

BIOGRAPHICAL SKETCHNAME: **Milena Bellin**, PhD

Research Unique Identifiers: Researcher ID: M-2311-2014
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POSITION TITLE: Full Professor of Genetics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Padua, Italy	M.S.	2002	Biological Sciences
University of Padua, Italy	Qualification to Biologist profession	2002	Biological Sciences
University of Padua, Italy	Ph.D	2005	Genetics & Developmental Molecular Biology

A. Personal Statement

The focus of my research is the study and treatment of human genetic cardiovascular diseases. Human pluripotent stem cells (hPSCs) provide unique opportunities to enable genetic information to be linked with cellular and molecular pathological mechanisms in human cardiac disease. We are using patient-specific hPSCs and gene editing for cardiac arrhythmia disease modelling and for developing hPSC-based platforms for drug-screening. We have recently developed a three-dimensional multicellular cardiac microtissue composed of the different cell types of the heart, all derived from hPSCs, which induced maturation of cardiomyocytes to post-natal stages. We have exploited this model to capture post-natal phenotypes of arrhythmic disease (Brugada syndrome) as well as complex and multicellular disorders (Arrhythmogenic cardiomyopathy). Our ambition is to realize the full potential of hPSC in Personalised Medicine by using cutting-edge technology to support gene therapy rationales.

Ongoing and funded projects include the following:

- European Research Council Consolidator Grant (101001746) - Bellin (PI) 2021-2026
Mini-HEART - *Human mini hearts: looking for culprits and victims in cardiac disease*
- LUMC PhD grant - Bellin (PI) 2021-2025
UNIONS: *Unified organoid system for modelling kidney and heart interaction in chronic disease and its treatment*
- HORIZON-EIC-2022-PATHFINDERCHALLENGES - Bellin (co-PI) 2023-2026
- IMPACT *Cardiogenomics meets Artificial Intelligence: a step forward in arrhythmogenic cardiomyopathy* diagnosis and treatment
- ERA4Health Joint Transnational NANOTECMEC project - Bellin (PI) 2025-2028
CELLBEAT - *Actuating nanostructured polymer microcarriers for pluripotent stem-cell derived cardiomyocyte expansion and maturation*
- Telethon Multiround Call – Project GMR24T1104 - Bellin (PI) 2025-2026
ARCADIA: *Human mini-hearts to decipher and correct RRGD cardiomyopathy*

- Human Technopole NF 24-G-Pilot Call - Project - Bellin (PI) 2025
MASTERMIND: Human cardiac microtissues to capture epigenetic and transcriptomic modifications in cardiomyopathies

Recent relevant publications from Bellin's lab:

- Nguyen PD et al., Bellin M, Bakkers J. Interplay between calcium and sarcomeres directs cardiomyocyte maturation during regeneration. *Science*. 2023;380(6646):758-764.
- Campostrini G et al., Bellin M*. Maturation of hiPSC-derived cardiomyocytes promotes adult alternative splicing of SCN5A and reveals changes in sodium current associated with cardiac arrhythmia. *Cardiovasc Res*. 2022:cvac059.
- Campostrini G et al, Orlova VV*, Mummery CL*, Bellin M*. Generation, functional analysis and applications of isogenic three-dimensional self-aggregating cardiac microtissues from human pluripotent stem cells. *Nat Protoc*. 2021;16(4):2213-2256.
- Giacomelli E et al., Orlova VV*, Mummery CL*, Bellin M*. Human-iPSC-Derived Cardiac Stromal Cells Enhance Maturation in 3D Cardiac Microtissues and Reveal Non-cardiomyocyte Contributions to Heart Disease. *Cell Stem Cell*. 2020;26(6):862-879.e11.

