

BIOGRAPHICAL SKETCHNAME: **Marselli, Lorella**

eRA COMMONS USER NAME: not applicable

POSITION TITLE: **Associate Professor of Technical Sciences of Laboratory Medicine****EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Pisa, Pisa	Master Degree	07/1995	Medicine and Surgery
University of Pisa, Pisa	Specialization	10/2000	Clinical Pathology
University of Rome "La Sapienza", Rome	PhD	03/2004	Endocrinology, Metabolism and Andrology Sciences

A. Personal Statement

I am an Associate Professor of Technical Sciences of Laboratory Medicine. My research focuses on the pathophysiology of diabetes mellitus, a topic I have investigated since the beginning of my career, exploring the morphological, morphometric, functional, and molecular aspects of pancreatic islet cells. I have an in-depth background in laboratory techniques applied in different experimental settings, including immunohistochemical and immunofluorescence techniques. These skills were further developed during my fellowship at the Islet Transplantation and Cell Biology Laboratory at the Joslin Diabetes Center (MA, USA) and have been applied in several studies, as documented in the publications listed below. I have personally performed these techniques and transferred this expertise to Master's students, PhD students, and postdoctoral fellows trained in the laboratory (see conference presentations). As a scientist involved in several European Union-funded projects, I supervised the establishment of a pancreas tissue collection available for histological, functional, and molecular studies. The current proposal is based on the use of a subset of these samples for immunohistochemical and immunofluorescence analyses. As principal investigator or co-principal investigator of national and international funded grants, I have successfully managed research projects, collaborated with other researchers, and produced peer-reviewed publications. Through these experiences, I have gained a strong awareness of the importance of frequent communication among project members and of developing a realistic research plan, with established and timely milestones, and accurate budget. I believe I have the expertise, leadership, training, and motivation necessary to successfully carry out the proposed research project.

Citations:

1. **Marselli L**, Bugliani M, Suleiman M, Olimpico F, Masini M, Petrini M, Boggi U, Filipponi F, Syed F, Marchetti P. β -Cell inflammation in human type 2 diabetes and the role of autophagy. *Diabetes Obes Metab.* 2013, 15 Suppl 3:130-136.
2. **Marselli L**, Suleiman M, Masini M, Campani D, Bugliani M, Syed F, Martino L, Focosi D, Scatena F, Olimpico F, Filipponi F, Masiello P, Boggi U, Marchetti P. Are we overestimating the loss of beta cells in type 2 diabetes? *Diabetologia.* 2014, 57(2):362-365.
3. **Marselli L**, Piron A, Suleiman M, Colli ML, Yi X, Khamis A, Carrat GR, Rutter GA, Bugliani M, Giusti L, Ronci M, Ibberson M, Turatsinze JV, Boggi U, De Simone P, De Tata V, Lopes M, Nasteska D, De Luca C, Tesi M, Bosi E, Singh P, Campani D, Schulte AM, Solimena M, Hecht P, Rady B, Bakaj I, Pocai A, Norquay L, Thorens B, Canouil M, Froguel P, Eizirik DL, Cnop M, Marchetti P. Persistent or Transient Human β Cell Dysfunction Induced by Metabolic Stress: Specific Signatures and Shared Gene Expression with Type 2 Diabetes. *Cell Rep.* 2020, 33(9):108466.

4. Suleiman M, Sawatani T, Tesi M, Yi X, Papadopoulou T, Rufer C, Lytrivi M, Bosi E, Burdet F, Fantuzzi F, De Luca C, Sebastiani G, Saponaro C, Pugliese LA, Del Guerra S, Pocai A, De Simone P, Ghinolfi D, Boggi U, Kessler C, Grieco GE, Fignani D, Kerr-Conte J, Pattou F, Nacher M, Montanya E, Mourad N, Buemi A, Citi V, Martelli A, Benedetti G, Calderone V, Rossi L, Paolicchi A, Cardarelli F, Dotta F, Eizirik DL, Ibberson M, Marchetti P, Cnop M, **Marselli L**. Functional recovery of islet β cells in human type 2 diabetes: Transcriptome signatures unveil therapeutic approaches. *Sci Adv*. 2025, 11(41):eads2905.

