

Luca Colnaghi, PhD
12.07.1983

Current Position

- 01.10.2021- Assistant Professor (Ricercatore RTDA), Human Physiology, Vita-Salute San Raffaele University, Milan, Italy
- 01.10.2021- Head of Laboratory of “Protein signaling in brain physiology and pathology”
Division of Neuroscience, San Raffaele Institute, Milan, Italy

Personal Statement

I am a junior faculty member at the Vita-Salute San Raffaele University, located at the San Raffaele Institute in Milan. I teach cellular and human physiology and run the laboratory of “Protein signaling in brain physiology and pathology”.

I have a broad background in computational, cellular, and molecular neuroscience, and biochemistry, with specific training and expertise in the pathophysiology of ubiquitin-like proteins, such as SUMO, and aggregation-prone proteins in both *in vitro* and *in vivo*.

My lab's research focuses on comprehending the function of ubiquitin-like and aggregation-prone proteins in nerve function and brain disorders, including rare neurodevelopmental conditions (such as NEDAMSS) and neurodegenerative diseases (including Alzheimer's disease).

We use computational, biochemical, and molecular approaches to investigate this area of study, as demonstrated by our more recent publications. Recently, I have also begun researching the role of micro- and nano-plastics in human health. Specifically, my research aims to determine whether plastics can interact with proteins that contain low-complexity domains, leading to pathological aberrations.

Education and training

2012-2015	Columbia University, NY, US	Postdoctoral training in Neuroscience
2007-2011	NYU, New York, US	Ph.D. in Cellular and Molecular Biology
2005-2007	University of Milan, Milan, Italy	M.Sc. Biotechnology
2003-2005	University of Milan, Milan, Italy	B.Sc. Biotechnology

Past positions and employment

2020-2021	Laboratory Head, Biological Regulation Unit, Department of Biochemistry, Mario Negri Institute, Milan, Italy
2019-2021	Lecturer, Human Anatomy, University of Milan, Italy
2018-2019	Researcher, Department of Biochemistry, Mario Negri Institute, Milan, Italy
2016-2017	Co-founder and Scientist, Plico Biotech, New York, USA

National Scientific Qualification (ASN)

03/06/2022 - 03/06/2032	“Seconda Fascia” 05/D1 – Physiology BIO/09
11/09/2019 - 11/09/2025	“Seconda Fascia” 05/E2 – Molecular Biology BIO/11

Grants (totaling more than 700,000 EURO) and Honors

1. NEURON JTC 2023, NEURON_RV-086 VIRAL-MI 2024/2026 Role: Collaborator
Title: “Profiling vulnerability and resilience for mental illness following viral infections: translating epidemiology to deep-phenotyping”. The project aims to uncover a connection between viral infections and depressive phenotypes.
2. The Swedish Research Council, 2023-02253 2024/2026 Role: Collaborator

- Title: “The role of m6A RNA methylation in alcohol use disorder”. The project aims to determine the still uncharacterized role of FTO in alcohol use disorder.
3. Prin PNRR 2022, P20225HP23 2023/2025 Role: Co-PI
Title: “Discerning dynamic SUMO-related liquid-liquid phase separation: a sUPramolecular Approach (SUM-UP)”. The project aims to how SUMOylation may regulate protein phase separation.
 4. Prin 2022, 20228BS45E 2023/2025 Role: PI
Title: “Phase separation and SUMOylation in the molecular pathogenesis of regressive neurological disorders”. The project aims to understand the physiology and pathophysiology of protein liquid-liquid phase separation and how SUMOylation may regulate it.
 5. Telethon-Cariplo, GJC22078 2023/2025 Role: Co-PI
Title: “Mechanisms and therapeutic targets of NEDAMSS, a novel regressive neurodevelopmental syndrome”. The project aims to study how IRF2BPL mutations cause NEDAMSS, a rare regressive neurodevelopmental disorder.
 6. Telethon, GSA22E005 2022/2024 Role: PI
Title: “SHANK3 mutations in Phelan–McDermid syndrome”. The project aims to study how patient-derived mutations in the proline-rich motifs of SHANK3 are pathogenic.
 7. BrightFocus ID A2019296F 2019/2022 Role: PI
Title: “Molecular Mechanisms in Alzheimer’s Disease”. The project aims to study how SUMOylation of tau affects the onset and progression of tau pathology in TauP301L mice.
 8. HPC@CINECA: 2021/2023 Role: PI
Title: “Expression of neuronal genes in primary breast cancer”. The grant covers expenses to run computational analysis (CPU/hours and storage) using the high-performance computing infrastructure of CINECA, a leading Italian supercomputer facility.
 9. Banca Intesa Sanpaolo 2019/2021 Role: PI
Title: “Novel Risk Factors in Alzheimer’s Disease”. The main aim of the grant was to study the genetic relevance of Ubiquitin and ubiquitin-like genes such as SUMO, NEDD8, and ISG15 in Alzheimer’s disease.
 10. The Fondazione Veronesi Post-Doc 2018 Fellowship
 11. The Bodini Post-Doc Fellowship 2013 Fellowship
 12. The Howard Hughes Medical Institute 2012-2014-2015 Fellowship
 13. NYU Travel Award for Best Student 2010 Award

