

BIOGRAPHICAL SKETCH

Provide the following information for all key personnel.
Follow the sample format for each person found in **Biosketch Sample**. **DO NOT EXCEED FIVE PAGES.**

NAME Michela Guglielmotto		POSITION TITLE Assistant Professor in General Pathology (MED/04)	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR (s)	FIELD OF STUDY
University of Turin	Doctor in Biology	2004	Dehydroepiandrosterone reduces expression and activity of BACE in NT2 neurons exposed to oxidative stress.
Department of Experimental Medicine and Oncology, University of Turin	PhD in Molecular and Experimental Pathology	2008	Study of the β -secretase induction mediated by oxidative stress: involvement of γ -secretase and role in the pathogenesis of Alzheimer's disease

A. Positions and Honors.

01 Feb 2009–31 Jan 2011

Post Doc Research Fellow at the Department of Experimental Medicine and Oncology, University of Turin, Turin (Italy). Title of project: Oxidative stress induces a positive "feedback" between β and γ secretase: role of the beta protein and significance in the pathogenesis of Alzheimer's disease.

01 Feb 2011–31 Jan 2013

Post Doc Research Fellow at the Department of Experimental Medicine and Oncology, University of Turin, Turin (Italy). Title of project: Oxidative stress and Sporadic Alzheimer's disease: hyper-regulation of β and γ -secretase and hyper-production of β -amyloid.

01 Feb 2013–31 Jan 2015

Post Doc Research Fellow at the Department of Neuroscience Rita Levi Montalcini and Neuroscience Institute Cavalieri Ottolenghi (NICO), University of Turin, Italy. Title of project: Role of autophagy in neurodegenerative disease models.

01 Feb 2015–31 Jan 2016

Post Doc Research Fellow Fondazione Veronesi (Grant 2015 Fondazione Umberto Veronesi, Milan, Italy) at Institute Cavalieri Ottolenghi (NICO), University of Turin, Italy.

Title of project: Amyloid-Beta accumulation: the role of Ubiquitin C-terminal Hydrolase L1 (UCH-L1).

01 Jun 2016–30 Nov 2016

Project researcher, University of Genoa, Genoa (Italy). Title of project: Nucleation effect of beta-amyloid species on the aggregation of tau. Project was carried out in Institute Cavalieri Ottolenghi (NICO), University of Turin, Italy.

01 Dec 2018 – 30 Nov 2021: Assistant Professor in General Pathology (MED/04) at the Department of Neuroscience Rita Levi Montalcini, University of Turin, Italy.

01 Dec 2021 – today: Associate Professor in General Pathology (MED/04) at the Department of Neuroscience Rita Levi Montalcini, University of Turin, Italy.

B. Selected peer-reviewed publications (in chronological order).

1. Tamagno E., Parola M., **Guglielmotto M.**, Santoro G., Bardini P., Davit A., Marra L., Danni O., Tabaton M. Multiple signaling events in amyloid beta-induced, oxidative stress-dependent neuronal apoptosis. *Free Radical Biol. Med.* 2003, 35, 45-58.
2. Tamagno E., **Guglielmotto M.**, Bardini P., Santoro G., Davit A., Di Simone D., Danni O., Tabaton M. Dehydroepiandrosterone reduces expression and activity of BACE in NT2 neurons exposed to oxidative stress. *Neurobiol Dis.* 2003, 14, 291-301.
3. Tamagno E., Parola M., Bardini P., Piccini A., Borghi R., **Guglielmotto M.**, Santoro G., Davit A., Danni O., Smith MA., Perry G., Tabaton M. Beta-site APP cleaving enzyme up-regulation induced by 4-hydroxynonenal is mediated by stress-activated protein kinases pathways. *J Neurochem.* 2005, 92, 628-636.
4. Tamagno E., Bardini P., **Guglielmotto M.**, Danni O., Tabaton M. The various aggregation states of beta- amyloid 1-42 mediate different effects on oxidative stress neurodegeneration and BACE-1 expression. *Free Radical Biol. Med.* 2006, 41, 202-212.
5. Tamagno E., **Guglielmotto M.**, Aragno M., Borghi R., Autelli R., Giliberto L., Muraca G., Danni O., Zhu X., Smith M.A., Perry G., Jo D.G., Mattson M.P., Tabaton M. Oxidative stress activates a positive feedback between the gamma- and beta-secretase cleavages of the beta-amyloid precursor protein. *J Neurochem.* 2008, 104, 683-695.
6. **Guglielmotto M.**, Tamagno E., Danni O. Oxidative stress and hypoxia contribute to Alzheimer's disease pathogenesis: two sides of the same coin. *ScientificWorldJournal.* 2009, 9,781-791.
7. **Guglielmotto M.**, Aragno M., Autelli R., Giliberto L., Novo E., Colombatto S., Danni O., Parola M., Smith M.A., Perry G., Tamagno E., Tabaton M. The up-regulation of BACE1 mediated by hypoxia and ischemic injury: role of oxidative stress and HIF1alpha. *J Neurochem.* 2009, 108, 1045-1056.
8. Testa G, Staurengli E, Giannelli S, Gargiulo S, **Guglielmotto M.**, Tabaton M, Tamagno E, Gamba P, Leonarduzzi G. A silver lining for 24-hydroxycholesterol in Alzheimer's disease: The involvement of the neuroprotective enzyme sirtuin 1. *Redox Biol.* 2018, 17:423-431.
9. Tamagno E, **Guglielmotto M.**, Monteleone D, Manassero G, Vasciaveo V, Tabaton M. The Unexpected Role of A β 1-42 Monomers in the Pathogenesis of Alzheimer's Disease. *J Alzheimers Dis.* 2018. doi: 10.3233/JAD-170581.

