
BIOSKETCH

NAME: Anna Fassio

POSITION TITLE: Associate Professor in Physiology

Personal Author ID: ORCID: 0000-0002-8801-038X

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Lyceum Gimnasium C. Colombo, Genova, Italy	B.S.	07/1987	Classical Studies
University of Genova, Italy	Master	07/1993	Pharmacy
Babraham Institute, Cambridge, UK	Fellow	12/1996	Neuroanatomy
University of Torino, Torino Italy	PhD	02/1999	Neuropharmacology
San Raffaele Hospital, Milano, Italy	Postdoctoral	04/2001	Cellular biology
University of Genova, Italy	Postdoctoral	05/2005	Neurophysiology

A. Personal Statement

I am a cellular and molecular neurophysiologist, expert in the study of neuronal development, synaptic transmission and plasticity. My research activity is focused on the physiology of synapse development and function and on the understanding of the molecular mechanisms by which mutations in genes coding for synaptic proteins result in neurodevelopmental disorders and epilepsy. At present, my group is composed of 2 researchers, 1 post doc, 1 PhD student and two master students. In the group, we utilize different neurophysiological techniques, ranging from live cell imaging, electrophysiology and molecular and cellular biology with the generation of murine and human models. We have full access to the facilities of the Department of Experimental Medicine at the University of Genoa and share two technicians with the other groups in the synaptic physiology laboratory and the administrative assistance from the Department office. I am also external collaborator at the Italian Institute of Technology and affiliate researcher at the IRCCS Ospedale Policlinico San Martino having full access into their multidisciplinary environment and core facilities, including confocal one photon and two photon microscopy and animal facility. Active collaborations are ongoing with the group of Renzo Guerrini (Meyer Children Hospital-Firenze), Federico Zara (Gaslini Children Hospital, Genova) Gianmichele Ratto (CNR-Pisa) Peter Oliver (Nucleic Acid Therapy Accelerator, Harwell, Oxford UK), Kevin Luthy (Institute of Human Genetics, Essen Germany); Philippe Campeau (Centre de Recherche Azrieli du CHU Sainte-Justine, Montreal Canada). I began working in the field of synaptic physiology during my PhD in Neuropharmacology, when I acquired expertise in brain preparation for the study of neurotransmission. I completed my studies as visiting fellow at the Babraham Institute, Cambridge UK, where I acquired expertise in morphological and ultrastructural analysis. My first post-doc was in molecular immunology in the group of Roberto Sitia, at San Raffaele Institute, Milano, where I acquired further expertise in cell biology and regulation of protein synthesis. My second post doc was in Neurophysiology, at the University of Genoa, in the group of Fabio Benfenati, studying the role of Synapsins in the regulation of synaptic vesicle cycling and plasticity. I obtained a permanent position at the University of Genoa in 2007 and started my independent research group back in 2008 with the obtainment of two competitive grants from Fondazione San Paolo and Ministero della Sanità, giovani ricercatori.

B. Positions, Scientific Appointments, and Honors

2005-2007 Non-tenured Assistant Professor in Physiology, University of Genoa, Italy.
2007-2017 Permanent position as Assistant Professor in Physiology, University of Genoa, Italy.
2017-present External Collaborator at the Italian Institute of Technology, Genoa, Italy.
2017-present Associate Professor in Physiology, University of Genoa, Italy.

2017	National qualification as full professor in Physiology (ASN).
2018-present	Research affiliate at IRCCS Ospedale Policlinico San Martino
2024	Coordinator of MEMBIOMED master's in biotechnology, financed by Erasmus Mundus.
2025	Appointed as full professor in Physiology, waiting for administrative issue to start the new position University of Genoa, Italy.

