
CURRICULUM VITAE

Paola Braghetta

ORCID ID: 0000-0003-2547-8679

POSITION TITLE: Associate Professor in Cell Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date	FIELD OF STUDY
University of Padova, Padova, Italy	M.Sc.	12/1984	Biological sciences
EMBL, Heidelberg, Germany	PhD fellow	04/1989	Cell biology
University of Padova, Padova, Italy	PhD	05/1992	Cell Biology
Glaxo Group Research, Greenford, U.K.	Guest Scientist	02/1991	Transgenic Research Unit

A. Personal Statement

Associate Professor of Cell Biology at the Medical School of The University of Padova. I authored 87 full-length publications in peer-reviewed journals, including several high impact journals such as *Cell*, *Nature Genetics*, *Immunity*, *Human molecular Genetics*, *Oncogene*, *Cell Stem Cell*, *JCI*, *J. Hepathology*; H-index (Scopus) 34; total citations: 5009; average citation per item: 58,93.

I am PI of the Functional Genomics Research Unit (<https://www.medicinamolecolare.unipd.it/ricerca/laboratori/functional-genomics-research-unit>) at the Department of Molecular Medicine, University of Padova. The complete Unit currently includes 3 staff scientists, 3 postdocs, 1 PhD students, 1 Research Assistant.

I have attended courses on mouse genomics ("Targeting Genome Editing using Zinc Finger Nuclease", EMBL, Heidelberg, Germany) and on cryopreservation of mouse lines ("Cryopreservation of mouse germplasm", "The Jackson Laboratories" Bar Harbor, Maine, USA)

I have a strong background in molecular biology, cell biology and functional genomics, in mouse and zebrafish models, with a long-lasting interest in extracellular matrix and its role during development and in disease. My research work is focused on the cardiovascular and skeletal muscle systems, on neuromuscular diseases and pathogenetic processes. I have a broad and long-standing expertise in mouse transgenesis and in the generation and characterization of animal models for diseases. I have always put much effort in establishing synergies and collaborations with different groups with specific interests in mouse transgenesis, in disease models and in development and application of innovative techniques for the generation of mutant animals (Zinc Finger Nuclease, CRISPR-Cas9). I am a founding member of a Research Spin-off of the University of Padova (MEMMIA s.r.l.), which offers services such as cryopreservation of mouse germplasms, production of transgenic mice by pronuclear injection and zygote electroporation and surgical techniques on animals.

B. Positions and Honors

Positions and Employment

- 1983-1984: University of Padova, Department of Biology, Graduation training
- 1985-1986: University of Padova, Department of Biology, Postgraduate training
- 1987-1989: European Molecular Biology Laboratory, Department of Cell Biology, Heidelberg, Germany, Ph.D fellow (K.K. Stanley Group, E. Wagner Group)
- 1990-1991: Glaxo Group Research, Department of Genetics, Greenford, U.K., Ph.D fellow (Transgenic Facility)
- 1993-2002: University of Padova, Institute of Histology and Embryology, Technical assistant
- 2003-2007: University of Padova, Institute of Histology and Embryology, Research assistant
- 2007-2015: University of Padova, School of Medicine, Assistant Professor of Cell Biology

- October 2015-present: University of Padova, School of Medicine, Associate Professor of Cell Biology (SSD BIO/13)

Other Experience and Professional Memberships

- Member, Italian Society of Biology and Genetics (A.I.B.G.)
- Member, International Society of Transgenic Technologies (ISTT)
- Member of Interuniversity Institute of Myology (IIM)

C. Research Topics

During the stay at the EMBL, I have been involved in the development of prokaryotic vectors for the production of fusion proteins and the production and use of antibodies for membrane proteins of the trans-Golgi network. I had also a deep training in embryonic stem cell culture, in their use *in vitro* as a tool to investigate cell differentiation and stemness and *in vivo* to produce chimeric mice. Since 1989 my main field of research has been the study of the organization and function of extracellular matrix proteins, such as collagen VI and all the members of the Emilin/Multimerin family in organ physiology and pathology and mouse transgenesis as a model for studying gene function *in vivo*. I performed analysis of the expression of extracellular matrix components in mouse embryos and adults' tissues and of the regulatory regions specifying temporal and spatial distribution, creating transgenic mice carrying reporter genes fused to different upstream and downstream regulatory regions. For this purpose, I started a training in mouse transgenesis, both at the EMBL (Germany) in the group of E. Wagner and at Glaxo Group Research (U.K.) in the group of G. Schmidt.

