Daniela Pietrobon
Curriculum vitae

Education
1979, Degree (Laurea) in Chemistry, Magna cum Laude, University of Padova.

Employment and Research experience
1979-1982, Research Fellow, Institute of General Pathology, University of Padova: Energy transduction in mitochondria.
1983-1991, CNR Researcher, CNR Unit Physiology of Mitochondria, Institute of General Pathology, University of Padova: Energy transduction in mitochondria.
1984-1985, Visiting Scientist, Dept of Membrane Research, Weizmann Institute of Science, Israel: Non-equilibrium thermodynamics of oxidative phosphorylation and kinetic modelling of mitochondrial H^+ pumps.
1987-1990, Visiting scientist, Dept of Cellular and Molecular Physiology, Harvard Medical School, U.S.A.: Biophysics of voltage-gated Ca^{2+} channels
1991-1993, CNR Director of Research, CNR Unit Physiology of Mitochondria, Dept. of Biomedical Sciences, University of Padova: Biophysics and physiology of neuronal Ca^{2+} channels.
1993-2000, Associate Professor of General Physiology, Dept. of Biomedical Sciences, University of Padova: Biophysics and physiology of neuronal Ca^{2+} channels.
2000-2024, Full Professor of Physiology, Dept. of Biomedical Sciences, University of Padova: Calcium channelopathies of the central nervous system, in particular familial hemiplegic migraine; pathophysiology of migraine.

Committees and Panels
1996-2000, Member of Council of the Italian Society of Pure and Applied Biophysics
1996-2002, Member of Council of IUPAB (Int. Union of Pure and Applied Biophysics)
2000-2003, Coordinator of the PhD Program in Molecular and Cellular Biology and Pathology, Univ. of Padova.
2005-2015, Coordinator of the PhD Program in Neurobiology, PhD School of Biosciences, Univ of Padova
2010-2017, Member of Faculty of 1000
2016-2022, Member of the Board of Directors of the Padova Neuroscience Center, University of Padova
2018-2023, Member of the Executive Committee of the Council of Physiology Professors

Honors and awards
1985, Luigi Galvani Prize of the Bioelectrochemical Society.
2001, President of the Republic National Prize, awarded by the Accademia dei Lincei for discoveries in the Mathematical, Physical and Natural Sciences.
2011- Member of the Venetian Institute of Letters Sciences and Art

Keynote and Plenary Lectures
2011, Pain in Europe Congress (Plenary)
2013, International Union of Physiological Societies Congress (Keynote)
2017, Italian Society of Neuroscience Congress (Plenary)
2018, International Congress on Cortical Spreading Depression (Keynote)

Editorial Boards
2006-2011, The Journal of Physiology
2007- Channels

2016- Neuroscience
2017- European Journal of Physiology
2018- Current Opinion in Neurobiology
2019- The Journal of Headache and Pain (Associate Editor)
2020- Frontiers in Cellular Neuroscience (Associate Editor)

***Ad hoc* reviewer**
For many prestigious scientific journals, including Science, Neuron, Nature Communications, Nature Reviews Neurology, The lancet Neurology, Proceedings of the National Academy of Sciences, eLife, Annals of Neurology, Brain, The Journal of Neuroscience, The Journal of Physiology
and international granting agencies including: Human Frontier Science Program, Wellcome Trust Foundation, NIH, ANR, Israel Science Foundation, Austrian Science Foundation.

Main contributions to Science (with selected publications)

1) Functional consequences of mutations causing familial hemiplegic migraine (FHM) and migraine pathophysiology.

We revealed that:

a) The migraine mutations in the CACNA1A gene causing FHM1:
i) produce gain of function of the human recombinant voltage-gated Ca^{2+} channel $Ca_V2.1$;
ii) increase the excitatory synaptic transmission without affecting the inhibitory synaptic transmission in the cerebral cortex of a genetic mouse model of the disease, and lead to dysregulation of the excitatory-inhibitory balance at key cerebral neuronal microcircuits;
iii) facilitate the induction and propagation of cortical spreading depression (CSD, the neurophysiological correlate of migraine aura and a trigger of the migraine pain mechanisms). This facilitation is due to the enhanced release of glutamate from cortical excitatory synapses.

b) The migraine mutations in the ATP1A2 gene causing FHM2 and loss-of-function of the human astrocytic α2 Na^+/K^+ ATPase:
i) reduce the rate of glutamate and K^+ clearance at cortical excitatory synapses during neuronal activity in a genetic mouse model of the disease
ii) facilitate the induction and propagation of cortical spreading depression. This facilitation is due to the reduced rate of glutamate clearance at cortical excitatory synapses.

c) Critical threshold levels of extracellular glutamate and NMDA receptors activation are necessary for ignition of CSD in the cerebral cortex. These threshold levels are similar in wild-type and FHM mutant mice; however, in the genetic mouse models of migraine they are reached with stimuli of lower intensity and more rapidly, thus explaining their increased susceptibility to CSD initiation.