B. Positions, Scientific Appointments, and Honors

POSITIONS

2006 - 2008 Postdoctoral fellow - CRIBI Biotechnology Center, University of Padua, Italy
 2008 - 2010 Postdoctoral fellow - Technical University of Munich, Germany
 2010 - 2014 Senior postdoctoral fellow and Marie Curie fellow, LUMC, The Netherlands
 2014 - 2016 Senior Researcher - Dept. of Anatomy and Embryology, LUMC, The Netherlands
 2016 - present Associate Professor, Leiden University Medical Center (LUMC), The Netherlands
 2019 - 2021 Assistant Professor and Group Leader - University of Padua and Veneto Institute of Molecular Medicine, Padua, Italy
 2021- present Full Professor of Genetics and Principal Investigator - University of Padua, Padua, Italy

INSTITUTIONAL RESPONSIBILITIES

2021 - present Committee Member of "Manzini prize" for young researchers, Veneto Institute of Molecular Medicine, Padova, IT
 2021 - present PhD thesis external advisory committee member - PhD Programs in Molecular Biomedicine, University of Trieste & University of Milan, IT and Biomedical Sciences PhD study programme, Jagiellonian University in Kraków, Poland
 2020 - 2021 Member of the "Communication committee" & editor of "meet the DiBio scientist series", Dept. of Biology, University of Padua, IT
 2019 - present Member committee PhD in Biosciences, University of Padova, IT
 2019 - present Member of PhD advisory committee, LUMC, NL
 2016 - present Organiser of Group Progress Meeting
 2016 - present Management team, Dept. Anatomy & Embryology, LUMC, NL
 2015 - 2018 Chair of PhD student Journal Club, Dept. Anatomy & Embryology, LUMC, NL
 2015 - present Member of 4 PhD thesis opposition committees, 2x Leiden University, NL, 1x University "Statale" of Milan, IT, 1x Imperial College, London, UK

AWARDS

2016 FEBS Anniversary Prize for outstanding achievements in Biochemistry & Molecular
 2012 EU FP7 Marie Curie Intra-European Fellowship for Career Development (IEF)
 2010 Young Investigator Award Competition, 8th Dutch-German Meeting Molecular Cardiology WG
 2005 & 2006 EMBO fellowships for participation to two EMBO Practical Courses

COMMISSIONS OF TRUST

- 2021 Delegation of Veneto Institute Molecular Medicine representatives to President of the Italian Republic Mattarella
- 2019 - 2021 Scientific Advisory Board, DENIM ERA-CVD project, Monzino Hospital, Milan, Italy
- 2019 - 2020 Managing Editor for ISSCR journal *Stem Cell Reports* (Cell press)
- 2017 - 2018 Section Editor for 'Crispr/Cas9 HR' in *Drug Discovery Today: Technologies*
- 2021 Comparative Reviewer for Application TUM-IAS Rudolf Mößbauer Tenure Track Professorship - Technical University of Munich, DE
- 2018 - present Italian Scientific Evaluation committee (Rita Levi Montalcini fellowship, PRIN-2017)
- 2016 - present Grant reviewer for: European Research Council (ERC CoG); the Friedreich's Ataxia Research Alliance (FARA), Australia; Medical Research Council UK (RCUK), UK; Dutch Heart Foundation (Hartstichting), NL; Israel Science Foundation (ISF), Israel; The Royal Society, UK; French National Research Agency (ANR); National Children's Research Center (NCRC), Ireland; Swiss National Science Foundation (SNF); Austrian Science Fund (FWF); German Research Foundation (DFG); Department Integrated Research Budget (university of Padua).
- 2010 - present Peer Reviewer for scientific journals (selection): *Circulation, Nature Methods, Stem Cell Reports, Scientific Reports, Cardiovascular Research, Stem Cells, Stem Cells & Development, Disease Models and Mechanisms, Cell Reports Medicine, Clin Transl Medicine, Stem Cell Res and Therapy, & others.* Ad hoc co-reviewer for: *Nature, Nature Biotechnology, Nature Medicine, Cell Stem Cell, Circulation Research.*

MEMBERSHIPS OF SCIENTIFIC SOCIETIES

- 2022 - present *Italian Genetics Association* (AGI)
- 2021 - present *The Italian Society of Biophysics and Molecular Biology* (SIBBM)
- 2021 - present *ERC in Italy*
- 2020 - present *International Society for Stem Cell Research* (ISSCR)
- 2016 - present Member, "Institute for human Organ and Disease Model technologies initiative (hDMT, <https://www.hdmt.technology>)" and hDMT "Heart-on-Chip" Group
- 2014 - present Member, "European Society of Cardiology (ESC)" and "Women in ESC Initiative"
- 2014 - present Member, "ESC Working Group on Cardiac Cellular Electrophysiology"
- 2012 - 2016 Member, "International Society of Differentiation"

