BIOGRAPHICAL SKETCH

NAME: FABIO BENFENATI, MD (orcid.org/0000-0002-0653-8368)

POSITION TITLE: Tenured Full Professor of Neurophysiology; Research Director, The Italian Institute of Technology (IIT)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Alma Mater University of Bologna	MD	10/1979	Neuroscience
Alma Mater University of Bologna	Neurologist	10/1983	Neuroscience
Karolinska Institutet (Sweden)	Postdoctoral fellow	12/1984	Neuroscience
The Rockefeller University, New York (USA)	Research Associate	12/1989	Neuroscience

A. Personal Statement

The main subjects of investigation of Dr Benfenati in the last 30 years have been the molecular mechanisms of information transfer among neurons and the application of new technologies to modulate neural activity in health and disease. He started working in the field of synaptic transmission first at the Karolinska Institutet, Stockholm in the laboratories of Kjell Fuxe and Thomas Hokfelt, who pioneered the field of neurotransmission in the central nervous system. Thereafter, he joined Paul Greengard's laboratory at the Rockefeller University in 1986. Since then, he has addressed the molecular and cellular mechanisms of neural and synaptic communication using a variety of experimental models of human diseases by using a combination of experimental techniques ranging from cell biology, biochemistry, biophysics, live imaging, electrophysiology and molecular biology. The double background of neurologist and cellular neurophysiologist allowed him to get in depth into the cellular mechanisms that underlie normal brain function and whose dysfunction leads to the pathogenesis of neurological diseases. He gave significant contributions to the following topics: (i) Molecular mechanisms of neurotransmitter release, synaptic vesicle trafficking and synaptic plasticity. A long array of papers has, for the first time, put forward the functional role of synaptic vesicle proteins in the regulation of the multi-step process of synaptic transmission; (ii) The membrane fusion machine acting during exocytosis and identification of the intracellular targets of tetanus/botulinum neurotoxins; (iii) Pathogenic mechanisms of synaptopathies and neurodegenerative diseases in genetically altered mice lacking synaptic vesicle proteins as models of human neurological disorders and investigation of disease gene function mouse and human reprogrammed neurons; (iv) Generation of engineered neuronal networks, neuro-electronic and opto-neural interfaces by exploiting optogenetics and photovoltaic interfaces.

In 2006 he was competitively selected to build the *Department of Neuroscience and Brain Technologies* at the newborn *Italian Institute of Technology* (IIT) in Genova with the mission to approach interdisciplinary research in Neuroscience by interacting with Nanochemistry, Nanophysics and Nanostructure Departments developed within the same Institute, with research programs regarding innovative neuroelectronic and opto-neural interfaces to pioneer new solution for neuroprosthetics. Starting from 2015, he is Director of the IIT Center of Synaptic Neuroscience and Technology (NSYN) that IIT developed together with the IRCCS University Hospital San Martino and the University of Genova Medical School with the aim of boosting the application of new technologies to central nervous system diseases. His current research group in NSYN consists of 40 people including researchers, postdocs and PhD students working in state-of-art equipped laboratories such as multiple in vitro/in vivo electrophysiology units with the most sophisticated patch-clamp, multielectrode arrays and optogenetics setups, molecular and cellular neurobiology units with a large cell culture facility and state-of-the art live neuroimaging and behavioral facilities. In the last 10 years, he exploited smart photovoltaic and photochromic materials for neuronal photostimulation with very innovative results that produced several papers in Nature, a few patents and the foundation of the NovaVido s.r.l. startup in May 2021 for retina prosthetics.

He is author of high rank research papers in top journals such as *Science* (1), *Nature* (2), *Neuron* (2), *Nature Materials* (1), *Nature Photonics* (1), *Nature Nanotechnology* (3), *Nature Communications* (6), *Nature Neuroscience* (1), *Nature Reviews Materials* (1), *J Cell Biology* (5), *J Clin Invest* (2), *EMBO J* (3), *Proc Natl Acad Sci USA* (12), *Cell Journals* (1 *Cell Stem Cell*, 3 *Cell Reports, 1 Aging Cell*), *Brain* (3) and co-inventor of 8 patents.

