

BIOGRAPHICAL SKETCH

NAME: Rivolta, Ilaria

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POSITION TITLE: Associate Professor of Physiology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Liceo Scientifico F. Enriques, Lissone (MB) Italy	High school diploma	07/1991	Scientific subjects
University of Milano, Milano (Italy)	Degree (BS+Master)	07/1998	Biological Sciences
Columbia University, New York, NY	Postdoctoral	09/1999-11/2001	Cardiac Cellular electrophysiology
University of Losanne, Losanne, Switzerland	Postdoctoral	12/2001	Biochemistry
Fondazione S. Maugeri, Pavia (Italy)	Postdoctoral	01/2002-01/2005	Cellular biology and cardiac cellular electrophysiology

A. Personal Statement

I am an associate Professor of Physiology and my research activities focus on cellular and systemic physiology, primarily in the field of membrane excitability. Over the years, my studies have primarily centered on characterizing the physiological and pathophysiological roles of ion channel activity. Through electrophysiological recordings on in vitro cells, I investigate the pathogenetic mechanisms responsible for cardiac, muscular, and more recently, neuronal channelopathies. The use of animal models has also allowed me to explore non-excitabile tissues, such as the pulmonary tissue, and to study the early stages of physiopathological transition in the cardio-pulmonary context. Additionally, a portion of my research activities has been dedicated to studying the interaction of nanoparticles synthesized for biomedical applications with biological membranes and the effects they may induce on normal physiological processes. Furthermore, I effectively managed the projects, overseeing aspects such as staffing, research protections, and budget management. I also engaged in collaborative efforts with fellow researchers and generated multiple peer-reviewed publications stemming from each project.

As PI, I laid the groundwork for the proposed research by characterizing the loss-of-function effect of the mutation in the HCN2 gene (p.G460D in the HCN2 protein), which we now aim to revert. The results of this work were successfully published in *Epilepsia* in 2023 (DiFrancesco JC et al. *Epilepsia*. 2023 Dec;64(12):e222–e228. doi:10.1111/epi.17777). The current application builds logically on this ongoing line of research, which experienced a significant interruption during the COVID-19 pandemic but has since resumed as part of a Ph.D. project.

We have access to patient-derived cells in which the mutation has already been characterized, and we are currently completing the functional characterization of patient neurons. Reverting the mutation in these same cells will allow us to directly corroborate the causative role of this variant in

the patient's disease (developmental and epileptic encephalopathy, DEE). The research group I lead has the expertise, resources, and motivation necessary to successfully carry out and complete the proposed project.

Ongoing and recently completed projects that I would like to highlight include:

PRIN 2022; Rivolta (Co-PI)

Title: A study investigating post-translational modifications in Brugada Syndrome and their effects on cardiac activity using hPSC-derived cardiomyocytes.

Funding period: 20/10/2023-19/09/2025

Myotonic Diseases Foundation; Rivolta (PI)

Title: Functional analysis of variants in myotonic disease genes in the context of personalized medicine.

Funding period: 31/10/2024-30/10/2025

Association SCN8A Italia ODV; Rivolta (PI)

Title: Functional analysis of variants in the SCN8A gene and preliminary assessment of a personalized medicine-based therapeutic approach.

Funding Period: May 2022-December 2023

B. Positions and Scientific Appointments

2008 - present	Associate Professor, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy
2022 - present	Scientific collaborator of the Institute of Molecular and Translational Cardiology (IMTC) and Head of the Cellular Electrophysiology Unit, San Donato Milanese (MI).
2021 - present	Member of the Editorial Board <i>Frontiers in Network Physiology</i>
2020 - present	Member of the Editorial Board <i>Life</i>
2019 - present	Member of the Editorial Board of <i>Scientific Reports</i>
2012 - present	Ordinary member of the European Working Group of Cardiac Electrophysiology (EWGCCE)
2007- 2018	Assistant Professor, Department of Experimental Medicine, University of Milano-Bicocca, Monza, Italy.
2005 - 2007	Senior Technician, Department of Experimental Medicine, University of Milano-Bicocca, Monza (Italy).
2009 - present	Ordinary member of the Italian Society of Physiology (SIF)

C. Contribution to Science

Cardiac Electrophysiology and Ion Channel Function

My early research focused on the cellular mechanisms of cardiac electrical activity, under the mentorship of Prof. Robert S. Kass at Columbia University. In these years I focused on the modulation of cardiac sodium channel activity

1. Cormier JW, Rivolta I, et al. J. Biol Chem. 2002 Mar 15;277(11):9233-9241; doi: 10.1074/jbc.M110204200
2. Rivolta I, et al. Physiol Genomics. 2002;10(3):191-197; doi: 10.1152/physiolgenomics.00039.2002
3. Rivolta I, et al. J Biol Chem. 2001;276(33):30623-30630; doi: 10.1074/jbc.M104471200

Later, in collaboration with Prof. Silvia Priori in Pavia I participate in studies that advanced our understanding of ion channel regulation and the mechanisms underlying arrhythmogenesis and identified the loss-of-function KCNJ2 mutations as causative of cardiac arrhythmias.

