

Curriculum vitae RAFFAELLA MASTROCOLA

Personal details

Born in CARMAGNOLA (TO)

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Educations

2005: Ph.D. in Molecular and Experimental Pathology, University of Turin.

2000: Master Degree in Biological Sciences, University of Turin.

Professional experiences and current position

Present position:

2011-Date: Contract Professor and Research Technician, Dept. of Clinical and Biological Sciences, University of Turin, Turin, Italy.

Previous appointments:

2017: National License as Associate Professor in General Pathology.

2017 March - May: visiting researcher at Maastricht University Medical Center, Dept. of Internal Medicine, Maastricht, The Netherlands.

2013-2014: Contract Professor of General Pathology at Dept. of Neurosciences, University of Turin, Italy.

2009-2011: Research Assistant, Dept. Experimental Medicine and Oncology, University of Turin.

2007-2009: Research Assistant, Dept. Internal Medicine, University of Turin.

2005-2007: Research Fellow, Dept. Experimental Medicine and Oncology, University of Turin.

Honors

Invited speaker:

- 8th Euro Global Diabetes Summit and Medicare Expo. Valencia, Spain, November 03-05, 2015.
- 3rd World Congress on Glycation & Maillard Reaction scheduled at Hungarian Academy of Sciences, Budapest, Hungary, on May 26-27, 2016.

Awards:

- The paper Collino M. et al., 2006 (Eur. J. Pharmacol., 530: 70-80, PMID: 16386242) has been awarded as "top-cited research paper published in 2006" from European Journal of Pharmacology.
- "Best Scientific Contributor" award at the 3rd World Congress on Maillard Reaction and Glycation, Budapest, Hungary, May 26-27, 2016.

Activity as Chairperson

- Chair of the session 5: "AGEs and RAGE, Strategies and Innovations" of the 3rd World Congress on Maillard Reaction and Glycation, Budapest, Hungary, May 26-27, 2016.
- Chair of the Session 2: "Diabetes and Metabolic Syndrome" at the 23rd Annual Meeting of the Society for Redox Biology and Medicine, San Francisco, USA, November 16-19, 2016.

International collaborations:

- Prof. Casper G. Schalkwijk, Maastricht University Medical Center, The Netherlands.
- Prof. Cristoph Thiemermann - Queen Mary University of London, Barts and The London School of Medicine & Dentistry, The William Harvey Research Institute, London, UK.
- Prof. Bernard Ryffel - INEM - UMR7355 - CNRS - University of Orléans, France.
- Prof. Carlo Gaetano, Goethe-Universität Frankfurt am Main, Francoforte, Germania.

Teaching activity:

2022/23:

- Contract Professor of Immunology at the BSc degree in Biological Sciences, University of Turin, Italy.
- Contract Professor of General Pathology, Immunology and General Pathophysiology at the BSc degree in Nursing, University of Turin, Italy.
- Contract Professor of Immunology at the MSc degree in Food and Human Nutrition Sciences, University of

Turin, Italy.

2021/22: Contract Professor of Immunology at the BSc degree in Biological Sciences, University of Turin, Italy.

2013/14: Contract Professor of General Pathology in BSc courses at the School of Medicine, University of Turin, Italy.

2002 - 2022: Adjunct professor and lecturer of Pathophysiology, Immunology and General Pathology in Bachelor of Sciences in Nursing.

Research main topics

Field of expertise:

Her research activity has been mainly focused on the role of advanced glycation end products (AGEs) in the development of metabolic impairment in obesity and diabetes. Specifically, she contributed to the clarification of the molecular mechanisms by which AGEs induce oxidative and inflammatory damage in target tissues, as kidney, brain, skeletal muscle and heart, in animal models of dysmetabolism. In an attempt to provide a more detailed understanding of the processes involved in the pathogenesis of insulin resistance and of diabetes complications, her research has progressed to the investigation of the biochemical pathways and tissue-specific transcription factors that are compromised by AGEs. She demonstrated that AGEs deriving from a high-fat or a high-sugar diet interfere with lipid metabolism through the induction of the lipogenic transcription factor SREBP and with sphingolipid metabolism inducing the unbalanced increase in ceramides and sphingosine-1-phosphate, leading to lipid accumulation, mitochondrial dysfunction and inflammation. She also significantly contributed to evaluate the potential efficacy of innovative therapeutic strategies aimed to prevent insulin-resistance and AGEs-induced dysmetabolism.