***Bibliometric indexes (SCOPUS): h*-index = 78; publications > 450; citations > 22,000.**

Key papers

1. Ghezzi D, Antognazza MR, Maccarone R, Bellani S, Lanzarini E, Martino N, Mete M, Pertile G, Bisti S, Lanzani G, **Benfenati F** (2013) A polymer optoelectronic interface restores light sensitivity in blind rat retinas. *Nature Photonics* 7: 400-406.
2. Maya-Vetencourt JF, Ghezzi D, Antognazza MR, Colombo E, Mete M, Feyen P, Desii A, Buschiazzo A, Di Paolo M, Di Marco S, Ticconi F, Emionite L, Shmal D, Marini C, Donelli I, Freddi G, Maccarone R, Bisti S, Sambuceti G, Pertile G, Lanzani G, **Benfenati F** (2017) A fully organic retinal prosthesis restores vision in a rat model of degenerative blindness. *Nature Materials* 16: 681-689.
3. DiFrancesco ML, Lodola F, Colombo E, Maragliano L, Bramini M, Paternò GM, Baldelli P, Serra MD, Lunelli L, Marchioretto M, Grasselli G, Cimò S, Colella L, Fazzi D, Ortica F, Vurro V, Eleftheriou CG, Shmal D, Maya-Vetencourt JF, Bertarelli C, Lanzani G, **Benfenati F** (2020) Neuronal firing modulation by a membrane-targeted photoswitch. *Nature Nanotechnology* 15: 296-306.
4. Maya-Vetencourt JF, Manfredi G, Mete M, Colombo E, Bramini M, Di Marco S, Shmal D, Mantero G, Dipalo M, Rocchi A, DiFrancesco ML, Papaleo ED, Russo A, Barsotti J, Eleftheriou C, Di Maria F, Piazza F, Cossu V, Emionite L, Ticconi F, Marini C, Sambuceti G, Pertile G, Lanzani G, **Benfenati F** (2020) Subretinally injected semiconducting polymer nanoparticles fully rescue vision in a rat model of retinal dystrophy. *Nature Nanotechnology* 15: 698-708.
5. Francia S, Shmal D, Di Marco S, Chiaravalli G, Maya-Vetencourt JF, Manterol G, Michetti C, Cupini S, Manfredi G, DiFrancesco ML, Rocchi A, Perotto S, Attanasio M, Sacco R, Bisti S, Pertile G, Lanzani G, Colombo E, Benfenati F (2022) Light-induced charge generation in polymeric nanoparticles restores vision in advanced-stage retinitis pigmentosa rats. *Nature Communications* 13: 3677.

B. Positions and Honors

1980-1983: "*Accademia Nazionale dei Lincei*" Giovanni Levi Neurobiology prize and fellowship.
1983-1984: **Postdoctoral fellow** at the Dept of Histology and Neurobiology at the Karolinska Institutet, Stockholm (Sweden).
1986-1989: **Fogarty Fellow & Research Associate**, Laboratory of Molecular and Cellular Neuroscience, The Rockefeller University, New York (USA) directed by Prof Paul Greengard (Nobel Laureate in 2000).
1990-present: **Foreign Member of the Adjunct Faculty,** The Rockefeller University, New York (USA).
1992-1999: **Associate Professor of Physiology**, University of Roma, School of Medicine (Italy).
2000-present: **Full Professor of Neurophysiology**, University of Genova, School of Medicine (Italy).
2006-2015: **Founder and Research Director**, Dept. Neuroscience and Brain Technologies, The Italian Institute of Technology.
2015-present: **Research Director**, Center of Synaptic Neuroscience and Technology, The Italian Institute of Technology.