I settled those techniques in the University of Padova, where I organized a lab in which many different techniques for the production and the use of transgenic mice are thoroughly applied (production of transgenic and knockout mice by microinjection of DNA in oocytes, culture and site directed mutagenesis of murine ES cells and microinjection into blastocysts, lentiviral production and embryos injection for *in vivo* knockdown via RNAi and overexpression of gene of interests, genome editing by ZFNs and CRISPR-Cas9 approaches). The use of these techniques and of cell and molecular biology procedures allowed the disclosure of the phenotype of knockout mice, both lacking extracellular matrix proteins. In collaboration with Prof. Paolo Bonaldo the dystrophic phenotype of collagen VI deficient mice was described and validated as a model of human inherited neuromuscular diseases. With the aim of dissecting the pathomolecular mechanisms, I carried out an ambitious and multidisciplinary study in collagen VI null mice and in patients affected by collagen VI-related myopathies. We established the important role of apoptosis, mitochondrial dysfunction and of impaired autophagy in the pathology. We used such model to validate possible therapeutic approaches for ameliorating the clinical picture of patients affected by collagen VI associated dystrophies. We pioneered the finding that an inefficient regulation of autophagy contributes to muscle wasting and weakness and showed that restoration of a proper autophagic flux by different means (genetic, pharmacological or nutritional) is beneficial and counteracts muscle pathology. We have also broadened the investigation on other tissues, like the CNS, the PNS and the gut and unveil defects on megakaryocytes function.

I deeply investigated the function of Emilin-1, a remarkable extracellular matrix protein, which carries at the N-terminus a cysteine-rich domain able to modulate TGF-beta bioavailability. The deficient mice appeared to be a striking model for monogenic hypertension linked to TGF-beta control, modulating myogenic tone in resistance arteries. Besides I broaden my interest on TGF-beta effects on the cardiovascular system focusing on the onset of aortic aneurysms in association also to mutation on Fibrillin1 gene. I am also investigating the effect of Emilin-1 absence in the heart, from the histological, biochemical, echocardiographic and inflammatory point of view. Recently we gained human aorta biopsies from patients bearing mutations in Emilin-1 gene and displaying aortic aneurysms, thanks to a collaboration with Dr J. Eleftheriades of the Yale University. We are currently investigating them at the histological and proteomics level. We have recently produced emilin-1 knockout zebrafish models by CRISPR-Cas9 strategy, that will enable us to dissect other signalling pathways that are dysregulated by the absence of Emilin-1.

Recently I have been involved in the production and characterization of mouse models for Arrhythmogenic Cardiomyopathy (ACM), a rare genetic cardiac disease phenotypically characterized by structural and functional alterations, in collaboration with Prof. Alessandra Rampazzo, Dott. Libero Vitiello and Dott. Martina Calore. For this purpose, I produced transgenic mice overexpressing in a cardiomyocyte's specific manner

the human DSG2 gene carrying mutations that have been previously mapped in families affected by ACM, and lately knockin mice for other different mutations. By means of these mice we were able to identify cFAPs cells as key player in the onset of the pathology. We are currently testing pharmacological compounds able to counteract the differentiation of these cells towards adipocytes and fibroblasts. In the IMPACT Project led by Prof. Rampazzo and in strict collaboration with Prof. Milena Bellin, we are currently producing “microhearts”. These sophisticated 3D models are generated through a multi-step process. Initially, human induced pluripotent stem cells (hiPSCs) carrying mutations in genes associated with Arrhythmogenic Cardiomyopathy (ACM) are differentiated into three distinct cell types: cardiac fibroblasts, endothelial cells, and cardiomyocytes. Subsequently, these differentiated cells are aggregated to form complex 3D structures that closely mimic the cellular composition and architecture of cardiac tissue.

