CURRICULUM VITAE
Emanuela Bottani

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PROFILE

I am a University Researcher with 15 years of experience in the field of rare genetic diseases. From 2009 to 2013, I worked as a research fellow at the Neurological Institute "Carlo Besta" in Milan (Italy), where I focused on characterizing and studying various murine models of mitochondrial genetic diseases. I used these models to investigate pathogenic mechanisms and identify novel pharmacological (*Viscomi*, Bottani* et al., Cell Metabolism 2011, *denotes equal contribution*) and gene therapy treatments (*Bottani et al, Molecular Therapy 2014*).

During my PhD in Translational and Molecular Medicine, I moved to the University of Cambridge (UK) as an *Investigator Scientist*, where I worked for over four and a half years. There, I successfully identified the molecular mechanisms underlying a severe, previously unknown mitochondrial disease (*Bottani et al., Molecular Cell 2017*).

I moved back to Italy in 2017 with the support of the *Umberto Veronesi Foundation*, which awarded me twice with a 1-year postdoctoral fellowship. On this occasion, I expanded my research interests to the study of mitochondrial bioenergetics in physiological and pathological conditions in neuronal cells and the central nervous system (*Bifari*, Dolci*, Bottani* et al., Pharmacol Res. 2020, *denotes equal contribution; Brunetti*, Bottani* et al., Front Pharmacol. 2020, *denotes equal contribution*).

In 2019, I obtained a position as Junior Researcher at the University of Verona (Italy), where I established my research group thanks to a *European Joint Program on Rare Diseases* grant (call 2020). The project, with over 2,4 million euros of funding, supported the establishment of the *CureMILS European Consortium* with the aim of identifying a pharmacological therapy for Maternally Inherited Leigh Syndrome, a severe paediatric neurological mitochondrial disorder. On that occasion, I was selected as an *Early Career Principal Investigator* by the Consortium Coordinator.

Since December 2024, I have held a Tenure Track position at the University of Verona. Here, I lead a research group focusing on novel pharmacological approaches for rare neurodevelopmental disorders, including Leigh Syndrome, Jamuar Syndrome, and Allan-Herndon-Dudley Syndrome. My research is supported by competitive national and international funding.

I hold the following National Scientific Qualifications for Associate Professor:

- 06/A1 - Medical Genetics (valid: 06.06.2023 to 06.06.2034)
- 06/N1 - Health Professions and Medical Technologies (valid: 06.06.2023 to 06.06.2034)
- 05/G1 - Pharmacology, Clinical Pharmacology and Pharmacognosy (valid: 24.06.2024 to 24.06.2035)

EDUCATION AND TRAINING

- **Oct 2012 – Nov 2015:** PhD in Translational and Molecular Medicine (SSD Med/03), University of Milan-Bicocca (Italy). Supervisor: Prof. Massimo Zeviani (MRC-MBU, Cambridge, UK). Thesis: "Mitochondrial diseases: from gene function to therapy" — Final assessment: Excellent.

➢ **Oct 2009 – Mar 2012:** MSc in Biology, Pathophysiology track – 107/110. University of Milan-Bicocca. Supervisor: Dr. Massimo Zeviani, IRCCS Carlo Besta, Milan (Italy). Thesis: "Pharmacological stimulation of mitochondrial biogenesis as a therapeutic approach in murine models of cytochrome c oxidase deficiency" — Published in *Cell Metabolism (Viscomi*, Bottani* et al, Cell Metabolism 2011; * denotes equal contribution).*

➢ **Oct 2000 – Apr 2006:** Five-year degree in Industrial Biotechnology – 110/110, University of Milan-Bicocca (Italy). Supervisor: Dr. Maria Foti. Thesis: "Colorectal cancer: Microsatellite instability and gene expression alteration".

WORK EXPERIENCE

➢ **Dec 2024 – Present:** Tenure Track Researcher (RTT), University of Verona, Department of Diagnostics and Public Health, Verona, Italy.