Honors:

1997: *Fullbright* Advanced Research and University Lecturing Award.
2003-2005: President, *The Italian Society for Neuroscience.*
2005-present: Member, Scientific Committee of the *International Genoa Science Festival.*
2009-2011: President, *The Italian Physiological Society.*
2009-2012: Member, *CNRS Conseil Scientifique du Dept. Sciences du Vivant*, Paris (France).
2012: *Foreign Scientist Award*, The Michael Stern Foundation for Parkinson's Disease, New York (USA).
2012-present: President, Board of the *Clinical Research Institute of Neurological Sciences*, Bologna (Italy).
2020: International 2020 *Cesare Casella Prize*, Pavia (Italy).
2020: International 2020 *Herlitzka Prize for Physiology* (Italy).
2020: Member of the *Academia Europaea (section: Physiology and Neuroscience).*
2021: President Elect, *The Federation of the European Physiological Societies* (FEPS).
2021-2022: Chair of the LS5 panel (Neuroscience) for the CNRS/INSERM International ATIP/Avenir Program.
2022: Fellow of the Academy of the International Union of Physiological Sciences (IUPS).

C. Contributions to Science

1. LIGHT-SENSITIVE NEURONAL INTERFACES FOR NEURONAL PHOTOSTIMULATION AND RETINA PROSTHETICS

Fabio Benfenati has pioneered and fully developed the extremely original field of light-controlled, gene-less organic nanoactuators to trigger light-driven neuronal activation. This allows to interrogate specific brain circuits and compensate for nervous system pathologies in which neuronal degeneration has induced a loss of function. Inspired by organic solar cells, the candidate was the first to propose a polymer (P3HT)/cell interface for achieving the optically controlled elicitation of electrical activity in primary neurons. The results supported the feasibility and the high translational potential of this approach. The same interface could rescue light sensitivity in blind retinas put in close subretinal contact with the polymer, with bursts of action potentials by retinal ganglion cells (RGC) in response to daylight-intensity stimuli. The polymer, layered onto an organic silk fibroin substrate, was also able to rescue light sensitivity, light-driven behavior and visual acuity after *in vivo* subretinal implantation in Royal College of Surgeons (RCS) rats, a well-accepted experimental model of human *Retinitis pigmentosa*. Dr. Benfenati recently engineered conjugated polymer nanoparticles (P3HY-NPs) transforming it into a "*liquid retina device*" that, injected in the retina, mediates light-evoked stimulation of retinal neurons and persistently recovers subcortical, cortical and behavioural visual responses in the blind RCS rats in the absence of trophic effects or retinal inflammation. P3HT-NPs provide a new avenue in neuronal photostimulation, with potential applications not only in retinal degeneration, but also for deep brain stimulation. To explore additional non-genetic strategies for neuronal photostimulation, dr. Benfenati also engineered novel membrane-targeted azobenzene photoswitches as light-driven nanomachine to perturb membrane dynamics. This novel molecular device (Ziapin2) stably partitions into the neuronal membrane and causes its thinning through trans-dimerization in the dark, resulting in an increased membrane capacitance and lower intrinsic excitability. Under these condition, millisecond pulses of visible light induce a sudden drop in capacitance followed by a fast depolarization triggering robust action potential firing. These effects are persistent and can be evoked in vivo, proving the potential of Ziapin2 for the modulation of the neuronal passive properties in the millisecond time scale, with high potential for future applications in neuroscience.

1.1 Maya-Vetencourt JF, Ghezzi D, Antognazza MR, Colombo E, Mete M, Feyen P, Desii A, Buschiazzo A, Di Paolo M, Di Marco S, Ticconi F, Emionite L, Shmal D, Marini C, Donelli I, Freddi G, Maccarone R, Bisti S, Sambuceti G, Pertile G, Lanzani G, **Benfenati F** (2017) A fully organic retinal prosthesis restores vision in a rat model of degenerative blindness. *Nature Materials* 16: 681-689.

