
BIOGRAPHICAL SKETCH

NAME: Isabella Barbiero

eRA COMMONS USER NAME: Isabella Barbiero

POSITION TITLE: Assistant professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Insubria, Varese, Italy	M.SC. in biology applied to biomedical research (cum laude)	07/2012	Molecular/Cellular/Neuro-biology
University of Insubria, Varese, Italy	PhD in Neurobiology	12/2015	Molecular/Cellular/Neuro-Biology

A. Personal Statement

I focused my professional career on the study of neurodevelopmental disorder including Rett syndrome (RS) and CDKL5 deficiency disorder (CDD). My academic training and research experience have provided me with a wide background in multiple biological disciplines including molecular biology, pharmacology, biochemistry, and genetics. My master studies have been focused on the characterization of the crosstalk between CDKL5 and MECP2, which mutations cause CDD and RT respectively. This work allowed me to expand my knowledge and technical skills on the design of short hairpin RNA and Illumina sequencing. I was further admitted to the PhD course in neuroscience at the university of Insubria during which I focused my studies on the role of CDKL5 in the regulation of microtubule dynamics and neuronal morphology. Through the use of Live imaging techniques and CDD animal models tests, I was able to demonstrate a reduction in the capacity of microtubules to invade dendritic spines, this finding correlates with hippocampal-dependent cognitive deficits in *Cdkl5*-KO mice. Since March 2023 I have become an assistant professor at the University and I have opened new projects to study the formation of inhibitory synapses and the consequences of CDKL5 pathological mutations (generated with CRISPR-Cas9 approach) on morpho-functional aspects related to MTs, including retrograde transport. I have activated various collaborations with national and international groups with proven experience in the field of iPSCs, neurology and neurogastroenterology. The latter open the way to a novel project focused on the characterization of gastrointestinal deficits associated with CDD.

B. Positions, Scientific Appointments, and Honors

- 2022-present: assistant professor, University of Insubria.
- 2016-2021: postdoctoral researcher, University of Insubria.
- 2019: Visiting scientist, Trinity college Dublin
- 2012-2015: Phd in Neurobiology, University of Insubria.
- 2022-present: Member of the Centre of Neuroscience - University of Insubria
- 2021-present: Member of Italian Society of Biophysics and Molecular Biology (SIBBM)

- 2023-present: Guest editor for IJMS. Special Issue "CDKL5 Deficiency Disorders: From Molecular Mechanisms to Therapeutics"
- Referee for international scientific journals: MDPI, PLOS ONE, Neurobiology of Disease

Honours and awards

- 2019: Selected candidate for "University of Insubria Senior Post doc grant"
- 2018: Selected candidate for "Cdkl5 forum junior award"
- 2017: Selected candidate for "University of Insubria Senior Post doc grant"
- 2013: Francesco de Luca international master thesis prize. Rotary club Sesto Calende Angera

C. Contributions to Science

I started my acquaintance with CDKL5 during my bachelor thesis in the laboratory of professor Charlotte Kilstrup-Nielsen at University of Insubria in 2005, with which I have done also my master's (2009) and PhD studies (2015). During these years, I have followed CDKL5 from the very beginning contributing since 2014 with 14 publications (and one submitted) to the current understanding of CDKL5. During my bachelor studies, I analyzed the functional consequences of some pathogenic mutations in CDKL5. My master's thesis was aimed at studying the molecular link between CDKL5 and MeCP2 (Bellini et al., *Frontiers Cell. Neurosci.*, 2014; Stefanelli et al., *Sci. Rep.*, 2016) and, finally, during my PhD studies I characterized the role of CDKL5 in regulating cell division and microtubule dynamics. In such regard I found that CDKL5, as MeCP2, is localized to the centrosome and at the midbody in proliferating cells; accordingly, CDKL5 depletion leads to defective cell division (Bergo et al., *J. Biol. Chem.* 2015; Barbiero et al., *Sci. Rep.*, 2017). Importantly, during my PhD studies, I also demonstrated for the first time a link between CDKL5 and microtubules. Indeed, I started analyzing the functional role of the interaction of CDKL5 with IQGAP1 that formed the basis of a publication in 2017 (Barbiero et al., *Hum. Mol. Genet.*, 2017). The link between CDKL5 and microtubules is likely to be of high relevance for future target based drug therapies. Indeed, my studies have suggested the relevance of evaluating the neurosteroid pregnenolone-methyl-ether, which promotes MT-dynamics, as a novel drug-based therapy for CDD (Barbiero et al., 2020 *Neuropharmacology*; Barbiero et al., 2022 *Hum Mol Gen*). In particular I have demonstrated a defective microtubule invasion into dendritic spines that may in part explain the defects in spine maturation and cognitive alteration associated with CDD. Besides this main stream of my research, I have collaborated on other projects in the lab, focusing on the role of CDKL5 in neuronal transmission and connectivity, thus contributing to the studies showing that CDKL5 levels are highly responsive to neuronal activity (La Montanara et al., *J. Biol. Chem.*, 2015) and to a recent publication showing that loss of CDKL5 leads to reduced surface exposure of glutamatergic AMPA-Rs, a defect that we showed can be restored with the antidepressant tianeptine (Tramarin et al., *Hum. Mol. Genet.*, 2018).

