

NAME Tongiorgi Enrico	POSITION TITLE Full Professor
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EDUCATION/TRAINING (Begin with initial professional education, and include postdoctoral training)

Institution and location	Degree	Year(s)	Field of study
University of Pisa, Pisa (Italy) Supervisor prof. Marcello Brunelli	Master Degree in Biology CUM LAUDE	1988	Biology, Neurobiology, protein kinases, leech (<i>Hirudo medicinalis</i>), learning and memory.
Department of Neurobiology at the University of Heidelberg (Germany) Supervisor prof. Melitta Schachner	Pre-doctoral fellow <u>Accademia Nazionale dei Lincei</u> fellowship	Jan/Dec 1990	Neurobiology, cell adhesion molecules, zebrafish (<i>Danio rerio</i>), embryonic development of the CNS.
Swiss Federal Institute of Technology (ETH) Zürich (Switzerland) Supervisor prof. Melitta Schachner	PhD	1994	Neurobiology, zebrafish (<i>Danio rerio</i>), embryonic development of the CNS.
International School for Advanced Studies (S.I.S.S.A./I.S.A.S.) of Trieste (Italy). Supervisor prof. Antonino Cattaneo.	Post-doctoral fellow <u>U.N.I.D.O.</u> fellowship	Oct 1994/ Sep1997	Neurobiology, neurotrophins, mRNA processing and intracellular signaling in rat CNS development.
Medical Research Council (M.R.C.) Cambridge (UK). Supervisor Prof. Antonino Cattaneo.	Short-term visitor	June 1996	Neurobiology, neurotrophins, mRNA processing and intracellular signaling in rat CNS.
International School for Advanced Studies (S.I.S.S.A./I.S.A.S.) of Trieste (Italy). Supervisor Prof. Antonino Cattaneo.	Post-doctoral fellow	Oct 1997/ Jan 1998	Neurobiology, neurotrophins, mRNA processing and intracellular signaling in rat CNS development.

A. Personal Statement

Prof. Tongiorgi is considered one of the leading Italian experts in the field of neurotrophic factors, and is internationally recognized for his contribution to the understanding of the cellular mechanisms that regulate local expression of the neurotrophin Brain-derived neurotrophic factor (*Bdnf*). He has contributed to consolidate the role of BDNF as serum biomarker in patients affected by neuropsychiatric diseases. In particular, in schizophrenic patients with cognitive deficits, in 6 genetically isolated populations with anxiety disorders, and in autism. In a recent study, his team has investigated BDNF together with 58 serum biomarkers in relation with work-related stress. In addition, he has contributed in setting the technical and theoretical bases for the establishment of a reliable protocol for measuring BDNF in serum samples. His current chief scientific interest is to identify a treatment (and its mechanism of action) to rescue neuronal atrophy in Rett syndrome and thereby alleviate patients and their families from the burden of this devastating disease. Prof. Tongiorgi's group has previously demonstrated that mirtazapine treatment is able to rescue cortical atrophy, GABAergic/Glutamatergic imbalance and restore to normal levels breath frequency in a male MeCP2-knock out mouse. More recently, they demonstrated the ability of mirtazapine to rescue motor deficits, somatosensory hypersensitivity in adult female mice and correct behaviours in the domain of Social communication/Responsiveness for the items Hypomimia, Unresponsiveness and Apathy, and in the domain of Aggressiveness for the items Irritability, Hyperactivity, Aggressiveness, Self-Aggressiveness and Biting in adult patients with Rett syndrome.