1.2 DiFrancesco ML, Lodola F, Colombo E, Maragliano L, Bramini M, Paternò GM, Baldelli P, Serra MD, Lunelli L, Marchioretto M, Grasselli G, Cimò S, Colella L, Fazzi D, Ortica F, Vurro V, Eleftheriou CG, Shmal D, Maya-Vetencourt JF, Bertarelli C, Lanzani G, **Benfenati F** (2020) Neuronal firing modulation by a membrane-targeted photoswitch. *Nature Nanotechnology* 15: 296-306.

1.3 Maya-Vetencourt JF, Manfredi G, Mete M, Colombo E, Bramini M, Di Marco S, Shmal D, Mantero G, Dipalo M, Rocchi A, DiFrancesco ML, Papaleo ED, Russo A, Barsotti J, Eleftheriou C, Di Maria F, Piazza F, Cossu V, Emionite L, Ticconi F, Marini C, Sambuceti G, Pertile G, Lanzani G, **Benfenati F** (2020) Subretinally injected semiconducting polymer nanoparticles fully rescue vision in a rat model of retinal dystrophy. *Nature Nanotechnology* 15: 698-708.

1.4 Francia S, Shmal D, Di Marco S, Chiaravalli G, Maya-Vetencourt JF, Manterol G, Michetti C, Cupini S, Manfredi G, DiFrancesco ML, Rocchi A, Perotto S, Attanasio M, Sacco R, Bisti S, Pertile G, Lanzani G, Colombo E, **Benfenati F** (2022) Light-induced charge generation in polymeric nanoparticles restores vision in advanced-stage retinitis pigmentosa rats. *Nature Communications*. Epub ahead of print. doi: 10.1038/s41467-022-31368-3

2. MECHANISMS OF NETWORK STABILITY: THE NOVEL PRRT2 GENE AND PAROXYSMAL DISORDERS

In the past few years, proline-rich transmembrane protein 2(PRRT)2 has been identified as the causative gene for several paroxysmal neurological disorders including the frequent kinesigenic dyskinesia. Recently, an important role of PRRT2 in synapse transmission has emerged. Knock down of the protein strongly impairs the formation of synaptic contacts and neurotransmitter release. At the nerve terminal, PRRT2 endows synaptic vesicle exocytosis with Ca^{2+}-sensitivity by interacting with proteins of the fusion complex, with the Ca^{2+} sensor synaptotagmin and enhancing density and expression of P/Q Ca^{2+} channels at the active zones. PRRT2 is intensely expressed in cerebellum and in restricted areas of the forebrain and PRRT2 KO mice mimic the pleiotropy of the PRRT2 dependent human pathology. They display paroxysmal movements at the onset of locomotion and in response to audiogenic stimuli, are more susceptible to convulsants and display an altered synaptic transmission in the cerebellum and hippocampus. Moreover, PRRT2 negatively modulates the membrane expression and biophysical properties of Na channels $Na_V1.2$ and $Na_V1.6$ in primary knockout neurons as well as in human iPSC-derived neurons. The stabilizing effects of PRRT2 on the activity of neural circuits depends on both an inhibition of synaptic facilitation and an inhibitory control of intrinsic excitability. Thus, the paroxysmal disorders due to mutations in the *PRRT2* gene can be defined as mixed channelopathies/synaptopathies.

2.1 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** (2016) PRRT2 is a key component of the Ca^{2+}-dependent neurotransmitter release machinery. *Cell Reports* 15: 117-1131.
2.2 Michetti C, Castroflorio E, Marchionni I, Forte N, Sterlini B, Binda F, Fruscione F, Baldelli P, Valtorta F, Zara F, Corradi A, **Benfenati F** (2017) The PRRT2 knockout mouse recapitulates the neurological diseases associated with PRRT2 mutations. *Neurobiol. Dis.* 99: 66-83.
2.3 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** (2018) PRRT2 controls neuronal excitability by negatively modulating Na^+ channel 1.2/1.6 activity. *Brain* 141: 1000-1016.
2.4 Ferrante D, Sterlini B, Prestigio C, Marte A, Corradi A, Onofri F, Tortarolo G, Vicidomini G, Petretto A, Muià J, Thalhammer A, Valente P, Cingolani LA, **Benfenati F*, Baldelli P*** (2021) PRRT2 modulates presynaptic Ca^{2+} influx by interacting with P/Q-type channels. *Cell Reports* 35: 109248. *co-last and corresponding authors