Grant as PI:

FONDAZIONE TELETHON: "Interaction of TBC1D24 with v-ATPase: pathophysiological mechanisms and novel therapeutic targets for rare TBC1D24 diseases" 2025-2027

MIUR PRIN 2022: "Temporal regulation of ionic and proteome homeostasis: implications for cortical excitability and brain physiopathology" 2023-2026

MIUR PNRR-PE Neuroscience project: "A multiscale integrated approach to the study of the nervous system in health and disease- MNESYS/spoke 2 Neural Plasticity and Connectivity" 2022-2025

ORPHAN DISEASE CENTER MILLION DOLLAR BIKE RIDE: "Boosting Autophagy: a novel therapeutic strategy for TBC1D24 epilepsy" 2023-2024

Compagnia di San Paolo: "An innovative molecular strategy, by non-coding RNAs, for treatment of neurodevelopmental synaptopathies" 2020-2023

Regione Toscana: "Developmental and epileptic encephalopathies: epidemiology, comorbidities, molecular diagnosis, personalized management, and costs analysis (DECODE-EE)" 2019-2021 external PI

FP7, COOPERATION 2013: "Development and Epilepsy Strategy for Innovative Research to improve diagnosis, prevention and treatment in children with difficult to treat Epilepsy-DESIRE" 2014-2028 coPI

Fondation Jerome Lejeune: "Dysregulation of Arf6 pathway and intellectual disability: impact on synapse function" 2013-2015

Fondazione Mariani, Milano: "Novel treatment for a genetic drug-resistant epileptic encephalopathy of infancy: virus delivered RNA interference in an animal model of Dravet syndrome" 2011-2015

Ministero della Sanità: "Canali ionici neuronali ed epilessia: meccanismi patogenetici e nuove strategie terapeutiche mediante "RNA interference" 2008-2011

Compagnia di San Paolo: "The Synapsins and membrane trafficking in nerve terminals" 2008-2011

MIUR bando PRINN: "Development and plasticity in networks of neurons grown onto micropatterned substrates" 2006-2008

Contributions to Science

I am author of 65 publications in indexed journal, 56 original articles and 9 reviews. In 14 publications I am first author and in 15 last/corresponding author. H-index 32 total citation 3386 (Scopus).

I contributed to the first description and functional characterization of *TBC1D24* mutations in epileptic patients and the elucidation of TBC1D24 role in neurodevelopment (1,2). More recently, I characterized the *Tbc1d24*KO mouse in terms of behavioral and synaptic phenotype and the neurodevelopmental defects associated with *Tbc1d24* loss of expression in murine and human models (3-5). I also identified Arf6 as TBC1D24 molecular interactor and dissected the role of Arf6 and the novel protein APACHE in synaptic vesicle cycling and neuronal development (6-8).

1. Falace A, Filipello F, La Padula V, Vanni N, Madia F, De Pietri Tonelli D, de Falco FA, Striano P, Dagna Bricarelli F, Minetti C, Benfenati F, **Fassio A***, Zara F*. TBC1D24, an ARF6-interacting protein, is mutated in familial infantile myoclonic epilepsy. Am J Hum Genet. 2010 Sep 10;87(3):365-70. *equal contribution. doi: 10.1016/j.ajhg.2010.07.020 i.f.:9.8
2. Falace A, Buhler E, Fadda M, Watrin F, Lippiello P, Pallesi-Pocachard E, Baldelli P, Benfenati F, Zara F, Represa A, **Fassio A***, Cardoso C*. TBC1D24 regulates neuronal migration and maturation through modulation of the ARF6-dependent pathway. Proc Natl Acad Sci U S A. 2014 111(6):2337-42. *equal contribution. doi: 10.1073/pnas.1316294111 If: 11.1
3. Finelli MJ, Aprile D, Castroflorio E, Jeans A, Moschetta M, Chessum L, Degiacomi MT, Grasegger J, Lupien-Meilleur A, Bassett A, Rossignol E, Campeau PM, Bowl MR, Benfenati F, **Fassio A***, Oliver PL*. The epilepsy-associated protein TBC1D24 is required for normal development, survival and vesicle trafficking in mammalian neurons. Hum Mol Genet. 2018 Oct 17. doi: 10.1093/hmg/ddy370. If: 4,544 * corresponding authors. i.f.: 3.5