10. Piras A, Schiaffino L, Boido M, Valsecchi V, **Guglielmotto M**, De Amicis E, Puyal J, Garcera A, Tamagno E, Soler RM, Vercelli A. Inhibition of autophagy delays motoneuron degeneration and extends lifespan in a mouse model of spinal muscular atrophy. *Cell Death Dis.* 2017 Dec 20;8(12):3223. doi: 10.1038/s41419-017-0086-4.

11. **Guglielmotto M**, Monteleone D, Vasciaveo V, Repetto I, Manassero G, Tabaton M, Tamagno E. The decrease of Uch-L1 activity is a common mechanism responsible for A β 42 accumulation in Alzheimer's and Vascular Disease. *Frontiers in Aging Neuroscience. Front Aging Neurosci.* 2017 Sep 29; 9:320. doi: 10.3389/fnagi.2017.00320. eCollection 2017.

12. Fucà E, **Guglielmotto M**, Boda E, Rossi F, Leto K, Buffo A. Preventive motor training but not progenitor grafting ameliorates cerebellar ataxia and deregulated autophagy in tambaleante mice. *Neurobiol Dis.* 2017 Feb 24;102:49-59. doi: 10.1016/j.nbd.2017.02.005.

13. Manassero G, **Guglielmotto M**, Monteleone D, Vasciaveo V, Butenko O, Tamagno E, Arancio O, Tabaton M. Dual Mechanism of Toxicity for Extracellular Injection of Tau Oligomers versus Monomers in Human Tau Mice. *J Alzheimers Dis.* 2017;59(2):743-751. doi: 10.3233/JAD-170298.

14. Barbero F, **Guglielmotto M**, Capuzzo A, Maffei ME. Extracellular Self-DNA (esDNA), but Not Heterologous Plant or Insect DNA (etDNA), Induces Plasma Membrane Depolarization and Calcium Signaling in Lima Bean (*Phaseolus lunatus*) and Maize (*Zea mays*). *Int J Mol Sci.* 2016 Sep 29;17(10). pii: E1659.

15. Manassero G, **Guglielmotto M**, Zamfir R, Borghi R, Colombo L, Salmona M, Perry G, Odetti P, Arancio O, Tamagno E, Tabaton M. Beta-amyloid 1-42 monomers, but not oligomers, produce PHF-like conformation of Tau protein. *Aging Cell.* 2016 Oct;15(5):914-23. doi: 10.1111/acer.12500.

16. **Guglielmotto M**, Reineri S, Iannello A, Ferrero G, Vanzan L, Miano V, Ricci L, Tamagno E, De Bortoli M, Cutrupi S. E2 Regulates Epigenetic Signature on Neuroglobin Enhancer-Promoter in Neuronal Cells. *Front. Cell Neurosci.* 2016 Jun 1;10:147. doi: 10.3389/fncel.2016.00147.

17. **Guglielmotto M**, Monteleone D, Piras A, Valsecchi V, Tropiano M, Ariano S, Fornaro M, Vercelli A, Puyal J, Arancio O, Tabaton M, Tamagno E. A β 1-42 monomers or oligomers have different effect on autophagy and apoptosis. *Autophagy.* 2014 Oct 1; 10(10):1827-43. doi: 10.4161/auto.30001. Epub 2014 Aug 12.

18. Gamba P, **Guglielmotto M**, Testa G, Monteleone D, Zerbinati C, Gargiulo S, Biasi F, Iuliano L, Giaccone G, Mauro A, Poli G, Tamagno E, Leonarduzzi G. Up-regulation of β -amyloidogenesis in neuron-like human cells by both 24- and 27-hydroxycholesterol: protective effect of N-acetylcysteine. *Aging Cell.* 2014 Jun;13(3):561-72. doi: 10.1111/acer.12206.

