Di Iorio G, **Melone MAB**, Sampaolo S. Successful long-term therapy with flecainide in a family with paramyotonia congenita. J Neurol Neurosurg Psychiatry. 2018 Feb 27.
9. **Melone MAB**, Valentino A, Margarucci S, Galderisi U, Giordano A, Peluso G. The carnitine system and cancer metabolic plasticity. Cell Death Dis. 2018 Feb 14;9(2):228. Review.
10. **Melone MAB**, Dato C, Paladino S, Coppola C, Trebini C, Giordana MT, Perrone L. Verapamil Inhibits Ser202/Thr205

Phosphorylation of Tau by Blocking TXNIP/ROS/p38 MAPK Pathway. Pharm Res. 2018 Feb 5;35(2):44.
11. Napolitano F, Di Iorio V, Testa F, Tirozzi A, Reccia MG, Lombardi L, Farina O, Simonelli F, Gianfrancesco F, Di Iorio G, **Melone MAB**, Esposito T, Sampaolo S.Autosomal-dominant myopia associated to a novel P4HA2 missense variant and defective collagen hydroxylation. Clin Genet. 2018 May;93(5):982-991.
12. Pascarella A, Terracciano C, Farina O, Lombardi L, Esposito T, Napolitano F, Franzese G, Panella G, Tuccillo F, la Marca G, Bernardini S, Boffo S, Giordano A, Di Iorio G, **Melone MAB,** Sampaolo S. Vacuolated PAS-positive lymphocytes as an hallmark of Pompe disease and other myopathies related to impaired autophagy. J Cell Physiol. 2018 Aug;233(8):5829-5837.
13. Cardinale A, Fusco FR, Paldino E, Giampà C, Marino M, Nuzzo MT, D'Angelo V, Laurenti D, Straccia G, Fasano D, Sarnataro D, Squillaro T, Paladino S, **Melone MAB**. Localization of neuroglobin in the brain of R6/2 mouse model of Huntington's disease. Neurol Sci. 2018 Feb;39(2):275-285.
14. Dhez AC, Benedetti E, Antonosante A, Panella G, Ranieri B, Florio TM, Cristiano L, Angelucci F, Giansanti F, Di Leandro L, d'Angelo M, **Melone M**, De Cola A, Federici L, Galzio R, Cascone I, Raineri F, Cimini A, Courty J, Giordano A, Ippoliti R. Targeted therapy of human glioblastoma via delivery of a toxin through a peptide directed to cell surface nucleolin. J Cell Physiol. 2018 May;233(5):4091-4105.
15. Squillaro T, Schettino C, Sampaolo S, Galderisi U, Di Iorio G, Giordano A, **Melone MAB**. Adult-onset brain tumors and neurodegeneration: Are polyphenols protective? J Cell Physiol. 2018
16. Esposito T, Schettino C, Polverino P, Allocca S, Adelfi L, D'Amico A, Capaldo G, Varriale B, Di Salle A, Peluso G, Sorrentino G, Lus G, Sampaolo S, Di Iorio G, **Melone MAB**. Synergistic Interplay between Curcumin and Polyphenol-Rich Foods in the Mediterranean Diet: Therapeutic Prospects for Neurofibromatosis 1 Patients.Nutrients. 2017 Jul 21;9(7).
17. Sampaolo S, Napolitano F, Tirozzi A, Reccia MG, Lombardi L, Farina O, Barra A, Cirillo F, **Melone MAB**, Gianfrancesco F, Iorio GD, Esposito T. Identification of the first dominant mutation of LAMA5 gene causing a complex multisystem syndrome due to dysfunction of the extracellular matrix. J Med Genet. 2017 Oct;54(10):710-720.
18. Vidoni C, Secomandi E, Castiglioni A, **Melone MAB**, Isidoro C. Resveratrol protects neuronal-like cells expressing mutant Huntingtin from dopamine toxicity by rescuing ATG4-mediated autophagosome formation. Neurochem Int. 2018 Jul;117:174-187.