B. Positions and Honors**CURRENT POSITION**

Since 2020	Full Professor in Comparative Anatomy and Cytology. Teacher for the courses: Cellular Neurobiology, Applied Neurosciences, Biology of Development
Since 2022	Coordinator of the International Master's Degree in Neuroscience, University of Trieste
Since 1 st March 2000	Group leader , Head of the Cellular and Molecular Neuroanatomy Laboratory

PAST POSITIONS AND PROFESSIONAL EXPERIENCE

2008 – 2022	Director of the Light Microscopy Core facility of the Department of Life Sciences, University of Trieste
Feb-March 2020	Visiting professor ("Inviti lunghi") Scuola Normale Superiore di Pisa (Italy)
May 2019 /May 2020	Deputy Director for the Third Mission of the Department of Life Sciences, University of Trieste
Oct 2008/Aug 2016	Responsible of the diagnostic service to detect biomarkers of neurological diseases for the Neurology Clinic

	of the Hospitals of Trieste, Portogruaro and Gorizia - Italy
May 2012/Apr 2016	Deputy-Rector for Public communication of Science of the University of Trieste
Jan 2008/May 2012	Scientific Responsible of the International Master in Neuroscience of the University of Trieste
July 2005/2008	Director of the BRAIN Interdepartmental Centre for Neuroscience, University of Trieste (20 faculty members)
1 st March 2000	Startup as independent group leader of the Cellular and Molecular Neuroanatomy Laboratory (with purchase of the equivalent of € 600.000 of lab instruments in the years 2000-2001)
Feb 1998/Dec 2012	University of Trieste (Italy). Assistant Professor in Comparative Anatomy and Cell Biology

HONORS

Fellow of the World Academy of Art and Science (since August 2012). Ranked at position 92 of the Macroarea Biomedical Sciences in the **Top Italian Scientists** classification of the VIA-Academy <http://www.topitalianscientists.org>. 1990 Accademia Nazionale dei Lincei pre-doctoral fellowship conferred by a committee chaired the Nobel Prize Prof. Rita Levi Montalcini; 1991 Bilateral Swiss-Italian Ministeries for Foreign Affairs fellowship; 1994-1997 United Nations-UNIDO Post-doctoral Fellowship; 1998 Invited speaker "International Neuroscience Meeting of the Brazilian Academy of Science"; 1998 and 2000 Telethon-Italy research grants; 2002 Invited speaker "VII Congress Société Européenne de Neurologie Pédiatrique" Paris, France; 2004 First Prize of the Start-Cup contest of the University of Trieste for the best innovation project; 2005 Invited speaker "International symposium: neuroplasticity, neurotrophic factors and affective disorders" Pisa, Italy; 2005 Research Award of the National Ataxia Foundation (USA); 2006 Invited speaker "Winter conference in Neuroscience" Solden, Austria; 2007 Invited speaker "IBRO International Meeting" Melbourne, Australia, 2007 Invited speaker at the Gordon Conference "Neurotrophic factors", 2009 Invited Speaker at the annual meeting of the American College Neuropsychiatry. Dec. 2011: Award by TÜV of the certification ISO-9001:2008 for the services offered by the laboratory (TABA service for the quantification of biomarkers of autoimmune and neurodegenerative neurological disorders for 4 Italian hospitals); 2017 Invited Speakers Gordon Conference on Neurotrophic Factors.