19. **Guglielmotto M.**, Aragno M., Tamagno E., Vercellinatto I., Visentin S., Medana C., Catalano M.G., Smith M.A., Perry G., Danni O., Boccuzzi G., Tabaton M. AGEs/RAGE complex upregulates BACE1 via NF-kappaB pathway activation. *Neurobiol Aging*. 2012 DOI:10.1016/j.neurobiolaging.2010.05.026.
20. Goitre L., De Luca E., Braggion S., Trapani E., **Guglielmotto M.**, Biasi F., Forni M., Moglia A., Trabalzini L., Retta SF. KRIT1 loss of function causes a ROS-dependent upregulation of c-Jun. *Free Radic Biol Med*. 2013 Nov 28; 68C: 134-147. doi: 10.1016/j.freeradbiomed. 2013.11.020.
21. Gamba P., **Guglielmotto M.**, Testa G, Monteleone D., Zerbinati C., Gargiulo S., Biasi F., Iuliano L., Giaccone G., Mauro A., Poli G., Tamagno E., Leonarduzzi G. Up-regulation of β -amyloidogenesis in neuron-like human cells by both 24- and 27hydroxycholesterol: protective effect of N-acetylcysteine. *Aging Cell*. 2014 Jun;13(3):561-72. doi: 10.1111/accel.12206.
22. **Guglielmotto M.**, Monteleone D., Piras A., Valsecchi V., Tropiano M., Ariano S., Fornaro M., Vercelli A., Puyal J., Arancio O., Tabaton M., Tamagno E. A β 1-42 monomers or oligomers have different effect on autophagy and apoptosis. *Autophagy*. 2014 Oct 1; 10 (10):1827-43. doi: 10.4161/auto.30001. Epub 2014 Aug 12.
23. **Guglielmotto M.**, Monteleone D., Piras A., Valsecchi V., Tropiano M., Ariano S., Fornaro M., Vercelli A., Puyal J., Arancio O., Tabaton M., Tamagno E. A β 1-42 monomers or oligomers have different effect on autophagy and apoptosis. *Autophagy*. 2014 Oct 1; 10 (10):1827-43. doi: 10.4161/auto.30001. Epub 2014 Aug 12.
24. Manassero G., **Guglielmotto M.**, Zamfir R., Borghi R., Colombo L., Salmona M., Perry G., Odetti P., Arancio O., Tamagno E., Tabaton M. Beta-amyloid 1-42 monomers, but not oligomers, produce PHF-like conformation of Tau protein. *Aging Cell*. 2016 Oct;15(5):914-23. doi: 10.1111/accel.12500. Epub 2016 Jul 12
25. Barbero F, **Guglielmotto M**, Capuzzo A, Maffei ME. Extracellular Self-DNA (esDNA), but Not Heterologous Plant or Insect DNA (etDNA), Induces Plasma Membrane Depolarization and Calcium Signaling in Lima Bean (*Phaseolus lunatus*) and Maize (*Zea mays*). *Int J Mol Sci*. 2016 Sep 29;17(10). pii: E1659.
26. Manassero G., **Guglielmotto M.**, Monteleone D., Vasciaveo V., Butenko O., Tamagno E., Arancio O., Tabaton M. Dual Mechanism of Toxicity for Extracellular Injection of Tau Oligomers versus Monomers in Human Tau Mice. *J Alzheimers Dis*. 2017;59(2):743-751. doi: 10.3233/JAD-170298.
27. Fucà E, **Guglielmotto M**, Boda E, Rossi F, Leto K, Buffo A. Preventive motor training but not progenitor grafting ameliorates cerebellar ataxia and deregulated autophagy in tambaleante mice. *Neurobiol Dis*. 2017 Feb 24;102:49-59. doi: 10.1016/j.nbd.2017.02.005.

28. **Guglielmotto M**, Monteleone D, Vasciaveo V, Repetto I, Manassero G, Tabaton M, Tamagno E. The decrease of Uch-L1 activity is a common mechanism responsible for A β 42 accumulation in Alzheimer's and Vascular Disease. *Frontiers in Aging Neuroscience*. Front Aging Neurosci. 2017 Sep 29; 9:320. doi: 10.3389/fnagi.2017.00320. eCollection 2017.

29. Piras A, Schiaffino L, Boido M, Valsecchi V, **Guglielmotto M**, De Amicis E, Puyal J, Garcera A, Tamagno E, Soler RM, Vercelli A. Inhibition of autophagy delays motoneuron degeneration and extends lifespan in a mouse model of spinal muscular atrophy. *Cell Death Dis*. 2017 Dec 20;8(12):3223. doi: 10.1038/s41419-017-0086-4.

30. Tamagno E, **Guglielmotto M**, Monteleone D, Manassero G, Vasciaveo V, Tabaton M. The Unexpected Role of A β 1-42 Monomers in the Pathogenesis of Alzheimer's Disease. *J Alzheimers Dis*. 2017 Oct 30. doi: 10.3233/JAD170581.