3. MECHANISMS HOMEOSTATIC PLASTICITY AND SURVIVAL: ROLE OF THE TRANSCRIPTIONAL REPRESSOR REST/NRSF
The repressor element 1-silencing transcription factor (REST) is a zinc-finger transcription factor highly expressed in embryonic stem-cells, that is rapidly downregulated during neural differentiation, thus enabling neurons to express the critical genes necessary for the acquisition and preservation of the neuronal phenotype We found that REST is also active in mature neurons as a molecular hub of a complex neuronal transcriptomic remodeling aimed at maintaining brain homeostasis. In mature excitatory and inhibitory neurons, REST is upregulated in response to hyperexcitability and translocates to the nucleus. We demonstrated that we the hyperactivity-dependent activation of REST furthers neuronal-network homeostasis by down-scaling intrinsic excitability and presynaptic function of excitatory neurons in response to chronic hyperactivity. At the same time, we recently found that REST response at inhibitory transmission consists of an upscaling of strength and density of perisomatic synapses only when the postsynaptic target is an excitatory neuron. Studies in conditional REST knockout mice also revealed that REST is essential to prevent the senescence phenotype in primary mouse neurons and that REST deficiency causes failure of autophagy, loss of proteostasis, increased oxidative stress, and higher rate of cell death. Our results strengthen the idea that the complex epigenetic pathways mediated by REST and downstream transcriptional cascades are essential for neuronal homeostasis and survival.
3.1 Pozzi D, Lignani G, Ferrea E, Contestabile A, Paonessa F, D'Alessandro R, Lippiello P, Boido D, Fassio A, Meldolesi J, Valtorta F, **Benfenati F**, Baldelli P (2013) REST/NRSF-mediated intrinsic homeostasis protects neuronal networks from hyperexcitability. *EMBO J* 32: 2994-3007.
3.2 Paonessa F, Criscuolo S, Sacchetti S, Amoroso D, Scarongella H, Pecoraro Bisogni F, Carminati E, Pruzzo G, Maragliano L, Cesca F, **Benfenati F** (2016) Regulation of neural gene transcription by optogenetic inhibition of the RE1-silencing transcription factor. *Proc Natl Acad Sci USA* 113: E91-100.
3.3 Prestigio C, Ferrante D, Marte A, Romei A, Lignani G, Onofri F, Valente P, **Benfenati F§**, Baldelli P (2021) REST/NRSF drives homeostatic plasticity of inhibitory synapses in a target-dependent fashion. *Elife* 10: e69058. §corresponder
3.4 Rocchi A, Carminati E, De Fusco A, Kowalska JA, Floss T, **Benfenati F** (2021) REST/NRSF deficiency impairs autophagy and leads to cellular senescence in neurons. *Aging Cell* 20: e13471.

4. SYN1/SYN2 AS AUTISM AND EPILEPSY CAUSATIVE GENES
Single, double and triple synapsin knockout mice, with the notable exception of the synapsin III knockout mice, show a severe epileptic and autistic phenotype without gross alterations in brain morphology and connectivity. In the last 10 years, the applicant has clarified the molecular and physiological mechanisms underlying the pathogenesis of the epileptic phenotype observed in synapsin deficient mice. Indeed, synapsins I and II regulate network excitability by exerting distinct roles in excitatory versus inhibitory synapses. They differentially affect crucial steps of presynaptic physiology, and their deletion causes a primary impairment of GABAergic transmission. Electrophysiological studies in synapsin I and synapsin II knockout mice have revealed that the two synapsins have distinct, yet complementary, effects on GABA transmission, with synapsin I that is essential for the fast synchronous GABA release, and synapsin II that is necessary for the delayed asynchronous GABA release that is the major source of tonic inhibition. Interestingly, an array of mutations in SYN1 and SYN2 in humans has been recently associated with ASD and epilepsy. Synapsin isoforms control the tone of activity of neural circuits and the balance between excitation and inhibition. As ASD pathogenesis is believed to result from dysfunctions in the balance between excitatory and inhibitory transmissions in neocortical areas, SYNs are novel ASD candidate genes. Accordingly, deletion of single Syn genes in mice, in addition to epilepsy, causes core symptoms of ASD