Research activities:

- Mitochondrial diseases: study of novel pharmacological treatments for maternally inherited Leigh syndrome (MILS) caused by homoplasmic mutations in the MT-ATP6 gene; analysis of neurodevelopmental alterations due genetic loss of mitochondrial genes NUBPL and COX15
- Genetic neurodevelopmental disorders: study of secondary mitochondrial dysfunctions in Allan-Herndon-Dudley syndrome caused by SLC16A2 loss-of-function mutations; development of new *in vitro* and *in vivo* therapeutic strategies targeting mitochondrial metabolism; prenatal metabolic modulation; investigation of neurodevelopmental defects in Jamuar syndrome (UGDH gene mutations); *in vitro* pharmacological treatments; generation of a new mouse model.

Teaching activities 2024–25: Pharmacology, Bachelor's Degree in Physiotherapy; Pharmacology, Bachelor's Degree in Medical Radiology Techniques for Imaging and Radiotherapy; Pharmacology for Dental Hygienists, Bachelor's Degree in Dental Hygiene; Pharmacology, Bachelor's Degree in Orthopedic Techniques; Pharmacology, Bachelor's Degree in Nutraceutical Sciences; Pharmacology, Bachelor's Degree in Cardiovascular Physiopathology and Cardiovascular Perfusion Techniques. *Full list here.*

➢ **Nov 2019 – Oct 2024:** Fixed-term Researcher Type A (RTD-A) University of Verona, Department of Diagnostics and Public Health, Verona, Italy.

Research activities:

- Mitochondrial genetic diseases: study of pharmacological treatments for MILS and functional analyses in cerebral organoids.
- Neurodevelopmental genetic diseases: mitochondrial dysfunction in Allan-Herndon-Dudley and Jamuar syndromes; therapeutic targeting of mitochondrial metabolism.
- Pharmacological modulation of mitochondrial metabolism in spinal cord injury and neuronal stem cell maturation.

Teaching activities:

2020–21: Clinical Pharmacology, Bachelor's Degree in Obstetrics; General Pharmacology, Bachelor's Degree in Obstetrics; Pharmacology, Bachelor's Degree in Medical Radiology Techniques, Imaging and Radiotherapy; *Full list here.*

2021–22: Pharmacology, Bachelor's Degree in Physiotherapy; Pharmacology, Bachelor's Degree in Medical Radiology Techniques, Imaging and Radiotherapy; Pharmacology for Dental Hygienists, Bachelor's Degree in Dental Hygiene; Pharmacology, Bachelor's Degree in Orthopedic Techniques.

2022–23: Pharmacology, Bachelor's Degree in Physiotherapy; Pharmacology, Bachelor's Degree in Medical Radiology Techniques, Imaging and Radiotherapy; Pharmacology for Dental Hygienists, Bachelor's Degree in Dental Hygiene; Pharmacology, Bachelor's Degree in Orthopedic Techniques.
2023–24: Pharmacology, Bachelor's Degree in Physiotherapy; Pharmacology, Bachelor's Degree in Medical Radiology Techniques, Imaging and Radiotherapy; Pharmacology for Dental Hygienists, Bachelor's Degree in Dental Hygiene; Pharmacology, Bachelor's Degree in Orthopedic Techniques; Pharmacology, Bachelor's Degree in Nutraceutical Sciences. *Full list here.*

- **Nov 2017 – Oct 2019:** Post-doctoral Research Fellow – Umberto Veronesi Foundation, University of Brescia, Department of Molecular and Translational Medicine, Brescia, Italy.

Research activities:

- Mitochondrial genetic diseases: biochemical and functional characterization of novel pathogenic variants in the MT-ATP6 gene associated with Leigh syndrome;
- Pharmacological modulation of mitochondrial metabolism in pathophysiological contexts, including neural stem cell development, non-alcoholic fatty liver disease (NAFLD), and frailty syndrome in aging, using murine models.

Teaching Activities:

Subject Expert in Pharmacology, Medical and Surgical Sciences (disciplinary sector BIO/14), within the Integrated Course of Biological and Pathological Foundations of Diseases and Pharmacology, Bachelor's Degree in Psychiatric Rehabilitation; and in Clinical Pharmacology (BIO/14), within the Integrated Course of Nursing Applied to Diagnostic and Therapeutic Pathways, Bachelor's Degree in Nursing.

- **May 2014 – Oct 2017:** Investigator Scientist, Mitochondrial Biology Unit, Medical Research Council, University of Cambridge, United Kingdom. Supervisor: Dr. Massimo Zeviani.