19. Sampaolo S, Liguori G, Vittoria A, Napolitano F, Lombardi L, Figols J, **Melone MAB**, Esposito T, Di Iorio G. First study on the peptidergic innervation of the brain superior sagittal sinus in humans. Neuropeptides. 2017 Oct; 65:45-55.
20. Santoro C, Giugliano T, **Melone MAB**, Cirillo M, Schettino C, Bernardo P, Cirillo G, Perrotta S, Piluso G. Multiple spinal nerve enlargement and SOS1 mutation: Further evidence of overlap between neurofibromatosis type 1 and Noonan phenotype. Clin Genet. 2018 Jan;93(1):138-143.
21. Mucerino S, Di Salle A, Alessio N, Margarucci S, Nicolai R, **Melone MA**, Galderisi U, Peluso G. Alterations in the carnitine cycle in a mouse model of Rett syndrome. Sci Rep. 2017 Feb 2;7:41824.
22. Squillaro T, Antonucci I, Alessio N, Esposito A, Cipollaro M, **Melone MAB**, Peluso G, Stuppia L, Galderisi U. Impact of lysosomal storage disorders on biology of mesenchymal stem cells: Evidences from in vitro silencing of glucocerebrosidase (GBA) and alpha-galactosidase A (GLA) enzymes. J Cell Physiol. 2017 Dec;232(12):3454-3467.
23. Nuzzo MT, Fiocchetti M, Totta P, **Melone MAB**, Cardinale A, Fusco FR, Gustincich S, Persichetti F, Ascenzi P, Marino M. Huntingtin polyQ Mutation Impairs the 17β-Estradiol/Neuroglobin Pathway Devoted to Neuron Survival. Mol Neurobiol. 2017 Oct;54(8):6634-6646.
24. Vidoni C, Castiglioni A, Seca C, Secomandi E, **Melone MA**, Isidoro C. Dopamine exacerbates mutant Huntingtin toxicity via oxidative-mediated inhibition of autophagy in SH-SY5Y neuroblastoma cells: Beneficial effects of anti-oxidant therapeutics. Neurochem Int. 2016 Dec;101:132-143.
25. Vidoni C, Follo C, Savino M, Melone MA, Isidoro C. The Role of Cathepsin D in the Pathogenesis of Human Neurodegenerative Disorders. Med Res Rev. 2016 Sep;36(5):845-70. Review.
26. Capasso S, Alessio N, Squillaro T, Di Bernardo G, **Melone MA**, Cipollaro M, Peluso G, Galderisi U. Changes in autophagy, proteasome activity and metabolism to determine a specific signature for acute and chronic senescent mesenchymal stromal cells. Oncotarget. 2015 Nov 24;6(37):39457-68.
27. Esposito T, Piluso G, Saracino D, Uccello R, Schettino C, Dato C, Capaldo G, Giugliano T, Varriale B, Paolisso G, Di Iorio G, **Melone MA**.A novel diagnostic method to detect truncated neurofibromin in neurofibromatosis 1. J Neurochem. 2015 Dec;135(6):1123-8.
28. Gentile MT, Ciniglia C, Reccia MG, Volpicelli F, Gatti M, Thellung S, Florio T, **Melone MA**, Colucci-D'Amato L. Ruta graveolens L. induces death of glioblastoma cells and neural progenitors, but not of neurons, via ERK 1/2 and AKT activation. PLoS One. 2015 Mar 18;10(3):e0118864.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/labs/bibliography/1XeLsnw7TvJo3M/bibliography/public/ or
https://iris.unicampania.it/simple-search?location=&query=&filtername=author&filtertype=authority&filterquery=rp05222&rpp=1000&sort_by=bi_sort_2_sort&order=desc#.XEghK1xKiUk , or http://cirn-na.com/people/marina-melone