Bibliography

Author ID scopus: 56507282700; **ORCID:** 0000-0003-2213-7932

Total number of referred publications on international scientific journals: 14

Google Scholar (21st march 2024): Citations: 307; H index: 11

Scopus (21st march 2024): Citations: 439; H index: 11

D. Publications

Baldin S, Carmone C, Valetti G, De Rosa R, Barbiero I. CDKL5 regulates the initiation of retrograde axonal transport through CLIP170-dynactin complex formation. *FEBS J.* Published online August 23, 2025. doi:10.1111/febs.70230

De Rosa R, Valastro S, Cambria C, Barbiero I, Puricelli C, Tramarin M, Randi S, Bianchi M, Antonucci F, Kilstrup-Nielsen C. Loss of CDKL5 causes synaptic GABAA-receptor defects that can be restored with the neuroactive steroid pregnenolone-methyl-ether. *Int J Mol Sci.* 2022 Dec 21;24(1):68. doi: 10.3390/ijms24010068.

Barbiero I, Zamberletti E, Tramarin M, Gabaglio M, Peroni D, De Rosa R, Baldin S, Bianchi M, Rubino T, Kilstrup-Nielsen C. (2022). Pregnenolone-methyl-ether enhances CLIP170 and microtubule functions improving spine maturation and hippocampal deficits related to CDKL5 deficiency" *Human Molecular Genetics* (accepted manuscript).

Barbiero, I., Bianchi, M., & Kilstrup-Nielsen, C. (2021). Therapeutic potential of pregnenolone and pregnenolone methyl ether on depressive and CDKL5 deficiency disorders: Focus on microtubule targeting. *Journal of neuroendocrinology*, e13033. Advance online publication. <https://doi.org/10.1111/jne.13033>

Trovò, L., Fuchs, C., De Rosa, R., Barbiero, I., Tramarin, M., Ciani, E., Rusconi, L., & Kilstrup-Nielsen, C. (2020). The green tea polyphenol epigallocatechin-3-gallate (EGCG) restores CDKL5-dependent synaptic defects in vitro and in vivo. *Neurobiology of disease*, 138, 104791. <https://doi.org/10.1016/j.nbd.2020.104791>

Barbiero, I., Peroni, D., Siniscalchi, P., Rusconi, L., Tramarin, M., De Rosa, R., Motta, P., Bianchi, M., & Kilstrup-Nielsen, C. (2020). Pregnenolone and pregnenolone-methyl-ether rescue neuronal defects caused by dysfunctional CLIP170 in a neuronal model of CDKL5 Deficiency Disorder. *Neuropharmacology*, 164, 107897. <https://doi.org/10.1016/j.neuropharm.2019.107897>

Barbiero, I., De Rosa, R., & Kilstrup-Nielsen, C. (2019). Microtubules: A Key to Understand and Correct Neuronal Defects in CDKL5 Deficiency Disorder?. *International journal of molecular sciences*, 20(17), 4075. <https://doi.org/10.3390/ijms20174075>