by affecting social behavior, social communication, and repetitive behaviors. The phenotype is particularly severe in synapsin II knockout mice that also present defects in auditory and hippocampal functional connectivity as measured with resting state functional fMRI. Taken together, our results reveal a permissive contribution of *Syn2* to the expression of normal socio-communicative behavior and suggest that *Syn2*-mediated synaptic dysfunction can lead to ASD-like behavior through dysregulation of cortical connectivity.

4.1 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, Mottron L, Valtorta F, Khoa Nguyen D, Rouleau GA, **Benfenati F*, Cossette P*** (2011) SYN1 loss-of-function mutations in autism and partial epilepsy cause impaired synaptic function. *Hum. Mol. Genet.* 20: 2297-2307. *co-last authors

4.2 Corradi A, Fadda M, Piton A, Patry L, Marte A, Rossi P, Cadieux-Dion M, Gauthier J, Lapointe L, Mottron L, Valtorta F, Rouleau GA, Fassio A, **Benfenati F*§, Cossette P*** (2014) SYN2 is an autism predisposing gene: loss-of-function mutations alter synaptic vesicle cycling and axon outgrowth. *Hum Mol. Genet.* 23: 90-103. * co-last authors; §corresponder.

4.3 Medrihan L, Ferrea E, Greco B, Baldelli P, **Benfenati F** (2015) Asynchronous GABA release is a key determinant of tonic inhibition and controls neuronal excitability: a study in the Synapsin $II^{-/-}$ mouse. *Cereb Cortex* 25: 3356-3368.

4.4 Rocchi A, Sacchetti S, De Fusco A, Giovedi S, Parisi B, Cesca F, Höltje M, Ruprecht K, Ahnert-Hilger G, **Benfenati F** (2019) Autoantibodies to synapsin I sequestrate synapsin I and alter synaptic function. *Cell Death Dis* 10: 864.

5. MOLECULAR MECHANISMS OF EXOCYTOSIS AND SYNAPTIC TRANSMISSION: SYNAPSINS AND SNARE PROTEINS

The applicant was one of the major contributors to the synapsin and SNARE protein fields worldwide. The synapsins are a family of neuronal phosphoproteins evolutionarily conserved in invertebrate and vertebrate organisms with the function of modulating neurotransmitter release at the pre-synaptic terminal, by reversibly tethering synaptic vesicles (SVs) to the actin cytoskeleton. However, many recent data have suggested novel functions for synapsins in other aspects of the pre-synaptic physiology, such as SV docking, fusion and recycling. Synapsin activity is tightly regulated by several protein kinases and phosphatases, which modulate the association of synapsins to SVs as well as their interaction with actin filaments and other synaptic proteins. In this context, synapsins act as a link between extracellular stimuli and the intracellular signaling events activated upon neuronal stimulation. Genetic manipulation of synapsins in various in vivo models has revealed that, although not essential for the basic development and functioning of neuronal networks, these proteins are extremely important in the fine-tuning of neuronal plasticity, as shown by the strong phenotype and behavioral abnormalities characterizing mouse lines lacking one or more synapsin isoforms. Thanks to his experience in the neurobiology of SVs, dr. Benfenati also had a leading role in the discovery, concomitantly with Nobel laureate dr. J. Rothman, the presynaptic SNARE proteins as components of the core fusion machine that allows membrane fusion events and, particularly, exocytosis of SVs to release neurotransmitter. The handle to discover these proteins was the search for presynaptic substrates of tetanus and botulinum neurotoxins. These toxins turned out to be as zinc proteases specific for the most indispensable proteins of neuroexocytosis, namely synaptobrevin, SNAP-25 and syntaxin (SNAREs).