4. Aprile D, Fruscione F, Baldassari S, Fadda M, Ferrante D, Falace A, Buhler E, Sartorelli J, Represa A, Baldelli P, Benfenati F, Zara F, **Fassio A**. TBC1D24 regulates axonal outgrowth and membrane trafficking at the growth cone in rodent and human neurons. *Cell Death Differ*. 2019 Nov;26(11):2464-2478. doi: 10.1038/s41418-019-0313-x. i.f.: 12.4
5. Pepe S, Aprile A, Castroflorio E, Marte A, Giubolini S, Hopestaine S, Parsons A, Soares T, Benfenati F, Oliver PL, **Fassio A**. TBC1D24 interacts with the v-ATPase and regulates intraorganellar pH in neurons. *iScience* 2024. doi.org/10.1016/j.isci.2024.111515 i.f.: 4.1
6. Tagliatti E, Fadda M, Falace A, Benfenati F, **Fassio A**. Arf6 regulates the cycling and the readily releasable pool of synaptic vesicles at hippocampal synapse. 2016 *eLife*. 2016 Jan 5;5. pii: e10116. doi: 10.7554/eLife.10116. i.f.: 7.7.
7. Piccini A, Castroflorio E, Valente P, Guarnieri FC, Aprile D, Michetti C, Bramini M, Giansante G, Pinto B, Savardi A, Cesca F, Bachi A, Cattaneo A, Wren JD, **Fassio A**, Valtorta F, Benfenati F, Giovedì S. APACHE Is an AP2-Interacting Protein Involved in Synaptic Vesicle Trafficking and Neuronal Development. *Cell Rep*. 2017 21(12):3596-3611. doi: 10.1016/j.celrep.2017.11.073. i.f.: 8.8
8. Parisi B, Esposito A, Castroflorio E, Bramini M, Pepe S, Marte A, Guarnieri FC, Valtorta F, Baldelli P, Benfenati F, **Fassio A**, Giovedì S. Apache is a neuronal player in autophagy required for retrograde axonal transport of autophagosomes. *Cell Mol Life Sci*. 2024 Oct 5;81(1):416. doi: 10.1007/s00018-024-05441-7. i.f.: 6.2

In parallel, I coordinated the research on the functional characterization of *de novo* and biallelic mutations in *ATP6V1A* and *DXML2* genes causing developmental disorders with epilepsy with the identification of impaired pH homeostasis and autophagy as a novel mechanism underlying neurodevelopmental and connectivity defects (9-12). To apply the iPSC-derived neurons for the study of the pathophysiology of v-ATPase related diseases, I recently contributed to the setting of standardized method for the culture and the differentiation of iPSC-derived glutamatergic neurons (13).

9. Esposito A., Pepe S., Cerullo MS, Cortese K., Tsushima Semini H., Giovedì S., Guerrini R., Benfenati F., Falace A., **Fassio A**. ATP6V1A is required for synaptic rearrangements and plasticity in murine hippocampal neurons. *Acta Physiologica* 2024. doi: 10.1111/apha.14186. i.f.: 6.4.
10. Guerrini R, Mei D, Kerti-Szigeti K, Pepe S, Koenig MK, Von Allmen G, Masuelli L, Conti V, Novarino G, **Fassio A**. 2022 Phenotypic and genetic spectrum of ATP6V1A encephalopathy: a disorder of lysosomal homeostasis. *Brain*. 145(8):2687-2703. doi: 10.1093/brain/awac145. i.f.: 14.5.
11. Esposito A, Falace A, Wagner M, Gal M, Mei D, Conti V, Pisano T, Aprile D, Cerullo MS, De Fusco A, Giovedì S, Seibt A, Magen D, Polster T, Eran A, Stenton SL, Fiorillo C, Ravid S, Mayatepek E, Hafner H, Wortmann S, Levanon EY, Marini C, Mandel H, Benfenati F, Distelmaier F, **Fassio A***, Guerrini R.* 2019 Biallelic DMXL2 mutations impair autophagy and cause Ohtahara syndrome with progressive course. *Brain*. 1;142(12):3876-3891. doi: 10.1093/brain/awz326. * equal contribution i.f.: 14.5.
12. **Fassio A**, Esposito A, Kato M, Saitsu H, Mei D, Marini C, Conti V, Nakashima M, Okamoto N, Olmez Turker A, Albuz B, Semerci Gündüz CN, Yanagihara K, Belmonte E, Maragliano L, Ramsey K, Balak C, Siniard A, Narayanan V; C4RCD Research Group, Ohba C, Shiina M, Ogata K, Matsumoto N, Benfenati F, Guerrini R. De novo mutations of the ATP6V1A gene cause developmental encephalopathy with epilepsy. *Brain*. 2018 Apr 13. doi: 10.1093/brain/awy092. i.f.: 14.5.
13. Servetti M, Caramia M, Parodi G, Loiacono F, Nano E, Biddau G, Ferrando L, Morinelli L, Valente P, Martinoia S, Escelsior A, Serafini G, Tamburro S, Baldassari S, **Fassio A**, Benfenati F, Corradi A, Sterlini B. Optimization of Transcription Factor-Driven Neuronal Differentiation from Human Induced Pluripotent Stem Cells for Disease Modelling and Drug Screening. *Stem Cell Rev Rep*. doi: 10.1007/s12015-025-10845-4. i.f.: 4.2