Peer-reviewed publications (in chronological order)

Pubmed ID: 37730697

ORCID: 0000-0002-9699-5318

Scopus: 37090619200

Average IF: 7.8

H Index (Scopus): 11

Citations (Scopus): 700

***First author; ^Corresponding author**

1. Callari M, Sola M, Magrin C, Rinaldi A, Bolis M, Paganetti P[^], **Colnaghi L[^]**, Papin S. Cancer-specific association between Tau (MAPT) and cellular pathways, clinical outcome, and drug response. *Scientific data*. 2023 10(1), 637. doi:10.1038/s41597-023-02543-y
2. Vaglietti S, Villeri V, Dell’Oca M, Marchetti C, Cesano F, Rizzo F, Miller D, LaPierre L, Pelassa I, Monje F, **Colnaghi L**, Ghirardi M, Fiumara F. PolyQ length-based molecular encoding of vocalization frequency in FOXP2. *iScience*. 2023 S2589-0042(23)02113 doi:10.1016/j.isci.2023.108036
3. Priori EC, Musi CA, Giani A, **Colnaghi L**, Milic I, Devitt A, Borsello T, Repici M. JNK Activation Correlates with Cognitive Impairment and Alteration of the Post-Synaptic Element in the 5xFAD AD Mouse Model. *Cells*. 2023 Mar 15;12(6):904. doi: 10.3390/cells12060904.