C. Contributions to Science

Prof. Tongiorgi's laboratory has given a major contribution to the understanding of the biological functions of Brain-Derived Neurotrophic Factor (BDNF). They demonstrated that BDNF splice variants provide a spatial and quantitative code for local expression and selective morphological shaping of dendrites during development. They investigated BDNF proteolytic forms as biomarkers of chronic stress, depression, multiple sclerosis, autism and cognitive impairment in schizophrenia. Current research focuses on the pharmacological rescue of **neuronal atrophy** in Rett syndrome. His group has identified 14 functional and morphological descriptors, defining 6 stages of the development of cultured mouse and rat hippocampal neurons (1). This assay enabled them to identify the stages at which Rett syndrome's neurons fail to grow and show the atrophic phenotype (1). Then, through miniaturization of this assay to a 96-well plate format, Tongiorgi's lab created a novel drug screening tool using high-content imaging methods to identify compounds of natural or synthetic origin capable of contrasting neuronal atrophy in Rett syndrome and other neurodevelopmental disorders (2). In a previous project funded by the Jerome Lejeune Foundation, this assay was successfully used to identify 14 FDA-approved drugs able to counteract the neuronal atrophy associated with Rett syndrome (Roggero et al., **unpublished**). Then, using a proprietary in vitro cell-based method that detects variations in BDNF levels within neurons (Patent PCT/EP2010/067081; 3) Tongiorgi's group found that four of the isolated FDA-approved hits, including the antidepressant mirtazapine, can promote an increase in cellular BDNF levels (Roggero et al., **unpublished**). Finally, they demonstrated the ability of mirtazapine to rescue neuronal atrophy, breathing and behavioral defects in a male animal model of Rett syndrome (4), in **adult** female mice and patients with Rett syndrome (5) and in juvenile female mice (Flores Gutierrez et al., 2022).

Relevant publications:

1. Baj G., Patrizio A., Montalbano A., Sciancalepore M. and Tongiorgi E. (2014). Developmental and maintenance defects in Rett syndrome neurons identified by a new mouse staging system in vitro. *Front Cell Neurosci.* 05 Feb 2014.
2. Nerli E, Roggero OM, Baj G, **Tongiorgi E.** (2020). In vitro modeling of dendritic atrophy in Rett syndrome: determinants for phenotypic drug screening in neurodevelopmental disorders. *Sci Rep.* 2020 Feb 12;10(1):2491.
3. Vaghi V, Polacchini A, Baj G, Pinheiro VL, Vicario A, Tongiorgi E. (2014). Pharmacological Profile of Brain-Derived Neurotrophic Factor (BDNF) Splice Variants Translation Using a Novel Drug Screening Assay: a "Quantitative Code". *J Biol Chem.* Jul 29. pii: jbc.M114.586719.
4. Bittolo T, Raminelli CA, Deiana C, Baj G, Vaghi V, Ferrazzo S, Bernareggi A, **Tongiorgi E.** (2016). Pharmacological treatment with mirtazapine rescues cortical atrophy and respiratory deficits in MecP2 null mice. *Sci Rep.* Jan 25 6:19796.
5. Flores Gutiérrez, J., De Felice, C., Natali, G, Leoncini S., Signorini C., Hayek J., Tongiorgi E. (2020) Protective role of mirtazapine in adult female Mecp2+/- mice and patients with Rett syndrome. *J Neurodevelop Disord* 12, 26.
6. Flores Gutiérrez J, Natali G, Giorgi J, De Leonibus E, Tongiorgi E. Mirtazapine treatment in a young female mouse model of Rett syndrome identifies time windows for the rescue of early phenotypes. *Exp Neurol.* 2022 Jul;353:114056.

D. Research Support

RESEARCH SUPPORT Total grant amount since 1998: > 2.5 Million € Euros (41 projects, coordinator in 34).

Research grants in the last 4 years (2017-2021):

November 2021	Angelini for Future: Coordinator “Repurposing mirtazapine in Rett syndrome: a multicentric randomized, placebo-controlled Phase II study”	€200.000
Sept 2020	Foundation Jerome Lejeune (France): Coordinator Advanced Project #1968 “A systems pharmacology approach for innovative therapies in Rett syndrome”	€80.000
Jan 2020	ProRett Ricerca ONLUS – Coordinator Project “Centro Drug Screening per la sindrome di Rett ”	€55.000
July 2019	MIUR –PRIN 2017 PRIN_ 2017HPTFFC.– Unit Responsabile Project “SYNACTIVE – Synactive Engrams in memory formation and recall”	€106.406
Sept 2018	ProRett Ricerca ONLUS – Coordinatore Cofunding grant for a fellowship “Centro Drug Screening per la sindrome di Rett ”	€10.000
Sept 2018	Consorzio Interuniversitario per le Biotecnologie: Coordinator Cofunding grant for a fellowship “Enhancers of BDNF translation for a neuroprotective therapy in Rett Syndrome”	€10.000
July 2017	European Union – Interreg ITA/SLO 5th programme: Coordinator “MEMORI-net - Network per la Riabilitazione Mentale e Motoria dell’Ictus; Združenje za kognitivno in gibalno rehabilitacijo po možganski kapi”	€808.406
July 2017	Foundation Jerome Lejeune (France): Coordinator “Enhancers of BDNF translation for a neuroprotective therapy in Rett Syndrome”	€40.000

