**Curriculum vitae of Dr Luigi Catacuzzeno**

Dr Luigi Catacuzzeno

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Born in Montefiore dell'Aso (Italy), 14/03/72
Present position: Researcher at the Department of Chemistry, Biology and Biotecnology, University of Perugia

**EDUCATION**
1991: Graduation High School "Liceo Scientifico"

1992-1997: Biology Student at the University of Perugia

1997: degree in Biolological Sciences at the University of Perugia. Thesis on the mechanism of verapamil block of voltage-gated K channels in DRG neurons, using the patch-clamp technique, approved with honours.

1997-1998: Internal Fellow in the Laboratory of Neuroscience of the Department of Chemistry, Biology and Biotecnology. He continued the study on the biophysical mechanism of block of verapamil block of voltage-gated K channels in DRG neurons.

2005-2007: phD specialization in "Biologia Cellulare e Molecolare" at the University of Perugia. He studied the pathophysiological mechanisms of the familial hemiplegic migraine, and more speficically the contribution of the trigeminal ganglion to the triggering and thevelopment of migraine headache.

**EMPLOYMENT**
1998-2000: postdoctoral fellow in Dr Nonner's lab, at the University of Miami, where he contributed to the development of a theory on Ca channel selectivity based on the Mean Spherical Approximation.

2001-2004: postdoctoral fellow in Prof Franciolini's lab, at the University of Perugia, where he has been involved in the study of the properties and role of ion channels in the growth and migration of glioblastoma cells.

2007-to date: As a researcher with a permanent position in the Dept. of Chemistry, Biology and Biotechnology, he has focused on the role of ion channels in the growth and migration of glioblastoma cells, and on the pathophysiological mechanisms of the familial hemiplegic migraine

**RESEARCH EXPERIENCE**
The research activity of Dr Catacuzzeno has been mostly focused on ion channels, with part of his activity being dedicated to biophysical studies of the structure/function relationship of these proteins, and part being dedicated to the study of pathophysiological consequences of their activity. His research has been mainly conducted using the patch-clamp technique to study ion channel activity and excitability, and programming in C language for theoretical models/predictions.

*Study of the pathophysiological consequences of ion channel activity*. A main topic of the research of Dr Catacuzzeno has been devoted on the role of ion channels in the pathophysiology of glioblastoma. More specifically, he found in GBM cell lines, primary cultures from human GBM, and GBM biopsies, the

presence of several ion channels normally absent in the central nervous system. Based on this evidence, the research has focused of the role of these channels in the aggressiveness of these tumors. Given the importance of the tumor microenvironment in setting the aggressiveness of GBMs, Dr Catacuzzeno has also studied effects on ion channels of chemical conditions known to be present is the GBM tissue, such as blood serum being in contact with the tumor because of tumor brain barrier breakdown, and tissue hypoxia. Dr Catacuzzeno has also been involved in the study of the role of ion channels in the phatophysiology of migraine, in collaboration with Dr Pietrobon, university of Padova. He studied the effects of genetic mutations causing a rare form of migrane, called familial hemiplegic migrane (FHM). Using a knockin mouse model containing an FHM mutation, he demonstrated that a diyfunction in the excitability of trigeminal ganglion neurons contributed to the development of migraine headache in FHM mice. More in particular he found that a subpopulation of trigeminal ganglion neurons isolated from knockin mice expressed a voltage-gated calcium current having activation properties different from that observed in wild-type mice. In turn, this electrophysiological difference causes a higher excitability of this neurons, that may be responsible for the development of headache.

*Study of the structure/function relationship in ion channels.* Dr Catacuzzeno acquired competences on the theoretical study of the structure/function relationship of ion channels in Dr Nonner's Lab, at the university of Miami. More specifically in Miami he studied ion channel permeation by applying theoretical models that take consistently into account the electrostatics, such as the Poisson-Nenrst-Planck theory to predict the ion flux and the Mean Spherical Approximation to study the ion selectivity. Applying these theoretical approaches on Ca channels he was able to explain the high selectivity for Ca vs Na ions as a compromise between the strong electrostatic attraction promoted by the four carboxyl groups and the energetic repulsion caused by the finite volume occupied by the ions inside the selectivity filter. Subsequently, when he came back to Italy, he continued to study the relevance of the electric field in ion permeation, this time trying to understand how electrostatics shapes the calcium microdomain forming at the intracellular mouth of a calcium channels. For the first time Dr Catacuzzeno predicted a strong role of the negative surface charges present at the intracellular mouth of the channel in changing the amount and spatial distribution of calcium ions entering the cell, a phenomenon likely important in neurotransmitter release an cell excitability. In these last years Dr Catacuzzeno is still trying to apply theories accounting for the effect of the electric field, this time to understand the movement of the voltage sensor in voltage-gated ion channels. More specifically he is working of a Brownian model of the voltage-sensor movement that, starting from the geometrical and electrostatic properties of the voltage sensor domain taken from the 3D crystal structure, is able to predict both the movement of a single voltage sensor as well as the macroscopic gating current. Notably, he successfully applied this model to the Shaker K channel, finding physical explanations for the peculiar shape of the macroscopic gating currents and for the origin of the multiple voltage-sensor substates previously suggested by discrete markov models. He is also trying to explant the brownian dynamic model to include the pore gating, so to find a physical explanation for the high cooperativity found among the four voltage-sensor domains for the opening of voltage-gated channels.