4. Elfers K, Menne L, **Colnaghi L**, Hoppe S, Mazzuoli-Weber G. Short- and Long-Term Effects of Cocaine on Enteric Neuronal Functions. *Cells*. 2023 Feb 10;12(4):577. doi:10.3390/cells12040577.
5. Gabbrielli S, **Colnaghi L**, Mazzuoli-Weber G, Redaelli ACL, Gautieri A. In Silico Analysis of Nanoplastics' and β -amyloid Fibrils' Interactions. *Molecules*. 2023 Jan 2;28(1):388. doi: 10.3390/molecules28010388.
6. Natale C, Barzago MM, **Colnaghi L**, De Luigi A, Orsini F, Fioriti L, Diomede L. A Combined Cell-Worm Approach to Search for Compounds Counteracting the Toxicity of Tau Oligomers In Vivo. *Int J Mol Sci*. 2022 Sep 24;23(19):11277.
7. Windheim J, Colombo L, Battajni NC, Russo L, Cagnotto A, Diomede L, Bigini P, Vismara E, Fiumara F, Gabbrielli S, Gautieri A, Mazzuoli-Weber G, Salmona M, **Colnaghi L**[^]. Micro-and Nanoplastics' Effects on Protein Folding and Amyloidosis. *International Journal of Molecular Sciences* 23 (18), 10329, 2022; <https://doi.org/10.3390/ijms231810329>
8. Musi AC, **Colnaghi L**, Giani A, Priori EC, Marchini G, Tironi M, Conci C, Cerullo G, Osellame R, Raimondi MT, Remuzzi A, Borsello T. Effect of 3D Synthetic Microscaffold Nichoid on the Morphology of Cultured Hippocampal Neurons and Astrocytes. *Cells*. 2022. 11(13), 2008; DOI: 10.3390/cells11132008
9. Musi CA, Marchini G, Giani A, Tomaselli G, Priori EC, **Colnaghi L**, Borsello T. Colocalization and Interaction Study of Neuronal JNK3, JIP1, and β -Arrestin2 Together with PSD95. *International Journal of Molecular Sciences*. 2022; 23(8):4113. DOI: 10.3390/ijms2308411
10. Marchetti C, Vaglietti S, Rizzo F, Di Nardo G, **Colnaghi L**, Ghirardi M, Fiumara F – Heptad stereotypy, S/Q layering, and remote origin of the SARS-CoV-2 fusion core – *Virus Evolution* - 2021 DOI: 10.1093/ve/veab097
11. Conz A*, Musi CA, Russo L, Borsello T, **Colnaghi L**[^] – Super-resolution study of PIAS SUMO E3-ligases in hippocampal and cortical neurons – *European Journal of Histochemistry* 65, 2021, DOI: 10.4081/ejh.2021.3241
12. Zanier ER*, Barzago MM, Vegliante G, Romeo M, Bertani I, Natale C, **Colnaghi L**, Colombo L, Russo L, Micotti E, Fioriti L, Chiesa R and Diomede L – *C. elegans* detects toxicity of traumatic brain injury generated tau – *Neurobiology of Disease*, 2021 DOI: 10.1016/j.nbd.2021.105330
13. **Colnaghi L**^{*,^}, Rondelli D, Muzi-Falconi M, Sertic S[^] - Tau and DNA Damage in Neurodegeneration. *Brain Sciences* 10 (12), 2020 946 DOI: 10.3390/brainsci10120946
14. Russo L*, Natale C, Conz A, Kelk J, Restelli E, Chiesa E, Salmona M, Fioriti L and **Colnaghi L**[^] - Super-resolution imaging of synaptic proteins in primary neurons – *JoVE*. Manuscript ID: JoVE61434. 2020 October. DOI: 10.3791/61434
15. **Colnaghi L**^{*,^}, Conz A*, Russo L, Musi CA, Fioriti L, Borsello T and Salmona M - Neuronal Localization of SENP Proteins with Super Resolution Microscopy –*Brain Sciences*. October 2020. DOI: 10.3390/brainsci10110778
16. Drisaldi B*, **Colnaghi L**,, Kandel ER[^] and Fioriti L[^] - Cytoplasmic Polyadenylation Element Binding proteins CPEB1 and CPEB3 regulate the translation of FosB and are required for maintaining addiction-like behaviors induced by cocaine – *Front. Cell. Neurosci*. 2020. DOI: 10.3389/fncel.2020.00207.
17. **Colnaghi L**^{*,^}, Russo L*,, Fioriti L[^] - Super Resolution Microscopy of SUMO proteins in neurons – *Front. Cell. Neurosci*. 2019 November. DOI: 10.3389/fncel.2019.00486
18. Griffin Jr EA, Melas PA, Zhou1 R, Li Y, Mercado P, Kempadoo KA, Stephenson S, **Colnaghi L**, Taylor K, Hu MC, Kandel ER and Kandel DB - Prior alcohol use enhances vulnerability to compulsive cocaine self-administration by promoting degradation of HDAC4 and HDAC5 – *Science Advances*. 2017 November. DOI: 10.1126/sciadv.1701682
19. **Colnaghi L**^{*,}, Clemenza K,, Levine AA - Social involvement modulates the response to novel and adverse life events (stimuli) in mice – *PLoS One*. 2016. DOI: 10.1371/journal.pone.0163077

20. Fioriti L, Myers C, Huang YY, Li X, Trifilieff P, **Colnaghi L**, Drisaldi B and Kandel ER - The Persistence of Memory in the Hippocampus Require Protein Synthesis mediated by the prion-like Protein CPEB3 – *Neuron*. 2015 June. DOI: 10.1016/j.neuron.2015.05.021
21. Stephan J, Fioriti L, Lamba N, **Colnaghi L**, Karl K, Derkatch I and Kandel ER - The CPEB3 protein is a functional prion that interacts with the actin cytoskeleton – *Cell Reports*. 2015 June. DOI: 10.1016/j.celrep.2015.04.060
22. Drisaldi B*, **Colnaghi L***,, Manley JL and Kandel ER- SUMOylation is an Inhibitory Constraint that Regulates the Aggregation and Activity of the Functional Prion CPEB3 – *Cell Reports*. 2015 June. DOI: 10.1016/j.celrep.2015.04.061
23. Chen YH, Jones MJK, Yin Y, Crist SB, **Colnaghi L**, Sims III RJ, Rothenberg E, Jallepalli PV and Huang TT - Phosphorylation-mediated monoubiquitination of FANCI uncouples dormant origin firing from replication stress response – *Mol Cell*. 2015 June. DOI: 10.1016/j.molcel.2015.02.031
24. Huang YY, Levine A, Kandel DB, Yin D, **Colnaghi L**, Drisaldi B and Kandel ER - D1/D5 receptors and histone deacetylation mediate the gateway effect of LTP in hippocampal dentate gyrus – *Learning and Memory*. 2013 December. DOI: 10.1101/lm.032292.113
25. Piatkov KI, **Colnaghi L**, Bekes M, Varshavsky A and Huang TT – The auto-generated fragment of the Usp1 deubiquitylase is a physiological substrate of the N-End rule pathway – *Mol Cell*. 2012 September. DOI: 10.1016/j.molcel.2012.10.012
26. Jones MJK*, **Colnaghi L** and Huang TT - Dysregulation of DNA polymerase κ recruitment to replication forks results in genomic instability – *EMBO*. 2011 December. DOI: 10.1038/emboj.2011.457
27. **Colnaghi L***, Jones MJK, Hanenberg H, Huang TT - Patient derived C-terminal mutation of FANCI causes protein mislocalization and reveals putative EDGE motif function in DNA repair – *Blood*. 2010 October. DOI: 10.1182/blood-2010-07-295758