5.1 **Benfenati F**, Valtorta F, Chieregatti E, Greengard P (1992) Interaction of free and synaptic vesicle-bound synapsin I with F-actin. *Neuron* 8: 377-386

5.2 **Benfenati F**, Valtorta F, Rubenstein JL, Gorelick F, Greengard P, Czernik AJ (1992) Synaptic vesicle-associated Ca^{2+}/calmodulin-dependent protein kinase II is a binding protein for synapsin I. *Nature* 359: 417-420, 1992.

5.3 Schiavo G, **Benfenati F**, Poulain B, Ross*etto O, Polverino de Laurato P, DasGupta BR, Montecucco C (1992) Tetanus and botulinum-B neurotoxins block neurotransmitter release by proteolytic cleavage of synaptobrevin-2. *Nature* 359: 832-835.

5.4 Medrihan L, Cesca F, Raimondi A, Lignani G, Baldelli P, **Benfenati F** (2013) Synapsin II desynchronizes neurotransmitter release at inhibitory synapses by a functional interaction with presynaptic Ca^{2+} channels. *Nature Comm.* 4:1512

D. Recent Research Support

Ongoing

- EU Horizon 2020 - EraNet JPND 2020, Project "*Neurophage: Phage-based targeted platform for neural stimulation".* Coordinator and PI: Fabio Benfenati (with IRCCS).
- EU Horizon 2020 - EuroNanoMed3 2019 call Project "*Nanolight: Photosensitive nanotools for neuronal stimulation and*

rescue of degenerative blindness". Coordinator and PI: Fabio Benfenati (with IRCCS).
- EU Horizon 2020 - FET Open 2020 – "*HyVis: Hybrid Synapse for VISion*". Co-PI: Fabio Benfenati.
- EU Horizon 2020 - Flagship Graphene Core 3 Project: "W*P4: Health and Environment* ". PI: Fabio Benfenati.
- EU Horizon 2020 - Flagship Graphene Core 3 Project: "W*P5: Biomedical Applications".* PI: Fabio Benfenati.
- European Space Agency (ESA), Project "*Advanced nanozymes for antioxidant therapy*". PIs: Fabio Benfenati, Pier Paolo Pompa
- EU Horizon 2020 Call: H2020-MSCA-ITN-2018 Project: "*Entrain Vision*". PI: Fabio Benfenati.
- Telethon Foundation, Project GGP19120: "*Interaction of PRRT2 with Na^+ channels: pathogenetic basis and new targets for the cure of PRRT2- associated paroxysmal disorders".* PI: Fabio Benfenati. Ranked first in the 2019 call.

Ended
- Ministry of Foreign Affairs Italy-Korea (MAECI), Project "*Graphene-based interfaces to foster neuronal regeneration and restore network excitability in neurodegenerative disorders*". PI: Fabio Benfenati.
EU Horizon 2020 - ERANET Neuron "*Mechanisms of neuropsychiatric genetic diseases of the SNARE complex: towards therapeutic intervention - SNAREopathy*". PIs: Federico Zara and Fabio Benfenati.
- Telethon/Glut-1 Foundations (GSP19002_PAsGlut009) Project "*GLUT1-deficiency: new therapeutic strategies to increase glucose transport across the blood brain barrier*". Co-PIs: Federico Zara, Fabio Benfenati.
- Cariplo Foundation - Bando 2018 Ricerca biomedica sulle malattie legate all'invecchiamento. Project: "*Nanosparks: high- resolution non-invasive photostimulation strategies to rescue vision and alleviate geriatric frailty in age-related macular degeneration*" PI: Fabio Benfenati.