Research activities:

- Mitochondrial diseases: investigation of the role of the mitochondrial protein TTC19, of unknown function, associated with fatal neurodegenerative disease in humans; study of the biochemical and molecular consequences of novel MT-ATP6 mutations in the mitochondrial genome associated with Leigh syndrome (in collaboration with Dr. Robert Pitceathly, UCL Queen Square Institute of Neurology, London, UK, and the Carlo Besta Neurological Institute, Milan, Italy).

- **Nov 2008 – Apr 2014:** Research Fellow, Molecular Neurogenetics Unit, Fondazione IRCCS Carlo Besta Neurological Institute, Milan, Italy. Supervisor: Dr. Massimo Zeviani. *(From 01/07/2013 to 30/04/2014: Visiting Scientist, Mitochondrial Biology Unit, Medical Research Council, University of Cambridge, UK).*

Research activities: Mitochondrial genetic diseases: generation and characterization of murine genetic models of human diseases; development of pharmacological and gene therapy approaches.

- **Nov 2007 – Oct 2008:** Research Fellow, Avantea s.r.l. Cremona Italy. Supervisor: Dr. Cesare Galli.

Research activities:

- Involved in the research project "High-tech network for the generation and use of animal models for gene and cell therapy in human diseases": characterisation of equine mesenchymal

stem cells; development of a regenerative medicine protocol for the treatment of tendon injuries;
- Embryo generation in bovine and swine models: in vitro fertilisation.

RESEARCH GRANTS:

As Principal Investigator or Co-Principal Investigator:

- 2019: "Prevention Of Western-Diet Induced Nafld: Preclinical Trial With A Peculiar Aminoacid Formula Preserving Liver Mitochondrial Health" Umberto Veronesi Foundation. Budget: **28,500 €.** Role: Applicant.
- 2020: "Prevention Of Western-Diet Induced Nafld: Preclinical Trial With A Peculiar Aminoacid Formula Preserving Liver Mitochondrial Health" Umberto Veronesi Foundation. Budget: **30,000 €.** Role: Applicant.
- 2021: CureMILS: "A reprogramming-based strategy for drug repositioning in patients with mitochondrial DNAassociated Leigh syndrome". European Joint Program for Rare Disease, Total Budget **2,360,668 €**, Budget to UniVR: **150.000 €.** Role: Early career-PI.
- 2021 "Definition of the disease mechanisms and identification of new therapeutic approaches in the NUBPL cerebral organoid model of mitochondrial disease." AMMeC Foundation. Budget **50.000 €.** Role: PI.
- 2021: "Targeting mitochondrial metabolism to promote full neuronal development in Allan-Herndon-Dudley syndrome". Telethon Foundation. Budget: **48.300 €.** Role: Co-PI.
- 2022: "Targeting mitochondrial metabolism to promote neuronal maturation in AHDS: developing new therapeutic approaches in 3D mouse and human brain models". Telethon Foundation. Budget: **50.000 €.** Role: Co-PI.
- 2023: "Novel pharmacological strategies for the treatment of the X-linked Allan-Herndon-Dudley Syndrome: targeting mitochondrial metabolism to promote neuronal and oligodendrocytic maturation" PRIN. Budget: **204.791 €.** Role : PI e National Coordinator.
- 2023: "Exploring pathogenetic mechanisms of Jamuar Syndrome: focus on transcriptomics and brain extracellular matrix changes". Telethon Seed Grant 2023. Budget: **49.350 €.** Role: PI
- 2023 "Definition of the disease mechanisms and identification of new therapeutic approaches in the NUBPL cerebral organoid model of mitochondrial disease." AMMeC Foundation. Budget **30.000 €.** Role: PI.
- 2024: "Investigating the Therapeutic Potential of UDP-Glucuronic Acid Supplementation in Mouse Brain Organoids Modeling Jamuar Syndrome". Telethon Foundation, Budget: **49.875 €** Role: PI.
- 2024: "Pharmacological stimulation of mitochondrial metabolism as a therapeutic approach in a mouse model of AHDS"; Telethon AHDS Seed Grant 2024 Budget: **49.980 €** Role: PI.
- 2025: Study of the mechanisms underlying Jamuar Syndrome and evaluation of potential therapeutic approaches through the development of innovative preclinical disease models. Banca d'Italia Liberal Contributions, 2024 edition. Budget: **€49,168.97**. Role: PI.
- 2025: ITALIAN SCIENCE FUND 2022–2023 (FIS Call 2) – "Dissecting the role of mitochondrial (dys)function in neurogenesis and in rare neurodevelopmental diseases" – approved by Ranking Decrees LS1, LS4, LS5, LS6, LS7, and LS8 – Protocol No. 2742 dated 14-02-2025. Project number: FIS-02296. Project start date: 01-10-2025. Budget: **1.320.000 €** Role: PI.