Invited speaker at conferences and seminars

1. 10 November 2023 – Title: "SUMOylation in brain physiology and pathology". Peptide and Protein Talks conference. Milan, Italy. *Talk*
2. 08 June 2022 - Title: "SUMO in Health and Diseases". Host: Cesar S. Mendes CEDOC, NOVA Medical School, Universidade Nova de Lisboa, Lisbon Portugal. *Talk*
3. 21 January 2022 – Title: "SUMO in Health and Disease". NeuroYoung Seminar Series. Host: Rossella Galli | San Raffaele Hospital, Milan, Italy. *Talk*
4. 07 May 2021 – Title: "SUMOylation in disease pathology". Host: Sarah Sertic | Department of Biosciences, University of Milan, Italy. *Talk*
5. 14 December 2020 – Nikon Webinar Series. Title: "Super-resolution microscopy of neuronal proteins". *Talk*
6. 26 September 2020 – "MORFOLOGIA E DINTORNI" Third National Conference. Plenary Lecture. Title: "Super resolution microscopy of proteins belonging to the SUMOylation machinery in neurons." *Talk*
7. 12 January 2020 – Title: "SUMO in tau pathology", Host: Paolo Paganetti, PhD | Neurocenter of Southern Switzerland. *Talk*
8. 21 May 2019 "Le cause del morbo di Alzheimer" Pint of Sience Event, Milan. *Talk*
9. 15 June 2011 – Title: "Fanconi Anemia regulation by SUMO", Host: Jean Gautier, PhD | Department of Genetics and Development, Columbia University, NYC, NY. *Talk*

Poster presentation at conferences and meetings

1. SINS 2023, 20th National Congress of the Italian Society for Neuroscience - Turin, September 14-17, 2023 Turin. "Effect of 3D Synthetic Microscaffold Nichoid on the Morphology of Cultured Hippocampal Neurons and Astrocytes" *Poster*.

Ph.D. Thesis Defense Committee Member

PhD candidate: Claudia Magrin.

Università della Svizzera italiana, Lugano, Switzerland.

Thesis defense: 11 July 2023.

External member of the thesis committee.

PhD candidate: Lucrezia Ribolla.

Vita-Salute San Raffaele University, Milan, Italy.

Thesis defense: 21 November 2023.

Internal member of the thesis committee.

Master Thesis

<i>Daniele Zanoni</i>	2022;	University of Milano Bicocca, Milan, Italy
<i>Fiumara Matteo</i>	2022-2023;	Vita-Salute San Raffaele University, Milan, Italy.
<i>Pietro Bianco</i>	2022-2023;	University of Milano Bicocca, Milan, Italy
<i>Michael Nicoli</i>	2022-2023;	University of Milano, Milan, Italy
<i>Tommaso Cabras</i>	2023-Ongoing;	University of Milano, Milan, Italy
<i>Pietro Munarin</i>	2023-Ongoing;	University of Milano, Milan, Italy
<i>Francesca Molinari</i>	2023-Ongoing;	University of Milano, Milan, Italy

Memberships

- Società Italiana di Neuroscienze <http://www.sins.it/EN/index.xhtml> 2021-2023
- Society for Neuroscience <https://www.sfn.org/>, 2012
- The New York Academy of Sciences <https://www.nyas.org/> 2007-2011

01.12.2023 Milan, Italy