I am also investigating the phenotypes of knockout mice, produced in our laboratory, for the other members of the Emilin-Multimerin family (Emilin-2, Emilin-3, Multimerin-2). I am involved in studies of the role of these proteins in different organs and tissues, and in pathological conditions. Moreover, I have been studying the expression pattern of the orthologue genes in zebrafish embryos and at the moment investigating other possible signalling pathways that are dysregulated in the absence of Emilin genes. For this purpose, we generated CRISPR-Cas9 zebrafish mutants that are currently under investigation.

I have been involved also in the development of new approaches for the recover of the dystrophic phenotype of *mdx* mice utilizing synthetic nanoparticles delivering oligonucleotides for exon-skipping.

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/>

D. Research Support

Ongoing Research Support

- | | |
|-----------|---|
| 2022-2025 | PNRR National Center for Gene Therapy and Drugs based on RNA Technology , Spoke 3 “ Metabolic and Cardiovascular diseases ” Role: co-investigator. |
| 2023-2025 | Horizon-EIC-2023-Pathfinderopen-01-03 : Role: co-investigator. (WP leader: A. Rampazzo) Proposal Acronym: IMPACT. Title: “ <i>Cardiogenomics meets artificial intelligence: a step forward in arrhythmogeniccardiomyopathy diagnosis and treatment.</i> ” (WP budget: € 766.793) |
| 2025-2028 | ERA4Health Joint Transnational Call for Proposals 2024 : Role: co-investigator. (WP leader: M. Bellin) Proposal Acronym: NANOTECMEC. Title: “ <i>Nano and advanced technologies for disease prevention, diagnostic and Therapy</i> ” (WP budget: € 175000) |

Completed Research Support since 2018

- | | |
|-----------|--|
| 2015-2018 | CaRiPaRo Foundation – Research Projects. Role: co-investigator. Title: <i>Collagen VI and autophagy in the nervous system: dissecting novel pathways in neurodegeneration and neuropathies</i> (Project acronym: AUTOGLIA). |
| 2017-2018 | University of Padova – Grant Application . Role: Principal Investigator. <i>Dissecting novel roles of autophagy in neurodegeneration and neuromuscular insults: from the nervous system to the muscle synapse.</i> |
| 2017 | ICE S.p.a. , Reggio Emilia. Role: Principal Investigator. Collaborative project: “ <i>Analisi di efficacia di diverse vie di somministrazione di oligonucleotidi per exon-skipping in topi mdx</i> ”. € 15.200 |
| 2018 | ICE S.p.a. , Reggio Emilia. Role: Principal Investigator. Collaborative project “ <i>Analisi di efficacia di diverse vie di somministrazione di oligonucleotidi per exon-skipping in topi mdx</i> ”. € 19.000 |
| 2019 | Gnosis S.p.a. , Desio (Mi). Role: Principal Investigator. Collaborative project “ <i>Testing of nutraceutical compounds able to counteract aging and osteoporosis processes in in vitro models</i> ”. € 32.341 |
| 2020 | PRID University of Padova. Role: Principal Investigator. Title “ <i>Characterization of the extracellular matrix deposition in murine models of arrhythmogenic right ventricular cardiomyopathy (ARVC)</i> ” |
| 2021 | PRID University of Padova. Role: co-investigator. (WP leader: E. Moro) Title: Title of the |

project: *“Development and application of a versatile and exploitable experimental platform to trace and modulate the NRF2-inflammasome axis”*.

E. Patents

PCT International publication number: WO2020084488A120200430. Title: *Conjugates of oligonucleotides and bile acids and their derivatives for pharmaceutical active molecules delivery*

F. Third Mission

University Spin off Memmia srl: founder, member of the board of directors and actively involved in laboratories activities. Memmia offers know-how and services on the utilization, manipulation, cryopreservation, and production of animal models applying classical transgenic techniques and CRISPR-Cas9 strategies in order to obtain knockout and knockin mice

Science4all 2022: “Non solo neuroni: un viaggio all’interno del cervello per capire il ruolo delle cellule gliali” in collaboration with the Department of Biology (Dott. L. Civiero, Dott. M. Cescon, Prof. E. Greggio)

Science4all 2023: “Come ci muoviamo? Il muscolo e le sue giunzioni” in collaboration with Dott. M. Cescon

