

BIOGRAPHICAL SKETCH

NAME: Andrea Saponaro

POSITION TITLE: Tenure-track assistant professor in Physiology (RTD-B)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Milan, Milan, Italy	BS	07/2008	Molecular Biology
University of Milan, Milan, Italy	MS	10/2010	Molecular Biology
New University of Lisbon, Lisbon, Portugal	research fellowship	12/2012	Structural Biology of soluble proteins (NMR)
University of Milan, Milan, Italy	PHD	01/2014	Molecular Biology
“Giuseppe Levi Foundation” for Neurobiology Research, Lincean Academy - Italian Science Academy (University of Milan, Milan, Italy)	Postdoctoral fellowship	04/2017	Structure-function of ion channels
Columbia University, NYC, USA	Visiting research fellowship	10/2019	Structural Biology of membrane proteins (cryo-EM)
University of Milan, Milan, Italy (CARIPLO grant 2018-0231 and TELETHON/CARIPLO grant GJC21084)	Postdoctoral fellowship	11/2023	Biophysics and structural biology of ion channels

A. Personal Statement

I am a young PI of the University of Milan, from November 2023 tenure-track assistant professor (RTD-B) in Physiology, Dept. Pharmacological and Biomolecular sciences.

My research is focused on the study of the **molecular mechanisms of ion channel gating**. I have a broad **background in ion channel biophysics**, with specific **training and expertise in structural biology of membrane proteins and macromolecular interactions**. As PI on several national and international-funded grants, I have demonstrated to be able to **establish a successful research line on membrane protein biophysics, recently including high-resolution cryogenic electron microscopy (cryo-EM)**. Notably, this has contributed to provide new expertise to the Italian research community of ion channels biophysics.

Teaching activities and responsibilities**Teaching**

- Physiology (bachelor's degree course in Chemical safety and Toxicological Environmental Sciences);
- Physiology of Nutrition (degree course in Pharmacy);

- Synthetic Biology (master's degree course in Molecular Biology of the Cell).

Responsibilities

- Tutoring of master and PhD students.

Ongoing and recently completed projects

- 2022 – 2024 Biomedical research (PI of the project), 250.000,00 €, co-granted by TELETHON and CARIPLO foundations (rif. GJC21084). Title of the project: “At the origin of congenital muscular dystrophy: shedding light on the Tdark proteins DPM2 and DPM3”. Collaborator: Prof Yvan Torrente, University of Milan.
- 2019 – 2023 Biomedical research conducted by young researchers (PI of the project), 250.000,00 €, granted by CARIPLO foundation (rif. 2018-0231). Title of the project: “The crucial role of HCN2 channels in inflammatory and neuropathic pain”. Collaborators: Prof Rajesh Khanna, NYU, YNC, USA; Dr Emmanuel Bourinet, CNRS, Montpellier, France.
- SEED 2019 grant for interdepartmental projects (responsible of the departmental unit of cellular electrophysiology), 10.000,00 €, granted by University of Milan. Title of the project: “Photo-activable Ivabradine: a spatiotemporal control of HCN channels function with added therapeutic potential”.
- Fulbright Visiting Research Program 2018-2019. Nine-month visiting research fellowship, Columbia University, NY, Dept. Physiology & Cellular Biophysics, laboratory of Prof Filippo Mancia. Structural study of membrane proteins by cryo-EM.
- 2015 - 2017, 40.000,00 € Postdoctoral fellowship granted by Accademia Nazionale dei Lincei. Title of the project: “A molecular prospective of memory: the interaction between HCN channels and their neural regulator TRIP8b”