Zamberletti, E., Gabaglio, M., Piscitelli, F., Brodie, J. S., Woolley-Roberts, M., Barbiero, I., Tramarin, M., Binelli, G., Landsberger, N., Kilstrup-Nielsen, C., Rubino, T., Di Marzo, V., & Parolaro, D. (2019). Cannabidiol completely rescues cognitive deficits and delays neurological and motor defects in male *Mecp2* mutant mice. *Journal of psychopharmacology* (Oxford, England), 33(7), 894–907. <https://doi.org/10.1177/0269881119844184>

Tramarin, M., Rusconi, L., Pizzamiglio, L., Barbiero, I., Peroni, D., Scaramuzza, L., Williams, T., Cavalla, D., Antonucci, F., & Kilstrup-Nielsen, C. (2018). The antidepressant tianeptine reverts synaptic AMPA receptor defects caused by deficiency of CDKL5. *Human molecular genetics*, 27(12), 2052–2063. <https://doi.org/10.1093/hmg/ddy108>

Barbiero, I., Peroni, D., Tramarin, M., Chandola, C., Rusconi, L., Landsberger, N., & Kilstrup-Nielsen, C. (2017). The neurosteroid pregnenolone reverts microtubule derangement induced by the loss of a functional CDKL5-IQGAP1 complex. *Human molecular genetics*, 26(18), 3520–3530. <https://doi.org/10.1093/hmg/ddx237>

Barbiero, I., Valente, D., Chandola, C., Magi, F., Bergo, A., Montefiorio, L., Tramarin, M., Fazzari, M., Soddu, S., Landsberger, N., Rinaldo, C., & Kilstrup-Nielsen, C. (2017). CDKL5 localizes at the centrosome and midbody and is required for faithful cell division. *Scientific reports*, 7(1), 6228. <https://doi.org/10.1038/s41598-017-05875-z>

Stefanelli, G., Gandaglia, A., Costa, M., Cheema, M. S., Di Marino, D., Barbiero, I., Kilstrup-Nielsen, C., Ausió, J., & Landsberger, N. (2016). Brain phosphorylation of MeCP2 at serine 164 is developmentally regulated and globally alters its chromatin association. *Scientific reports*, 6, 28295. <https://doi.org/10.1038/srep28295>

La Montanara P, Rusconi L, Locarno A, et al. Synaptic synthesis, dephosphorylation, and degradation: a novel paradigm for an activity-dependent neuronal control of CDKL5. J Biol Chem. 2015;290(7):4512-4527. doi:10.1074/jbc.M114.589762

Bergo A, Strollo M, Gai M, et al. Methyl-CpG binding protein 2 (MeCP2) localizes at the centrosome and is required for proper mitotic spindle organization. J Biol Chem. 2015;290(6):3223-3237. doi:10.1074/jbc.M114.608125

Bellini E, Pavesi G, Barbiero I, et al. MeCP2 post-translational modifications: a mechanism to control its involvement in synaptic plasticity and homeostasis? Front Cell Neurosci. 2014;8:236. Published 2014 Aug 13. doi:10.3389/fncel.2014.00236

D. Additional Information: Ongoing, pending and recently completed projects

- 2024-present PI of the project "FAR-University of Insubria - Gut deficits in CDKL5 deficiency disorder: analysis of CLIP170-IQGAP1-NINEIN complex in the microtubule organization and cellular adhesion of intestinal epithelial barrier" (tot 25.000€ per 2 years: 12.500€/year).
- 2023-present PI of the project "Bank of Italy - Generation and morpho-functional analysis of neuronal and cellular models characterized by pathological mutations in the CDKL5 gene" (tot 30.000€ per 2 years: 15.000€/year).
- 2022-present PI of the project "Cariplo Telethon Alliance GJC2021 - Functional characterization of the InSyn1-CDKL5 interaction for dystrophin/dystroglycan complex dependent inhibitory synapse formation".GJC21015. (tot 190.000 € per 2 years: 95.000 €/year)
- 2019-2020 Responsible of the grant from the University of Insubria: funding for a one-year post-doc Research Fellow position (25.000€).
- 2017-2018 Responsible of the grant from the University of Insubria: funding for a one-year post-doc Research Fellow position (25.000€).

Busto Arsizio, 25st September 2025

Signed