Ongoing and recently completed Research Support:

- INNODIA Harvest. Translational approaches to disease modifying therapy of type 1 diabetes. 01/05/2020-30/04/2023. Role: **Scientist**.
- PRIN 2022. Cod. 2022L9PMZZ. Multi-omics analysis of pancreatic islet cells to unravel and validate new functional loci for beta cell targeted prediction, prevention and treatment of human type 2 diabetes. 01/11/2024-28/02/2026. Role: **Responsible of Unit**.
- Grant EFSD/Lilly. Peripancreatic adipose tissue and its impact on islet beta cells in human type 2 diabetes. 01/06/2025-31/05/2027. Role: **PI**.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2024 - Present	Associate Professor, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa
2023 - Present	Medical executive, Clinical Pathology Laboratory, University Hospital of Pisa, Italy
2022 - 2024	Researcher (under the Italian Law 240/2010, article 24, subparagraph 3, point b), Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Italy
2012 - 2021	Researcher, Department of Clinical and Experimental Medicine, University of Pisa, Italy
2006 - 2012	Researcher, Department of Endocrinology and Metabolism, Orthopedics and Traumatology, Occupational Medicine, University of Pisa, Italy
2002 - 2006	Postdoctoral Fellow, Islet Transplantation and Cell Biology Laboratory, Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA
2001 - 2002	Research fellow, Department of Endocrinology and Metabolism, University of Pisa, Italy
1995 - 2000	Internship, Clinical Pathology, University of Pisa, Italy

Other Experience and Professional Memberships

2021 - Present	Editorial Board Member, Journal "il Diabete"
2021 - Present	Editorial Board Member, International Journal of Molecular Sciences
2018 - 2021	Co-Director, Journal "il Diabete", official organ of the Italian Society of Diabetes, for the section "Translational Medicine: clinical application of basic research"
2017 - Present	Member, Italian Society of Organ and Tissue Transplantation (SITO)
2005 - Present	Member, European Association for the Study of Diabetes (EASD)
1998 - Present	Member, Italian Society of Diabetes (SID)

Honors

1998	Award for the study "Rilascio di citochine da parte di linfo-monociti e linfociti umani incubati con xeno-isole pancreatiche", Italian Society of Diabetes
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C. Contributions to Science

The focus of my research is the pathophysiology of diabetes mellitus, with particular interest in the endocrine pancreas. For this purpose, in the early years of my career, I contributed to the development of methods for the isolation of pancreatic islets from large mammals and humans. In the field of type 1 diabetes, I defined the mechanisms of islet damage induced by proinflammatory cytokines and the direct protective effect of Th2 and Th3 cytokines, and demonstrated the involvement of the mitochondrial permeability transition pore on beta cell damage induced by pro-inflammatory cytokines. In the field of type 2 diabetes, I explored the impact of free fatty acid-induced beta cell dysfunction and the mechanisms involved. I further investigated the functional and molecular characteristics of pancreatic islets obtained from type 2 diabetic subjects and the protective effects of pharmacological molecules. These studies identified key aspects and molecular mechanisms involved in beta-cell dysfunction in type 2 diabetes and paved the way for further research.

- a. **Marselli L**, Dotta F, Piro S, et al. Th2 cytokines have a partial, direct protective effect on the function and survival of isolated human islets exposed to combined proinflammatory and Th1 cytokine. *J Clin Endocrinol Metab* 2001; 86:4974-4978.
- b. Trincavelli ML, **Marselli L**, Falleni A, et al. Upregulation of mitochondrial peripheral benzodiazepine receptor expression by cytokine-induced damage of human pancreatic islets. *J Cell Biochem* 2002; 84:636-644.
- c. **Marselli L**, Trincavelli L, Santangelo C, et al. The role of peripheral benzodiazepine receptors on the function and survival of isolated human pancreatic islets. *Eur J Endocrinol* 2004, 151:207-214.
- d. Lupi R, Dotta F, **Marselli L**, et al. Prolonged exposure to free fatty acids has cytostatic and pro-apoptotic effects on human pancreatic islets. *Diabetes*, 2002, 51:1437-1442.
- e. Del Guerra S, Lupi R, **Marselli L**, et al. Functional and molecular defects of pancreatic islets in human type 2 diabetes. *Diabetes* 2005, 54:727-735.
- f. Marchetti P, Del Guerra S, **Marselli L**, et al. Pancreatic islets from type 2 diabetic patients have functional defects and increased apoptosis that are ameliorated by metformin. *J Clin Endocrinol Metab* 2004, 89: 5535-5541.

During my postdoctoral fellowship at the Islet Transplantation and Cell Biology Laboratory, Joslin Diabetes Center, Harvard Medical School in Boston, I developed an original protocol for the identification and isolation of human beta cells from the pancreas using the laser capture microdissection technique. The procedure was utilized to study, for the first time, the transcriptome of beta cell enriched preparations obtained from type 2 diabetic subjects. The approach was afterwards applied to other studies on human islet cells by our and other groups.