B. Scientific Appointments, and Honors

Scientific Appointments

2023– Present	Tenure-track assistant professor in Physiology (RTD-B), University of Milan, Milan, Italy
2019	Fulbright Visiting Research fellow, Columbia University, NY, Dept. Physiology & Cellular Biophysics, laboratory of Prof Filippo Mancia. Structural study of membrane proteins by cryo-EM.
2021 – 2022	Council member of the Italian Society for Pure and Applied Biophysics.
2021 – Present	Guest associate editor of “Frontiers in Physiology - Membrane Physiology and Membrane Biophysics”
2021 – Present	Review editor of “Frontiers in Physiology - - Cardiac Electrophysiology”
2020 – Present	Reviewer for Soft Matter and other Royal Society of Chemistry journals which fall within my area of expertise: Biophysics, Biochemistry, Molecular Biology

Honors

2013	Award for Best Poster Presentation (European Biophysical Society)
2014	Award for Best PhD thesis in Biophysics (Italian society of Pure and Applied Biophysics)

2021 – 2033	National Scientific Qualifications: Biochemistry (05/E1); Molecular Biology (05/E2); Physiology (05/D1)
2024	Italian Physiological Society award

C. Contributions to Science

Oral communications

- “Structural basis for the dual regulation of HCN channel activity by cAMP and their auxiliary subunit TRIP8b”, XXII Italian Society of Pure and Applied Biophysics meeting – 2014, Palermo, Italy.
- “HCN channels: the molecular basis for their cAMP-TRIP8b regulation”, 59th Biophysical Meeting 2015, Baltimore, Maryland, U.S.A.
- “HCN channel modulation: the competition between cAMP and TRIP8b explained in molecular detail” Gordon Research Conference (ion channels) 2016, Il Ciocco, Italy.
- “An atomic view of memory: the “complex” structure of HCN channels and TRIP8b”. XXIII Italian Society of Pure and Applied Biophysics meeting – 2016, Cortona, Italy.
- “Exploring new pharmacological perspectives of Fusicoccin, a stabilizer of 14-3-3 – target protein complex”. 61th Biophysical Meeting 2017, New Orleans, U.S.A.
- “Structure-guided design of synthetic peptides for orthogonal control of HCN channels” Gordon Research Seminar/Conference 2018, South Hadley, U.S.A.
- “Developing synthetic peptides to regulate native HCN channels”. 63th Biophysical Meeting 2019, Baltimore, U.S.A.
- “Structure-driven rational design of synthetic proteins to regulate native HCN channels”. Janelia Protein Engineering Workshop, 2019. Howard Hughes Medical Institute, Janelia Research Campus, U.S.A.
- “Gating movements and ion permeation in HCN4 pacemaker channels”. 46th FEBS Congress, 2021, virtual format.
- “Gating movements and ion permeation in HCN4 pacemaker channels”. XXV Italian Society of Pure and Applied Biophysics meeting - 2021, virtual format.
- “Mass photometry to study challenging macromolecules: The case of study of eukaryotic ion channels”. Invited speaker of a webcast organized in May 2022 by Refeyn Inc, 200 Dexter Avenue, Suite 178, Watertown, Massachusetts, 02472, U.S.A.
- “Structural determinant of the Ivabradine-induced block of pacemaker HCN channels”. 67th Biophysical Meeting 2023, San Diego, U.S.A.
- Italian Physiological Society award: “HCN channels: From molecular physiology to synthetic biology”. 74th Italian Society of Physiology meeting 2024, Rome, Italy.
- Saponaro A. “Conventional and unconventional pharmacology of HCN pacemaker channels”. Invited speaker of the 40th International Union of Physiological Sciences (IUPS) 2025. Frankfurt, Germany.
- Saponaro A., “Conventional and unconventional pharmacology of HCN pacemaker channels”. Invited speaker of SGP-EpIC 2026 (the Society of General Physiologists - Electrophysiology and Ion Channel seminar series) symposium entitled: “Emerging Research on Ion Channels in Health and Disease”. Davis, U.S.A.