E. Granted Patents
1. Publication number: 2009107069 "M*icroelectrode array based on optically transparent conductive polymer materials and a method of fabrication thereof*" Inventors: A Blau, F Benfenati. Publication Date: Sept 3, 2009. Filed: Feb 25, 2009.
2. Publication number: 20160168561 "*Organic device for photoinhibition of excitable cells*" Inventors: D Ghezzi, F Benfenati, G Lanzani, G Pertile et al. Publication date: June 16, 2016.
3. Patent number: 9938518 "*Organic device for photoinhibition of excitable cells*" Inventors: D Ghezzi, F Benfenati, G Lanzani, G Pertile et al. Filed: August 1, 2014. Date of Patent: April 10, 2018.
4. Patent number: 102018000005987 (PT180423) "*Photochromic compounds*" Inventors: G Lanzani, F Benfenati et al.

F. Invited presentations to international conferences/advanced schools (selected from >150 in the period)
- Invited Lecture "Photovoltaic polymers: towards a bioorganic artificial retina". University of Tubingen, Werner Reichardt Centrum fur Integrative Neurowissenschaften, March 11, 2014
- Invited Lecture "Neuronal interfaces for tissue engineering and photostimulation". Paris Symposium on "Integrated Cell-Material Sciences". Paris, October 12-13, 2015
- Invited Lecture "Neuronal Interfaces: Innovative Therapies and Neuroprostheses". Lundbeck Neuroscience Forum. Rome (Accademia Lincei), December 3, 2015
- Pinelli Lecture "Modulation of neural activity with light: bases and applications of optogenetics". International Brain Awareness Week, IRCCS Mondino Pavia. March 14, 2016
- Invited Lecture "A fully organic retinal prosthesis restores vision in a rat model of degenerative blindness". Institut de la Vision & Pixium. Paris, December 7, 2016
- Invited Lecture "Physiological role and optogenetic modulation of the transcription factor REST/NSRF in the nervous system". Dunn School, Oxford University. December 14, 2016.
- Invited Lecture "A fully organic retinal prosthesis restores vision in a rat model of degenerative blindness"; European Retina Meeting, Paris. October 5, 2017
- Keynote Lecture " *Opto-epigenetic strategies for modulating brain plasticity and excitability",* Park City Epilepsy Meeting, Park City (UT) October 5-8, 2019
- Invited Lecture "*Light-sensitive neuronal interfaces to rescue vision in retinal degeneration*", Rockefeller-Cornell-Sloan Kettering Tri-Institutional Seminar Series, New York October 11, 2019
- Invited Lecture University College London, Queen Square Institute of Neurology Virtual Seminar Series "*Neuronal firing modulation by a membrane-targeted photoswitch".* March 26, 2020.

G. Organization of International Conferences

Director of the International School "The use of virus vectors in Neuroscience: virus-mediated gene-delivery into the rodent brain" (MSCA-ITN-2014-ETN), Bogliasco (Genova), June 6-8, 2016.
President and organizer of the "66th National Congress of the Italian Physiological Society", Genova, September 2015. Chairman, International Program Committee, 8th IBRO World Congress, Florence

H. Prizes, Awards, Academy Memberships

Fellow of the Academy of the International Union of Physiological Sciences; International 2020 Cesare Casella Prize; International 2020 Herlitzka Prize for Physiology; UK-Italy Business Award and Smart Cup/National Innovation Prize; Foreign Scientist Award, The Michael Stern Foundation for Parkinson's Disease; Fellow of the Academia Europaea (Physiology & Neuroscience).

I. Contributions to the early career of excellent researchers

His talented postdocs got research associate positions at Rockefeller University (L Medrihan), UCL (G Lignani) and Tufts (M Chiacchiaretta); D Ghezzi became associate professor at EPFL; several senior researchers obtained tenured associate professor (P Valente, A Corradi, S Giovedi, F Onofri, A Corradi, L Cingolani, F Cesca, JF Maya-Vetencourt) and full professor (P Baldelli, A Fassio) positions in the Italian University.

K. Leadership in industrial innovation

Founder and scientific advisor of the start-up NOVAVIDO funded by investors and charities with a capital of 6M€ for the exploitation in humans of organic retinal prosthetics.