C. Contributions to Science

Expertise on cardiac disease modelling using hPSCs

We have more than 15 years' experience in using hPSC-derived cardiomyocytes to study cardiac arrhythmia syndromes. We contributed significantly to the field by describing one of the first hiPSC models of long-QT syndrome 1. We developed several hPSC-based models, shown that they recapitulated human cardiac arrhythmia and used them to create platforms to test any-arrhythmic drugs.

- Campostrini G et al., Bellin M*. Maturation of hiPSC-derived cardiomyocytes promotes adult alternative splicing of SCN5A and reveals changes in sodium current associated with cardiac arrhythmia. *Cardiovasc Res.* 2022:cvac059
- Sala L et al, Bellin M*. A new hERG allosteric modulator rescues genetic and drug-induced long-QT syndrome phenotypes in cardiomyocytes from isogenic pairs of patient induced pluripotent stem cells. *EMBO Mol Med.* 2016;8(9):1065-81
- Zhang M et al., Greber B*#, Bellin M*#. Recessive cardiac phenotypes in iPS cell models of Jervell and Lange-Nielsen Syndrome: disease mechanisms and pharmacological rescue. *Proc Natl Acad Sci USA.* 2014;111(50):E5383-92.
- Bellin M*, Moretti A*, Welling A*, et al., Laugwitz KL. Patient-Specific Induced Pluripotent Stem-Cell Models for Long-QT Syndrome. *N Engl J Med.* 2010; 363(15):1397-409.

Expertise on gene editing in hPSCs

We were the first group to generate isogenic hPSC lines for cardiac diseases. We successfully applied gene editing technology in hPSCs to reveal the causative effect of gene mutations and to expand CRISPR-Cas versatility.

- a. Meraviglia V et al., Bellin M#. Generation of human induced pluripotent stem cell line LUMCi027-A and its isogenic gene-corrected line from a patient affected by arrhythmogenic cardiomyopathy and carrying the c.2013delC PKP2 mutation. *Stem Cell Res.* 2020;46:101835.
- b. Chen X, et al., ... Bellin M, ... Gonçalves MAFV. Expanding the editable genome and CRISPR-Cas9 versatility using DNA cutting-free gene targeting based on in trans paired nicking. *Nucleic Acids Res.* 2020. 48(2):974-995.
- c. Bellin M#, Casini S, Davis RP, D'Aniello C, Haas J, Ward-van Oostwaard D, Tertoolen LGJ, Jung CB, Elliott DA, Welling A, Laugwitz KL, Moretti A#, Mummery CL. Isogenic human pluripotent stem cell pairs reveal the role of a KCNH2 mutation in long-QT syndrome. *EMBO J.* 2013;32(24):3161-75.

Expertise on developing advanced models of the heart based on hPSCs

We developed 3D multicellular cardiac microtissues that enable post-natal maturation of hPSC-cardiomyocytes

- a. Nguyen PD et al., Bellin M, Bakkers J. Interplay between calcium and sarcomeres directs cardiomyocyte maturation during regeneration. *Science.* 2023;380(6646):758-764.
- b. Campostrini G et al., Bellin M*. Generation, functional analysis and applications of isogenic three dimensional self-aggregating cardiac microtissues from human pluripotent stem cells. *Nature Protocols.* 2021;16(4):2213-2256.
- c. Giacomelli E, et al., Orlova VV*#, Mummery CL*#, Bellin M*#. Human-iPSC-Derived Cardiac Stromal Cells Enhance Maturation in 3D Cardiac Microtissues and Reveal Non-cardiomyocyte Contributions to Heart Disease. *Cell Stem Cell.* 2020;26(6):862-879.e11

*shared authorship

#corresponding author

Full list of publications can be found at

<https://pubmed.ncbi.nlm.nih.gov/?term=milena+bellin&sort=date>