Patent

Co-author of TICK, Temperature Induced K⁺ channel (102021000023987, University of Milan). TICK is a fully synthetic ion channel designed to gate upon 2.5 fold-increase in temperature (°C) (from 37°C to 39.5°C, physiological values for mammals). TICK expression in neurons (ex vivo and in vivo results) causes a T-induced sustained K⁺ flux that inhibits neuronal activity. Thus, TICK has been designed for analgesic purposes as it is able to silence aberrant nociceptive firing in a temperature dependent manner.

Publications

I have co-authored 30 articles (16 as first and 7 as corresponding author) published in high-impact factor, peer-reviewed international scientific journals, **h-index = 13 (Web of Science)**.

These publications are the result of **collaborations with scientists from prestigious international research centers**:

Prof Steven A Siegelbaum, Columbia University, New York, USA;

Prof Filippo Mancia, Columbia University, New York, USA;

Dr Bina Santoro, Columbia University, New York, USA;

Prof Gerhard Thiel, Technische Universität Darmstadt, Darmstadt, Germany;

Prof Kay Hamacher, Technische Universität Darmstadt, Darmstadt, Germany;

Prof Dario DiFrancesco, University of Milan, Milan, Italy;

Prof Lucia Banci, Magnetic Resonance Center, University of Florence, Florence, Italy;

Prof Anna Moroni, Department of Biosciences, University of Milan, Milan, Italy.

Most relevant publications

1. Sharifzadeh AS, Castelli R, Porro A, Mesirca P, Perrier R, Gómez AM, Mekrane N, Benoit H, Meli AC, Palloni LMG, DiFrancesco D, Mangoni ME, Thiel G, Saponaro A* & Moroni A*. Nat Commun. 2025 Dec 1;16(1):10804. doi: 10.1038/s41467-025-65852-3. * co-corresponding authors.
2. Saponaro A. et al., "Structural determinants of ivabradine block of the open pore of HCN4". Proc Natl Acad Sci U S A. 2024 Jul 2;121(27):e2402259121. doi: 10.1073/pnas.2402259121.
3. Porro A., & Saponaro A.* et al., "A high affinity switch for cAMP in the HCN pacemaker channels". Nat Commun. 2024 Jan 29;15(1):843. doi: 10.1038/s41467-024-45136-y. * co-first author.
4. Saponaro A.* et al. "Validation of the binding stoichiometry between HCN channels and their neuronal regulator TRIP8b by single molecule measurements". Front Physiol. 2022 Sep 26;13:998176. doi: 10.3389/fphys.2022.998176. eCollection 2022. * Also, corresponding author.
5. Saponaro A. et al., "Gating movements and ion permeation in HCN4 pacemaker channels". Mol Cell. 2021 81(14):2929-2943.e6. doi: 10.1016/j.molcel.2021.05.033.
6. Porro A, Binda A, Pisoni M, Donadoni C, Rivolta I, Saponaro A*. "Rational design of a mutation to investigate the role of the brain protein TRIP8b in limiting the cAMP response of HCN channels in neurons". J Gen Physiol. 2020 152(9):e202012596. doi: 10.1085/jgp.202012596 *Corresponding author.
7. Saponaro A. et al., "A synthetic peptide that prevents cAMP regulation in mammalian Hyperpolarization-activated Cyclic Nucleotide-regulated (HCN) channels". Elife. 2018, pii: e35753. doi: 10.7554/eLife.35753.
8. Saponaro A. et al., Fusicoccin Activates KAT1 Channels by Stabilizing Their Interaction with 14-3-3 Proteins. Plant Cell. 2017, 29(10):2570-2580. doi: 10.1105/tpc.17.00375.
9. Saponaro A. et al. "Structural basis for the mutual antagonism of cAMP and TRIP8b in regulating HCN channel function", Proc Natl Acad Sci U S A., 2014, 111(40) :14577-82. doi:10.1073/pnas.1410389111.

Complete List of Published Work: <https://orcid.org/0000-0001-5035-5174>