COORDINATION OF RESEARCH PROJECTS:
2007-2010: PRIN 2007: Analisi funzionale ed implicazioni terapeutiche della eterogeneità cellulare in gliomi ad alto grado. Indagini su popolazioni selezionate in vitro con caratteri di multipotenza.

2014-2016: Fondazione Cassa di Risparmio di Perugia: "Ipossia e aggressivita' dei glioblastomi"

PARTECIPATION TO OTHER RESEARCH PROJECTS:
PRIN 2000: Ruolo, natura e distribuzione dei canali Ca voltaggio-dipendenti, canali K Ca-attivati, Ca-ATPasi e scambiatori Na/Ca nelle cellule ciliate vestibolari.

PRIN 2002: Ruoli, proprietà e distribuzione delle diverse correnti di calcio nelle cellule ciliate vestibolari

Prin 2005: Canali del sodio, calcio e potassio neuronali: ruolo fisiologico e canalopatie

Progetto di ricerca della Fondazione Cassa di Risparmio di Perugia – anno 2005 - COD. 2005.0055.020

Telethon 2006 - GGP06234 - Functional consequences of mutations associated to familial hemiplegic migraine type 1 and migraine mechanisms

Progetto di ricerca della Fondazione Cassa di Risparmio di Perugia – BANDO 2007

Progetto di ricerca della Fondazione Cassa di Risparmio di Perugia – anno 2009 - COD. 2009.020.0025

Progetto di ricerca della Fondazione Cassa di Risparmio di Perugia – anno 2012 - COD. 2012.0240.021

PUBLICATIONS


1. Catacuzzeno L, Franciolini F. Simulation of gating currents of the Shaker K channel using a Brownian model of the voltage sensor. 2018 arXiv:1809.05464 [physics.bio-ph]

2. Catacuzzeno L , Orfei F , Di Michele, A, Sforna L,i Franciolini F, Gammaitoni, L. (2018). Energy harvesting from a bio cell. Nano Energy. 56. 10.1016/j.nanoen.2018.12.023.

3. Sforna L, Franciolini F, Catacuzzeno L. Ca(2+) -dependent and Ca(2+) -independent somatic release from trigeminal neurons. J Cell Physiol. 2018 Dec 7.

4. Catacuzzeno L, Franciolini F. Role of KCa3.1 Channels in Modulating Ca(2+) Oscillations during Glioblastoma Cell Migration and Invasion. Int J Mol Sci. 2018 Sep 29;19(10). pii: E2970.

5. Rosa P, Catacuzzeno L, Sforna L, Mangino G, Carlomagno S, Mincione G, Petrozza V, Ragona G, Franciolini F, Calogero A. BK channels blockage inhibits hypoxia-induced migration and chemoresistance to cisplatin in human glioblastoma cells. J Cell Physiol. 2018 Sep;233(9):6866-6877.

6. Zampino C, Ficacci R, Checcacci M, Franciolini F, Catacuzzeno L. Pain Control by Proprioceptive and Exteroceptive Stimulation at the Trigeminal Level. Front Physiol. 2018 Aug 7;9:1037.

7. Grimaldi A, D'Alessandro G, Di Castro MA, Lauro C, Singh V, Pagani F, Sforna L, Grassi F, Di Angelantonio S, Catacuzzeno L, Wulff H, Limatola C, Catalano M. Kv1.3 activity perturbs the homeostatic properties of astrocytes in glioma. Sci Rep. 2018 May 16;8(1):7654.

8. Catacuzzeno L, Franciolini F. Editorial: The Role of Ca2+-activated K+ Channels of Intermediate Conductance in Glioblastoma Malignancy. Curr Neuropharmacol. 2018;16(5):607.

9. Sforna L, Megaro A, Pessia M, Franciolini F, Catacuzzeno L. Structure, Gating and Basic Functions of the Ca2+-activated K Channel of Intermediate Conductance. Curr Neuropharmacol. 2018;16(5):608-617.

10. Rosa P, Sforna L, Carlomagno S, Mangino G, Miscusi M, Pessia M, Franciolini F, Calogero A, Catacuzzeno L. Overexpression of Large-Conductance Calcium-Activated Potassium Channels in Human Glioblastoma Stem-Like Cells and Their Role in Cell Migration. J Cell Physiol. 2017 Sep;232(9):2478-2488.

11. Sforna L, Cenciarini M, Belia S, Michelucci A, Pessia M, Franciolini F, Catacuzzeno L. Hypoxia Modulates the Swelling-Activated Cl Current in Human Glioblastoma Cells: Role in Volume Regulation and Cell Survival. J Cell Physiol. 2017 Jan;232(1):91-100.

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13. D'Adamo MC, Sforna L, Visentin S, Grottesi A, Servettini L, Guglielmi L, Macchioni L, Saredi S, Curcio M, De Nuccio C, Hasan S, Corazzi L, Franciolini F, Mora M, Catacuzzeno L, Pessia M. A Calsequestrin-1 Mutation Associated with a Skeletal Muscle Disease Alters Sarcoplasmic Ca2+ Release. PLoS One. 2016 May 19;11(5):e0155516.

14. Lanciotti A, Brignone MS, Visentin S, De Nuccio C, Catacuzzeno L, Mallozzi C, Petrini S, Caramia M, Veroni C, Minnone G, Bernardo A, Franciolini F, Pessia M, Bertini E, Petrucci TC, Ambrosini E.

Megalencephalic leukoencephalopathy with subcortical cysts protein-1 regulates epidermal growth factor receptor signaling in astrocytes. Hum Mol Genet. 2016 Apr 15;25(8):1543-58.

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