Science4all 2024: “Match perfetto!” in collaboration with Dott. M. Cescon

Patient Association “Beat the Beat” and “La stella di Lorenzo”: patient association aiming at fund raising for pharmacological strategies to inhibit the progression of arrhythmogenic right ventricular cardiomyopathy

Patient Association “Collagene VI italia onlus”: a non-profit social promotion association that represents patients with diseases due to collagen VI deficiency

Advanced course in Bioethics: Coordinator Prof. Viafora. **Public Session:** *“Animal experimentation: scientific rationale and ethical-public debate”*

Annual project of the Department of Molecular Medicine “Invecchiare bene: istruzioni per l’uso”: podcast consisting in 4 episodes focused on the effect of aging in the cells

G. Teaching Activities

School of Medicine: Courses of General Biology (SSD BIO/13) in “CdS di Medicina e Chirurgia” (Padova and Treviso) and “CdS in Odontoiatria e Protesi Dentaria”; Course of Cell Biology (SSD BIO/13) in “CdS in Medicine and Surgery”; Courses of Biology and Genetics (SSD BIO/13) in “CdS in Infermieristica” and in “CdS in Tecniche di radiologia medica, per immagini e radioterapia”. Course of Applied Biology (SSD BIO/13) in Specialization School in Genetics.

School of Science: Course of Functional Genomics (SSD BIO/13) in “CdS in Biotecnologie”.

Summer/Winter School Program, Ph.D. Courses of The School of Medicine: Title: “Animal model in Biomedical Research”

Teaching4Learning Training Program: Basic course (T4L basic 1.0) Open Badge

Thesis advisor for Biotechnology, Industrial and Medical Biotechnologies and Molecular Biology students

Member of the committee for the defence of PhD thesis Maastricht University, The Netherland

H. Organizational/managerial assignments

School of Medicine: Coordinator of teaching activities in the second semester “CdS di Medicina e Chirurgia” (Padova); Professor in charge of OFA acquittal “CdS di Medicina e Chirurgia” and “CdS in Odontoiatria e Protesi Dentaria”; Professor in charge for student career evaluation; Professor in charge for the coordination of medical students’ internship; Member of the Teaching Staff-Student Joint Committee

University of Padova: scientific member of the “Ethical Committee for Animal experimentation” (OPBA)

I. Collaborations and networks

Prof. C. Gelfi, University of Milano: proteomic analyses

Prof. G. Vozzi, University of Pisa, Centro Piaggio: biomaterial production and testing

Prof. A. Rampazzo, University of Padova: cardiomyopathies and animal models

Prof. F. Rossi, The University of British Columbia, Vancouver, Canada: cardiomyopathies, animal models and fibroadipogenic precursors

Dr. M. Calore, University of Maastricht, The Netherland: miRNAs and hiPSCs

Prof. M. Bellin, University of Padova: hiPSCs

Prof. I. Castagliuolo, Prof. P. Brun, University of Padova: inflammation analyses

Prof. F. Anglani, University of Padova: kidney diseases, CRISPR-Cas9

Prof. A. Balduini, University of Pavia: megakaryocytes dysfunction and extracellular matrix

Dr. C. Stainkuhler, Dr. G. Fossati, Dr. M. Forino, Italfarmaco SpA, Milano: compounds against fibrosis

Dr. M. Mazzucato, IRCSS Aviano: bone marrow niche

Prof. E. Pegoraro, University of Padova: peripheral and central neuropathies

Prof. R. Wagener, University of Cologne, Germany: extracellular matrix functions

Prof. G. Lembo, Prof. D. Carnevale Neuromed IRCSS, Pozzilli, Isernia: cardiovascular system investigations

Prof. A. Calvo, Department of Neuroscience, University of Turin, ALS Center, Turin: peripheral and central neuropathies

Dott. J. Elefteriades, Aortic Institute at Yale-New Haven Hospital (YALE), Yale University School of Medicine, New Haven, Connecticut, USA: thoracic aortic aneurysms

Prof. A. Ghigo, University of Torino: ECG analyses

Prof. G. Farrauto, University of Torino: cMRI analyses

Padova, September 29, 2025