Selected articles

M. Hans, S. Luvisetto, M.E. Williams, M. Spagnolo, A. Urrutia, A. Tottene, P.F. Brust, E.C. Johnson, M.M. Harpold, K.A. Stauderman and D. Pietrobon. Functional consequences of mutations in the human α1A calcium channel subunit linked to familial hemiplegic migraine.
J Neurosci (1999) 19, 1610-1619.

A. Tottene, T. Fellin, S. Pagnutti, S. Luvisetto, J. Striessnig, C. Fletcher and D. Pietrobon.

Familial hemiplegic migraine mutations increase Ca2+ influx through single human CaV2.1 channels and decrease maximal CaV2.1 current density in neurons.
Proc Natl Acad Sci (2002) 99, 13284-13289.

A.M.J.M. van den Maagdenberg*, D. Pietrobon*, T. Pizzorusso, S. Kaja, L.A.M. Broos, T. Cesetti, R.A.G. van de Ven, A. Tottene, J. van der Kaa, J.J. Plomp, R.R. Frants, M.D. Ferrari. A cacna1a knockin migraine mouse model with increased susceptibility to cortical spreading depression.
Neuron (2004) 41, 701-710
*Shared first authorship and shared corresponding authorship.

Tottene A., Conti R., Fabbro A, Vecchia D, Shapovalova M, Santello M, van den Maagdenberg AMJM, Ferrari M and Pietrobon D. Enhanced excitatory transmission at cortical synapses as the basis for facilitated spreading depression in CaV2.1 knockin migraine mice.
Neuron (2009) 61: 762-773

Vecchia D, Tottene A, van den Maagdenberg AM, Pietrobon D. Mechanism underlying unaltered cortical inhibitory synaptic transmission in contrast with enhanced excitatory transmission in $Ca_V2.1$ knockin migraine mice.
Neurobiol Dis (2014) 69:225-34

Capuani C, Melone M, Tottene A, Bragina L, Crivellaro G, Santello M, Casari G, Conti F, Pietrobon D. Defective glutamate and K+ clearance by cortical astrocytes in familial hemiplegic migraine type 2.
EMBO Mol Med (2016) 8:967-86

Tottene A., Favero M, Pietrobon D. Enhanced thalamocortical synaptic transmission and dysregulation of the excitatory-inhibitory balance at the thalamocortical feedforward inhibitory microcircuit in a genetic mouse model of migraine.
J. Neurosci. (2019) 39:9841-51

Crivellaro G, Tottene A, Vitale M, Melone M, Casari G, Conti F, Santello M, Pietrobon D. Specific activation of GluN1-N2B NMDA receptors underlies facilitation of cortical spreading depression in a genetic mouse model of migraine with reduced astrocytic glutamate clearance.
Neurobiol Dis. (2021) 156:105419.

Parker PD, Suryavanshi P, Melone M, Sawant-Pokam PA, Reinhart KM, Kaufmann D, Theriot JJ, Pugliese A, Conti F, Shuttleworth CW, Pietrobon D*, Brennan KC*. Non-canonical glutamate signaling in a genetic model of migraine with aura.
Neuron (2021) 109(4):611-628.
* Shared corresponding authorship

Marchionni I, Pilati N, Forli A, Sessolo M, Tottene A, Pietrobon D. Enhanced Feedback Inhibition Due to Increased Recruitment of Somatostatin-Expressing Interneurons and Enhanced Cortical Recurrent Excitation in a Genetic Mouse Model of Migraine.
J Neurosci. (2022) 42(34):6654-66

Vitale M, Tottene A, Zarin Zadeh M, Brennan KC, Pietrobon D. Mechanisms of initiation of cortical spreading depression.
J Headache Pain. (2023) 24(1):105.

Selected invited reviews

Pietrobon D and Striessnig J. Neurobiology of Migraine.
Nature Rev Neurosci (2003) 4, 386-398 C. 387

Pietrobon D Insights into migraine mechanisms and $Ca_V2.1$ channel function from animal models of familial hemiplegic migraine.
J Physiol (2010) 588: 1871-1878

Vecchia D and Pietrobon D. Migraine: a disorder of brain excitatory-inhibitory balance?
Trends Neurosci. (2012) 35:507-520 C. 91

Pietrobon D and Moskowitz M. Pathophysiology of migraine.

Ann Rev Physiol (2013) 75:365-91 C. 189
Pietrobon D and Moskowitz M. Propagation of chaos and commotion in the wake of cortical spreading depression and spreading depolarizations.
Nature Rev. Neurosci. (2014) 15:379-93 C. 96
Brennan KC and Pietrobon D. A systems neuroscience approach to migraine.
Neuron (2018) 97:1004-21

2) $Ca_V2.1$ channelopathies

We revealed that the mutations in the CACNA1A gene causing episodic ataxia type 2 produce loss-of-function of the human recombinant voltage-gated Ca^{2+} channel $Ca_V2.1$.

