

BIOGRAPHICAL SKETCH

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NAME: Perico, Luca

eRA COMMONS USER NAME: 15846223

POSITION TITLE: Head, Laboratory of Targeted Therapies in Autoimmune Diseases

EDUCATION/TRAINING:

INSTITUTION AND LOCATION	DEGREE	END DATE MM/YYYY	FIELD OF STUDY
Istituto David Maria Turoldo, Bergamo	HS	06/2002	Scientific High School
University of Milan, Milan	BS	10/2005	Biology
University of Milan, Milan	MS	07/2007	Biology
Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan	OTH	07/2010	Pharmacological Research Specialist
Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo	PHD	12/2014	Cell biology, Renal diseases

A. Personal Statement

My research interests focus on understanding the molecular pathways underlying renal cell injury and their contribution to the progression of kidney diseases. Over the past decade, my work has been primarily dedicated to investigating the role of mitochondria in the pathogenesis of both acute and chronic kidney diseases.

More recently, I have expanded my research to explore how mitochondrial dysfunction contributes to the breakdown of immune tolerance in renal autoimmune diseases, such as membranous nephropathy and lupus nephritis. I have extensive expertise in both cellular and molecular biology, equipping me with the technical proficiency necessary to fulfill the objectives of this project.

During my ten years of research at the Istituto di Ricerche Farmacologiche Mario Negri, I have developed a strong skill set in advanced cell culture techniques, flow cytometry, live-cell imaging, immunofluorescence, Western blotting, and ELISA, key methodologies required for this study. Additionally, I successfully established protocols for mitochondrial isolation from both cultured cells and tissue samples, enabling in-depth analysis of mitochondrial function. Furthermore, I have designed and optimized biochemical assays to assess mitochondrial metabolism and dynamics in renal cells, both *in vivo* and *in vitro*. Notably, I have developed *in vitro* models to evaluate the effects of patients' sera on renal cells, providing a powerful tool to investigate disease-specific mechanisms. My expertise in these areas positions me well to contribute to the advancement of this project and to generate novel insights into the mitochondrial regulation of kidney disease.

Since 2007, I have been qualified to use laboratory animals for scientific experimentation in accordance with current European and Italian regulations. In this capacity, I have served as the responsible researcher for various projects involving laboratory animal use, ensuring compliance with ethical and legal standards in animal research.

1. **Perico L**, Morigi M, Rota C, Breno M, Mele C, Noris M, Introna M, Capelli C, Longaretti L, Rottoli D, Conti S, Corna D, Remuzzi G, Benigni A. Human mesenchymal stromal cells transplanted into mice stimulate renal tubular cells and enhance mitochondrial function. *Nat Commun*. 2017 Oct 17;8(1):983.
2. **Perico L**, Mandalà M, Schieppati A, Carrara C, Rizzo P, Conti S, Longaretti L, Benigni A, Remuzzi G. BRAF Signaling Pathway Inhibition, Podocyte Injury, and Nephrotic Syndrome. *Am J Kidney Dis*. 2017 Jul;70(1):145-150.
3. Buelli S, **Perico L**, Galbusera M, Abbate M, Morigi M, Novelli R, Gagliardini E, Tentori C, Rottoli D, Sabadini E, Saito T, Kawano M, Saeki T, Zoja C, Remuzzi G, Benigni A. Mitochondrial-dependent Autoimmunity in Membranous Nephropathy of IgG4-related Disease. *EBioMedicine*. 2015 May;2(5):456-66.
4. Morigi M, **Perico L**, Rota C, Longaretti L, Conti S, Rottoli D, Novelli R, Remuzzi G, Benigni A. Sirtuin 3-dependent mitochondrial dynamic improvements protect against acute kidney injury. *J Clin Invest*. 2015 Feb;125(2):715-26.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2025 - Present	Head, Laboratory of Targeted Therapies in Autoimmune Diseases, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo
2020 - 2025	Senior researcher, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo
2019 - 2020	Visiting Scientist, MD Anderson cancer center, Houston, TX
2014 - 2019	Postdoctoral fellow, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo
2011 - 2014	PhD student, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo
2007 - 2011	Post graduate fellow, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milan
2005 - 2007	Trainee, University of Milan, Milan

Honors

2019 - 2020	First rank in the "Roche for research" award for the study of lupus nephritis, Roche
2019 - 2019	Research Scholarship, Associazione Ricerca Malattie Rare (A.R.M.R.)
2019 - 2019	Travel Award for Training in the USA, Associazione Ricerca Malattie Rare (A.R.M.R.)
2019 - 2019	Travel Award for participation at the "2019 Kidney Week" organised by the American Society of Nephrology, Associazione Ricerca Malattie Rare (A.R.M.R.)
2018 - 2018	Research Scholarship, Associazione Ricerca Malattie Rare (A.R.M.R.)
2017 - 2017	Research Scholarship, Associazione Ricerca Malattie Rare (A.R.M.R.)
2017 - 2017	Travel Award for participation at the "8th Targeting Mitochondria" congress, Associazione Ricerca Malattie Rare (A.R.M.R.)
2016 - 2016	Research Scholarship, Associazione Ricerca Malattie Rare (A.R.M.R.)
2016 - 2016	Travel Award for participation at the "2016 Kidney Week" organised by the American Society of Nephrology, Associazione Ricerca Malattie Rare (A.R.M.R.)
2015 - 2015	Research Scholarship, Associazione Ricerca Malattie Rare (A.R.M.R.)
2015 - 2015	Early Scientist Support for the study of membranous nephropathy, Halpin Foundation
2015 - 2015	Travel Award for participation at the "56th Congress of the Italian Society of Nephrology", Associazione Ricerca Malattie Rare (A.R.M.R.)
2014 - 2014	Research Scholarship, Associazione Ricerca Malattie Rare (A.R.M.R.)
2014 - 2014	Travel Award for participation at the "5th Targeting Mitochondria" congress, Associazione Ricerca Malattie Rare (A.R.M.R.)