- a. **Marselli L**, Thorne J, Ahn YB, et al. Gene expression of purified beta cell tissue obtained from human pancreas with laser capture microdissection. *J Clin Endocrinol Metab* 2008, 93:1046-1053.
- b. **Marselli L**, Sgroi DC, Bonner-Weir S, Weir GC. Laser Capture Microdissection of Human Pancreatic beta-Cells and RNA Preparation for Gene Expression Profiling. *Methods Mol Biol* 2009, 560:87-98.
- c. **Marselli L**, Thorne J, Dahiya S, et al. Gene expression profiles of Beta-cell enriched tissue obtained by laser capture microdissection from subjects with type 2 diabetes. *PLoS One*. 2010 Jul 13;5(7):e11499.
- d. Solimena M, Schulte AM, **Marselli L**, et al. Systems biology of the IMIDIA biobank from organ donors and pancreatectomised patients defines a novel transcriptomic signature of islets from individuals with type 2 diabetes. *Diabetologia*. 2018, 61(3):641-657.

As a scientist involved in several European Union funded projects, I supervised the creation of a unique biobank of pancreas tissue available for histological, functional, and molecular studies. In the context of such projects, aiming to the identification of biomarkers for the risk assessment and progression of type 2 diabetes, tissue samples, nucleic acids and/or proteins of high quality were prepared from isolated islets for the evaluation of islet properties.

- a. Marchetti P, Suleiman M, **Marselli L**. Organ donor pancreases for the study of human islet cell histology and pathophysiology: a precious and valuable resource. *Diabetologia*. 2018, 61(4):770-774.
- b. Marchetti P, Schulte AM, **Marselli L**, et al. Fostering improved human islet research: a European perspective. *Diabetologia*. 2019, 62:1514-1516.
- c. Alonso L, Piron A, Morán I, Guindo-Martínez M, Bonàs-Guarch S, Atla G, Miguel-Escalada I, Royo R, Puiggròs M, Garcia-Hurtado X, Suleiman M, **Marselli L**, et al. TIGER: The gene expression regulatory variation landscape of human pancreatic islets. *Cell Rep*. 2021, 37:109807.
- d. Atla G, Bonàs-Guarch S, Cuenca-Ardura M, Beucher A, Crouch DJM, Garcia-Hurtado J, Moran I; T2DSysCons Consortium; Irimia M, Prasad RB, Gloy AL, **Marselli L**, et al. Genetic regulation of RNA splicing in human pancreatic islets. *Genome Biol*. 2022, 23(1):196.

More recently, I have assessed the possible reversibility of beta cell functional damage in lipo-/gluco-toxic conditions and in type 2 diabetes, identified the mechanisms involved and tested targeted pharmacological strategies, with possible clinical impact. This approach is currently being applied with beta cells exposed to pro-inflammatory cytokines, as a paradigm of type 1 diabetes pathogenesis.

- a. **Marselli L**, Piron A, Suleiman M, et al. Persistent or Transient Human β Cell Dysfunction Induced by Metabolic Stress: Specific Signatures and Shared Gene Expression with Type 2 Diabetes. *Cell Rep*. 2020, 33:108466.

- b. Suleiman M, Sawatani T, Tesi M, Yi X, Papadopoulou T, Rufer C, Lytrivi M, Bosi E, Burdet F, Fantuzzi F, De Luca C, Sebastiani G, Saponaro C, Pugliese LA, Del Guerra S, Pocai A, De Simone P, Ghinolfi D, Boggi U, Kessler C, Grieco GE, Fignani D, Kerr-Conte J, Pattou F, Nacher M, Montanya E, Mourad N, Buemi A, Citi V, Martelli A, Benedetti G, Calderone V, Rossi L, Paolicchi A, Cardarelli F, Dotta F, Eizirik DL, Ibberson M, Marchetti P, Cnop M, **Marselli L**. Functional recovery of islet β cells in human type 2 diabetes: Transcriptome signatures unveil therapeutic approaches. *Sci Adv*. 2025 Oct 10;11(41):eads2905.

In parallel, I am assessing the proteomic characteristics of pancreatic islets and peripancreatic adipose tissue and am exploring the impact of intra- and peripancreatic adipose tissue on the morphological, morphometric, and molecular characteristics of the endocrine pancreas.

Pisa, 19-01-2026

Prof.ssa Lorella Marselli