1. Priori SG, Pandit SV, Rivolta I, et al. *Circulation Research*. 2005; 96(7):800-807. doi.org/10.1161/01.RES.0000162101.76263.8c.

Pulmonary Physiology and Membrane Barrier Function

Upon joining the University of Milano-Bicocca in 2005, I expanded my research to pulmonary physiology with Prof. Giuseppe Miserocchi, with a specific focus on the role of cellular membranes and barriers in edema formation. This work emphasized the critical role of membrane physiology in maintaining tissue homeostasis under pathological conditions.

1. Miserocchi G, Beretta E, Rivolta I. *Thoracic Surgery Clinics*. 2010;20(3):345-57; doi: 10.1016/j.thorsurg.2010.03.001.
2. Rivolta I, et al. *European Respiratory Journal*. 2011;37(4):943-949; doi: 10.1183/09031936.00066710.

Nanoparticle–Membrane Interactions

Through two European-funded projects (BONSAIL, 2006; NAD, 2008), I investigated the interactions of excitable and non-excitable cell membranes with biomedical nanoparticles. This work highlighted novel safety considerations for nanomaterials and their potential impact on excitable cell physiology.

1. Panariti A, Lettierio B, Alexandrescu R, Collini M, Sironi L, Chanana M, Morjan I, Wang D, Chirico G, Miserocchi G, Bucci C, Rivolta I. *Journal of Biomedical Nanotechnology*. 2013;9(9):1556-1569
2. Binda A, Panariti A, Barbuti A, Murano C, Dal Magro R, Masserini M, Re F, Rivolta I. *Int J of Nanomed*. 2018; 13: 4059-4071. doi: 10.2147/IJN.S161563.

Molecular Basis of Ion Channelopathies

Over the last decade, I have led an independent research group focused on the molecular physiology of altered electrical activity and ion channel dysfunction. My studies have contributed to defining gene-specific risk factors, genotype–phenotype correlations, and the electrophysiological consequences of ion channel mutations. These insights have informed about the discovery of genetic modifiers that increase susceptibility to myotonia

1. Binda A, Renna LV, Bosè F, Brigonzi E, Botta A, Valaperta R, Fossati F, Rivolta I (#), Meola G, Cardani R. *Scientific Reports*. 2018;8:11058 | DOI:10.1038/s41598-018-29302-z.
2. Bugiardini E*, Rivolta I*, et al. *Neuromuscular Disorders*. NMD 01/2015; DOI: 10.1016/j.nmd.2015.01.006;

the development of mutation-specific strategies for managing cardiac

1. Frosio A, Micaglio E, Polsinelli I, Calamaio S, Melgari D, Prevostini R, Ghiroldi A, Binda A, Carrera P, Villa M, Mastrocinque F, Presi S, Salerno R, Boccellino A, Anastasia L, Ciconte G, Ricagno S, Pappone C, Rivolta I. *IJMS*. Accepted 9/10/2023 doi: 10.3390/ijms242015089:
2. Tarantino A, et al. *Eur Heart J*. 2024 Jul 30:ehae480. doi: 10.1093/eurheartj/ehae480
3. Ghiroldi A, et al. *Int J Mol Sci*. 2022 Oct 29;23(21):13154. doi: 10.3390/ijms232113154

More recently, my research has increasingly focused on neuronal alterations in the pediatric age, in particular on elucidating the pathogenic mechanisms of different types of epilepsies and developmental and epileptic encephalopathies (DEE), all with a genetic basis.

1. DiFrancesco J, Ragona F, Murano C, Frosio A, Melgari D, Binda A, Calamaio S, Prevostini R, Mauri M, Canafoglia L, Castellotti B, Messina G, Gellera C, Previtali R, Veggiotti P, Milanese R, Barbuti A, Solazzi R, Freri E, Granata T, Rivolta I. *Epilepsia*. 2023 Sep 25. doi: 10.1111/epi.17777
2. Porro A, Abbandonato G, Veronesi V, Russo A, Binda A, Antolini L, Granata T, Castellotti B, Marini C, Moroni A, DiFrancesco JC, Rivolta I. *Prog Biophys Mol Biol*. 2021 Jul 23:S0079-6107(21)00089-4. doi: 10.1016/j.pbiomolbio.2021.07.008
3. Rivolta I, Binda A, Masi A, DiFrancesco JC. *Pflügers Archiv - European Journal of Physiology*. 2020; *Pflugers Arch*. 2020 May 18. doi: 10.1007/s00424-020-02384-3

Complete list of published works

<https://pubmed.ncbi.nlm.nih.gov/?term=Rivolta+I>

or

<https://www.scopus.com/authid/detail.uri?authorId=6602454670>