In collaboration with Fabio Benfenati, I contributed to the elucidation of the functional role of Synapsins and PRRT2 in the regulation of synaptic vesicle cycling and synaptic transmission and the first description and functional characterization of pathogenic *SYNAPSIN* mutations leading to epilepsy and autism (14-20).

14. **Fassio A**, Patry L, Congia S, Onofri F, Piton A, Gauthier J, Pozzi D, Messa M, Defranchi E, Fadda M, Corradi A, Baldelli P, Lapointe L, St-Onge J, Meloche C, Motttron L, Valtorta F, Nguyen DK, Rouleau GA, Benfenati F, Cossette P. SYN1 loss-of-function mutations in ASD and partial epilepsy cause impaired synaptic function. *Hum Mol Genet.* 2011, 20: 2297-307. i.f.: 3.5
15. Corradi A, Fadda M, Piton A, Patry L, Marte A, Rossi P, Cadieux-Dion M, Gauthier J, Lapointe L, Motttron L, Valtorta F, Rouleau GA, Fassio A, Benfenati F, Cossette P. SYN2 is an autism predisposing gene: loss-of-function mutations alter synaptic vesicle cycling and axon outgrowth. *Hum Mol Genet.* 2014 23(1):90-103. i.f.: 3.5.
16. Verstegen AMJ, Tagliatti E, Lignani G, Marte A, Stolerio T, Atias M, Corradi A, Valtorta F, Gitler D, Onofri F, **Fassio A***, Benfenati F*. Phosphorylation of Synapsin I by Cyclin-Dependent Kinase-5 sets the ratio between the resting and the recycling pool of synaptic vesicles at hippocampal synapses. *J. Neurosci* 2014 34:7266-80. *equal contribution. i.f.: 5.3
17. Valente P, Castroflorio E, Rossi P, Fadda M, Sterlini B, Cervigni RI, Prestigio C, Giovedì S, Onofri F, Mura E, Guarnieri FC, Marte A, Orlando M, Zara F, **Fassio A**, Valtorta F, Baldelli P, Corradi A, Benfenati F. PRRT2 Is a Key Component of the Ca(2+)-Dependent Neurotransmitter Release Machinery. *Cell Rep.* 2016 Apr 5;15(1):117-31. doi: 10.1016/j.celrep.2016.03.005. i.f.: 8.8
18. Fruscione F, Valente P, Sterlini B, Romei A, Baldassari S, Fadda M, Prestigio C, Giansante G, Sartorelli J, Rossi P, Rubio A, Gambardella A, Nieus T, Broccoli V, **Fassio A**, Baldelli P, Corradi A, Zara F, Benfenati F. PRRT2 controls neuronal excitability by negatively modulating Na⁺channel 1.2/1.6 activity. *Brain.* 2018 Apr 1;141(4):1000-1016. doi: 10.1093/brain/awy051. i.f.: 14.5
19. Sterlini B, Romei A, Parodi C, Aprile D, Oneto M, Aperia A, Valente P, Valtorta F, **Fassio A**, Baldelli P, Benfenati F, Corradi A. (2021) An interaction between PRRT2 and Na⁺/K⁺ ATPase contributes to the control of neuronal excitability. *Cell Death Dis.* 12 (4):292. doi: 10.1038/s41419-021-03569-z. i.f.: 9.0
20. Moschetta M, Ravasenga T, De Fusco A, Maragliano L, Aprile D, Orlando M, Sacchetti S, Casagrande S, Lignani G, **Fassio A**, Baldelli P, Benfenati F. Ca²⁺ binding to synapsin I regulates resting Ca²⁺ and recovery from synaptic depression in nerve terminals. *Cell Mol Life Sci.* 2022 Nov 21;79(12):600. doi: 10.1007/s00018-022-04631-5. i.f.: 8.0