As Collaborator:

- Participated in 6 research projects (2011–2020): including ERC Advanced Grant, Telethon, Cariplo, and MUR.
- 2021: PANTHER project on precision medicine for Leigh Syndrome, funded by Regione Lombardia (€557,800).

Contract Research Projects:

- 2021: Tumor-associated macrophage pathways in spinal cord injury. Scientific coordinator. (€116,000 + VAT, Hemera s.r.l.);
- 2023: Safety profile of TEMs in spinal cord injury. Scientific coordinator (€70,000 + VAT, Hemera s.r.l.).

COLLABORATORS:

International Collaborations:

- From 2021: European "CureMILS" Consortium: Prigione, Alessandro (DE); Pless, Ole (DE); Edenhofer, Frank (AT); Koopman, Werner (NL); Suomalainen, Anu (FI); Lisowski, Pawel (PL); Bottani, Emanuela (IT); Del Sol, Antonio (LU); International Mito Patients (NL).
- From 2024: Ana Guadaño-Ferraz, Department of Neurological Diseases and Aging, Instituto de Investigaciones Biomédicas Sols-Morreale, Consejo Superior de Investigaciones Científicas (CSIC), Universidad Autónoma de Madrid (UAM), Madrid, Spain.

National Collaborations:

Ongoing/past collaborations with Dr Lucia Biasutto, CNR, Padova; Dr. Gaia Colasante, San Raffaele Research Institute, Milano; Dr. Giorgio Malpeli, Università di Verona; Prof. Carlo Viscomi, Università di Padova; Dr. Dario Brunetti, Università di Milano; Prof. Ilaria Dando, Università di Verona; Prof. Massimo Donadelli, Università di Verona; Dr. Francesco De Sanctis, Università di Verona.

INVITED TALKS AND CONFERENCES:

- Speaker at 13 national and 6 international conferences.
- *Chair and Scientific Committee Member* of the international conference "Euromit: International Meeting of Mitochondrial Pathology", Bologna, June 11–15, 2023.
- *Invited Moderator* at the "International Workshop to Identify and Address Opportunities Towards Therapeutic Development in Beta-Propeller Protein-Associated Neurodegeneration (BPAN)", Warsaw, October 16–18, 2023. Funded by the European Joint Programme on Rare Diseases (EJP-RD), in collaboration with the consultancy Science Compass, Italy.

SCIENTIFIC PUBLICATIONS:

Author of 30 scientific publications, H-index: 17, Citations: 1,247 (Scopus)
ORCID: 0000-0003-1217-8722

Selected Publications:

- *Viscomi C*, Bottani E*, et al.* In vivo correction of COX deficiency by activation of the AMPK/PGC-1α axis. **Cell Metabolism 2011** (* denotes equal contribution)
- *Bottani E, et al.* AAV-mediated liver-specific MPV17 expression restores mtDNA levels and prevents dietinduced liver failure. **Molecular Therapy 2014**

- *Bottani E, et al.* TTC19 Plays a Husbandry Role on UQCRFS1 -Turnover in the Biogenesis of Mitochondrial Respiratory Complex III. **Molecular Cell, 2017**
- *Bugiardini, E*, Bottani, E*, et al.* Expanding the molecular and phenotypic spectrum of truncating MT-ATP6 mutations. **Neurology Genetics, 2020** (* denotes equal contribution)
- *Inak, et al.* Defective metabolic programming impairs early neuronal morphogenesis in neural cultures and an organoid model of Leigh syndrome. **Nature Communications, 2021**

Languages: Italian (native), English (fluent)
Maternity Leave: Sep 2003–Sep 2004; Nov 2016–June 2017

Consent According to Regulation (EU) 2016/679 of the European Parliament (27 April 2016), I hereby consent to the processing of my personal data provided in this CV.