PATENTS

- Patent PCT/EP2010/067081 – Priority Date: 09 November 2010 - “Method for the selection of compounds useful for the treatment of neuropsychiatric and neurodegenerative diseases” (Status: A1)

- Patent ITALIA n. 10202000032423- Priority Date: 24 December 2020 (exp. 2040)- “Metodo per la produzione di forme processate proteoliticamente di fattori trofici o fattori di crescita”

REVIEWER FOR GRANTS AGENCIES (12 nations, 5 continents)

2018 MS Research, Australia; 2002-present Third World Academy for Africa, South America and Asia (Basic Science Grant Scheme; 2002, 2003). Lundbeckfunds Denmark, Member of the Biotech/Biomed Basic Research Evaluation Panel for all Ireland’s Universities; 2003 Wellcome Trust Research Grants (UK); 2005 Estonian Science Foundation (Estonia)., 2006-2009 External Referee of the Open Programme for Earth and Life Sciences (ALW) of the Netherlands Organisation for Scientific Research (NWO), 2009 Ministry of Education of Chile (CONDECYT), 2009 Third World Organization for Women in Science; 2010 Reviewer of TEAM programme for the Foundation for Polish Science (Poland), 2012, 2016, 2017 ANR-France. Member of the Conseil Scientifique of the Jerome Lejeune Foundation, Paris 2021, 2022– France.

EDITORIAL/REVIEWER ACTIVITY

Ad-hoc Reviewer for 38 journals.

Brain Research Bulletin, Brain Research Interactive, Molecular Brain Research, Bipolar Disorders, Journal of Neurochemistry, Neurobiology of Aging, European Journal of Neurology, Molecular and Cellular Biochemistry, Journal of Neuroscience, Neurobiology of disease, Behavioural Brain Research, Journal of Nanobiotechnol, BMC Neuroscience, Journal of affective disorders, Hippocampus, Neuroscience Research, Cerebral Cortex, Progress in Neuro-Psychopharmacology & Biological Psychiatry, Traffic, Frontiers in Neuroscience, Genes Brain & Behavior, Neuroscience Letters, Psychiatry Research, Neuropharmacology, Experimental Brain Research, International Journal of Neuropsychopharmacology, Developmental Neuroscience, Biological Psychiatry, Oxidative Medicine and Cellular Longevity, Neuroscience & Biobehavioral Reviews, Pharmacological Research, Research in Veterinary Science, Science Advances, Science Signaling, RNA, Traffic, Journal of Autism and Developmental Disorders.

Membership of Editorial boards

Since 2020, **Review Editor** of **Cellular Neurophysiology** (specialty section of Frontiers in Cellular Neuroscience)

Since 2018, **Associate Editor** of **Frontiers in Molecular Neuroscience**

Since 2011, Member of the Editorial Board of **Scientific Reports** (Nature Publishing Group).

2011-2017, Member of the Editorial Board of **The Scientific World JOURNAL**(Indawi Publishing Group).

PUBLICATIONS

Total 80 publications: [http://www.ncbi.nlm.nih.gov/pubmed/?term=Tongiorgi E](http://www.ncbi.nlm.nih.gov/pubmed/?term=Tongiorgi+E) Google Scholar H-index = 42, i10-index = 68; Scopus H-index = 40; total n. citations 5950