C. Contribution to Science

During my career, I have published 43 articles in peer-reviewed journals, with a total of 23 publications as first author and an H-index of 21, according to Scopus (Author ID: 55773505100). I also published 4 book chapters, two of which as first author.

Over the past decade, my research has focused on the critical role of mitochondria in the pathogenesis of acute and chronic kidney diseases. In acute kidney injury (AKI), I discovered that mitochondrial dysfunction exacerbates kidney damage by impairing energy production and increasing oxidative stress. A key regulator of mitochondrial function is SIRT3, a mitochondrial deacetylase that helps preserve mitochondrial integrity by regulating oxidative stress and energy metabolism. In this context, I demonstrated that mesenchymal stromal cells (MSCs) protect mitochondrial function by preserving mitochondrial mass, structure, and antioxidant capacity. MSCs promote mitochondrial trafficking and fusion by stimulating the formation of microtubule-rich projections in tubular cells, which supports mitochondrial function restoration and cell recovery in a SIRT3-dependent manner.

I also investigated mitochondrial function during nephrogenesis, where SIRT3 regulates mitochondrial bioenergetics and post-translational modifications, influencing glycolysis and energy production during kidney development. By boosting SIRT3 activity with nicotinamide riboside, I showed improvements in nephron number and kidney structure.

In chronic kidney disease, I identified that mitochondrial dysfunction contributes to renal injury, with SIRT3 protecting against glomerular damage and podocyte injury, particularly under nephrotoxic stress. Restoring mitochondrial function in these cells could offer therapeutic potential for improving kidney outcomes.

Additionally, I explored the role of SIRT3 in aging hearts, demonstrating its essential role in maintaining mitochondrial bioenergetics. I found that its deficiency leads to cardiac hypertrophy, fibrosis, and reduced lifespan. Gene transfer of deacetylated OPA1, a SIRT3 target, reversed these alterations, highlighting the therapeutic potential of targeting mitochondrial function in age-related heart diseases.

In the past five years, I have also investigated the role of mitochondrial dysfunction in the induction of neoantigens involved in the development of membranous nephropathy (MN), an autoimmune kidney disease. As part of my research on MN, I focused on identifying the key immunogenic epitopes of the disease's main autoantigen, PLA2R. Building on these findings, I developed a promising therapeutic approach: a bispecific autoantigen-T cell engager designed to selectively target the small subset of autoreactive B cells in MN, while sparing normal B cells. A patent has been filed for this compound.

Since 2020, following the COVID-19 emergency, I have also been involved in studying the spread of the virus in Bergamo, one of the most affected areas worldwide. In the context of SARS-CoV-2, I have investigated long-term cellular and humoral immune responses in individuals vaccinated with mRNA vaccines. Additionally, I studied, both in vitro and in vivo, the mechanisms by which the spike protein of SARS-CoV-2 induces endothelial damage and thromboembolic phenomena in severe forms of COVID-19, contributing to the understanding of virus-induced pathological mechanisms.

Most recent publications:

- a. **Perico L**, Casiraghi F, Benigni A, Remuzzi G. Is there a place for engineered immune cell therapies in autoimmune diseases? Trends Mol Med. 2025 Feb 20; PubMed PMID: 39984382.
- b. **Perico L**, Remuzzi G, Benigni A. Sirtuins in kidney health and disease. Nat Rev Nephrol. 2024 May;20(5):313-329. PubMed PMID: 38321168.

- c. Ruggenti P, Reinhard L, Ruggiero B, Perna A, **Perico L**, Peracchi T, Fidone D, Gennarini A, Benigni A, Cortinovis M, Hoxha E, Remuzzi G. Anti-Phospholipase A2 Receptor 1 and Anti-Cysteine Rich Antibodies, Domain Recognition and Rituximab Efficacy in Membranous Nephropathy: A Prospective Cohort Study. Am J Kidney Dis. 2024 May;83(5):588-600.e1. PubMed PMID: 38151224.
- d. **Perico L**, Casiraghi F, Sônego F, Todeschini M, Corna D, Cerullo D, Pezzotta A, Isnard-Petit P, Faravelli S, Forneris F, Thiam K, Benigni A, Remuzzi G. Bi-specific autoantigen-T cell engagers as targeted immunotherapy for autoreactive B cell depletion in autoimmune diseases. Front Immunol. 2024;15:1335998. PubMed Central PMCID: PMC10926275.

Complete List of Published Work in My Bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/luca.perico.1/bibliography/public/>