31. Testa G, Staurengi E, Giannelli S, Gargiulo S, **Guglielmotto M**, Tabaton M, Tamagno E, Gamba P, Leonarduzzi G. (2018). A silver lining for 24-hydroxycholesterol in Alzheimer's disease: The involvement of the neuroprotective enzyme sirtuin 1. *Redox Biol*. 17:423-431.

32. **Guglielmotto M**, Repetto IE, Monteleone D, Vasciaveo V, Franchino C, Rinaldi S, Tabaton M, Tamagno E. Stroke and Amyloid- β Downregulate TREM-2 and Uch-L1 Expression that Synergistically Promote the Inflammatory Response. *J Alzheimers Dis*. 2019 Aug 21. doi: 10.3233/JAD-190494.

33. Valsecchi V, Boido M, Montarolo F, **Guglielmotto M**, Perga S, Martire S, Cutrupi S, Iannello A, Gionchiglia N, Signorino E, Calvo A, Fuda G, Chiò A, Bertolotto A, Vercelli A. The transcription factor Nurr1 is upregulated in amyotrophic lateral sclerosis patients and SOD1-G93A mice. *Dis Model Mech*. 2020 May 15;13(5):dmm043513. doi: 10.1242/dmm.043513. PMID: 32188741; PMCID: PMC7240304.

34. **Guglielmotto M**, Manassero G, Vasciaveo V, Venezia M, Tabaton M, Tamagno E. Estrogens Inhibit Amyloid- β -Mediated Paired Helical Filament-Like Conformation of Tau Through Antioxidant Activity and miRNA 218 Regulation in hTau Mice. *J Alzheimers Dis*. 2020;77(3):1339-1351. doi: 10.3233/JAD-200707. PMID: 32804095.

35. Amante E, Alladio E, Rizzo R, Di Corcia D, Negri P, Visintin L, **Guglielmotto M**, Tamagno E, Vincenti M, Salomone A. Untargeted metabolomics in Forensic Toxicology: a new approach for the detection of Fentanyl intake in urine samples. *Molecules*. 2021 Aug 18;26(16):4990. doi: 10.3390/molecules26164990.

36. Hoxha E, Balbo I, Parolisi R, Audano M, Muratori L, Montarolo F, Ravera F, **Guglielmotto M**, Raimondo S, DiGregorio E, Buffo A, Brusco A, Borroni B., Mitro N., Caruso D, Tempia F. Elovl5 is required for proper

action potential conduction along peripheral myelinated fibers. *Glia* 2021 Oct;69(10):2419-2428. doi: 10.1002/glia.24048.

37. Barbero F, **Guglielmotto M**, Islam M, Maffei M. Fragmented self-DNA (eDNA) is involved in plant responses to biotic stress. *Front Plant Sci.* 2021 Jul 26;12:686121. doi: 10.3389/fpls.2021.686121. eCollection 2021.
38. Tamagno E, **Guglielmotto M**, Vasciaveo V, Tabaton M. Oxidative Stress and Beta Amyloid in Alzheimer's Disease. Which Comes First: The Chicken or the Egg? *Antioxidants (Basel)*. 2021 Sep 16;10(9):1479. doi: 10.3390/antiox10091479.
39. Tamagno E, **Guglielmotto M**. Estrogens still represent an attractive therapeutic approach for Alzheimer's disease. *Neural Regen Res.* 2022 Jan;17(1):93-94. doi: 10.4103/1673-5374.314295.
40. Vasciaveo V., Iadarola A., Casile A., Dante D., Morello G., Minotta L., Tamagno E., Cicolin A., **Guglielmotto M**. Sleep fragmentation affects glymphatic system through the different expression of AQP4 in wild type and 5xFAD mouse models. *Acta Neuropathol Commun* 11, 16 (2023). <https://doi.org/10.1186/s40478-022-01498-2>

C. Research Support.

PI: University finalized research call for the year 2019. Local Research Support 2019 (RILO2019) entitled: Relationship between disturbed sleep / wake rhythm and Ubiquitin C-Terminal Hydrolase -L1 (Uch-L1) activity.

PI: University finalized research call for the year 2020. Local Research Support 2020 (RILO2020) entitled: mRNA-218 modulation in Alzheimer's disease female patients.

PI: University finalized research call for the year 2021. Local Research Support 2021 (RILO2021) entitled: Study of the bidirectional relationship between chronic sleep fragmentation and Alzheimer's disease in hTau and 5xFAD transgenic mice.

PI: University finalized research call for the year 2022. Local Research Support 2022 (RILO2022) entitled: Effect of AAV-delivered DNase I in transgenic mouse model of Alzheimer disease.