Selected article
S. Guida, F. Trettel, S. Pagnutti, E. Mantuano, A. Tottene, L. Veneziano, T. Fellin, M. Spadaro, K. Stauderman, M.E. Williams, S. Volsen, R.A. Ophoff, R.R. Frants, C. Jodice, M. Frontali and D. Pietrobon. Complete loss of P/Q calcium channel activity caused by a CACNA1A missense mutation carried by patients with episodic ataxia type 2.
Am J Hum Genet (2001), 68, 759-764

Selected invited review
Pietrobon D. Function and dysfunction of synaptic calcium channels: insights from mouse models
Curr Opin Neurobiol (2005) 15, 257-269

3) Biophysics and physiology of voltage-gated Ca^{2+} channels

We revealed and characterized:

a) a new mechanism of regulation of the conductance of L-type Ca^{2+} channels by protons and a new mechanism of voltage-dependent gating of L-type Ca^{2+} channels.
b) different gating modes of human $Ca_V2.1$ channels.
c) a new "anomalous" neuronal voltage-gated L-type Ca^{2+} channel
d) a novel neuronal P-type and two novel neuronal R-type Ca^{2+} channels.

Selected articles
B. Prod'hom, D. Pietrobon and P. Hess. Direct measurement of proton transfer rates to a group controlling the dihydropyridine-sensitive Ca^{2+} channel.
Nature (1987) 329, 243-246.
D. Pietrobon, B. Prod'hom and P. Hess. Conformational changes associated with ion permeation in L-type calcium channels.
Nature (1988) 333, 373-376.
D. Pietrobon and P. Hess. Novel mechanism of voltage-dependent gating in L-type calcium channels.
Nature (1990) 346, 651-655.
L. Forti and D. Pietrobon. Functional diversity of L-type calcium channels in rat cerebellar neurons.
Neuron (1993) 10, 437-450.
L. Forti, A. Tottene, A. Moretti and D. Pietrobon. Three novel types of voltage-dependent calcium channels in rat cerebellar neurons.

J Neurosci (1994) 14, 5243-5256

A. Tottene, A. Moretti and D. Pietrobon. Functional diversity of P-type and R-type calcium channels in rat cerebellar neurons.
J Neurosci (1996) 16, 6353-6363.

B. Hivert, S. Luvisetto, A. Navangione, A. Tottene and D. Pietrobon. Anomalous L-type calcium channels of rat spinal motoneurons.
J Gen Physiol (1999) 113, 679-693

A. Tottene, S. Volsen and D. Pietrobon. α1E subunits form the pore of three cerebellar R-type calcium channels with different pharmacological and permeation properties.
J. Neurosci. (2000) 20, 171-178.

S. Luvisetto, T. Fellin, M. Spagnolo, B. Hivert, PF Brust, M.M. Harpold, K.A. Stauderman, M.E. Williams and D. Pietrobon. Modal Gating of Human CaV2.1 (P/Q-type) Calcium Channels: I. The Slow and the Fast Gating Modes and their Modulation by {beta} Subunits.
J Gen Physiol. (2004) 124, 445-461.

T. Fellin, S. Luvisetto, M. Spagnolo, and D. Pietrobon. Modal Gating of Human CaV2.1 (P/Q-type) Calcium Channels: II. The b Mode and Reversible Uncoupling of Inactivation.
J Gen Physiol. (2004) 124, 463-74.

4. Biophysical properties of mitochondrial proton pumps and energy transduction in mitochondria.

We revealed that the mitochondrial proton pumps are not completely coupled and developed detailed kinetic models of the mitochondrial H^+ pumps and their chemiosmotic coupling.

Selected articles

D. Pietrobon, G.F. Azzone and D. Walz. Effect of funicolosin and antimycin A on the redox-driven H^+-pumps in mitochondria: on the nature of leaks.
Eur J Biochem (1981) 117, 389-394

D. Pietrobon, M. Zoratti, G.F. Azzone, J.W. Stucki and D. Walz. Non equilibrium thermodynamic assesment of redox-driven H+ pumps in mitochondria.
Eur J Biochem (1982) 127, 483-494

D. Pietrobon, M. Zoratti and G.F. Azzone. Molecular slipping in redox and ATPase H^+-pumps.
Biochim Biophys Acta (1983) 723, 317-321

D. Pietrobon and S.R. Caplan. Flow-force relationships for a six-state proton pump model: intrinsic uncoupling, kinetic equivalence of input and output forces, and domain of approximate linearity.
Biochemistry (1985) 24, 5764-5776

D. Pietrobon, M. Zoratti, G.F. Azzone and S.R. Caplan. Intrinsic uncoupling of mitochondrial proton pumps. II. Modelling studies.
Biochemistry (1986) 25, 767-775