Current research interests:

The modulation of either the production of AGEs from dicarbonyl precursors or the activation of the main detrimental receptor for AGEs, RAGE, may represent effective strategies to prevent the metabolic alterations and the inflammatory response induced by AGEs. We are currently evaluating the efficacy of both pyridoxamine supplementation, an analog of vitamin B6 provided of peculiar anti-glycating properties, and of pharmacological antagonism of RAGE in models of diet-induced obesity and insulin-resistance. Moreover, we are planning to investigate the potential of peripherally-restricted pharmacological modulation of selected cannabinoid receptors in the prevention of AGEs accumulation and AGE-RAGE signaling.

Main projects as PI and research unit component:

- Research Unit component of a JPI - ERA-HDHL grant, “Biomarkers for Nutrition and Health”, with a 3-years research programme on “Innovative Technological Approaches for validation of Salivary AGEs as novel biomarkers in evaluation of risk factors in diet-related diseases – SALIVAGES”, 2017-2018.
- Recipient of an EMBO Short-term Fellowship for international mobility (90 days at Maastricht University), “Advanced glycation end products (AGEs) in the ceramide/sphingosine/sphingosine-1-phosphate disequilibrium in insulin resistance: mechanisms and molecular targets”, 2017.
- Principal investigator of the research grant: Piedmont region, Ricerca sanitaria finalizzata 2008bis, for a 2-years project on “Role of the heat shock proteins alterations induced by oxidative stress in the onset of diabetic cardiomyopathy”, 2008-2009.
- Principal Investigator of grants from the University of Turin, Ricerca Locale (RILO, ex 60%), 2015-2023.

Bibliometry (2002-present) (www.scopus.com)

- Published original research and review articles on peer-reviewed indexed international journals: **67**
- Average Impact Factor: **4.885**
- Total number of citations: **3150**
- H index: **34**

Publications of the last five years (2017-2022)

1. Kar S, Perrelli A, Bali KK, Mastrocola R, Kar A, Khan B, Gand L, Nayak A, Hartmann C, Kunz WS, Samii A, Bertalanffy H, Retta SF. Identification of Galectin-3 as a novel prognostic/predictive biomarker and therapeutic target candidate for Cerebral Cavernous Malformation disease. *Genes and Disease*, in press 2023.
2. Mastrocola R, Aimaretti E, Ferreira Alves G, Cento AS, Fornelli C, Dal Bello F, Ferraris C, Goitre L, Perrelli A, Retta SF. Heterozygous Loss of KRIT1 in Mice Affects Metabolic Functions of the Liver, Promoting Hepatic Oxidative and Glycative Stress. *Int J Mol Sci* 23(19):11151, 2022. doi: 10.3390/ijms231911151.
3. Alves GF, Stoppa I, Aimaretti E, Monge C, Mastrocola R, Porchietto E, Einaudi G, Collotta D, Bertocchi I, Boggio E, Gigliotti CL, Clemente N, Aragno M, Fernandes D, Cifani C, Thiemermann C, Dianzani C, Dianzani U, Collino

- M. ICOS-Fc as innovative immunomodulatory approach to counteract inflammation and organ injury in sepsis. *Front Immunol* 13:992614, 2022. doi: 10.3389/fimmu.2022.992614.
4. Alves GF, Aimaretti E, Einaudi G, Mastrocola R, de Oliveira JG, Collotta D, Porchietto E, Aragno M, Cifani C, Sordi R, Thiemermann C, Fernandes D, Collino M. Pharmacological Inhibition of FAK-Pyk2 Pathway Protects Against Organ Damage and Prolongs the Survival of Septic Mice. *Front Immunol* 13:837180, 2022. doi: 10.3389/fimmu.2022.837180.
 5. Wouters K, Cento AS, Gaens KH, Robertus M, Scheijen J, Barutta F, Chiazza F, Collotta D, Aragno M; Gruden G; Collino M, Schalkwijk CG, Mastrocola R. Deletion of RAGE fails to prevent hepatosteatosis in obese mice due to impairment of other AGEs receptors and detoxifying systems. *Scientific Reports* 30;11(1):17373, 2021. doi: 10.1038/s41598-021-96859-7.
 6. Mastrocola R, Dal Bello F, Cento AS, Gaens K, Collotta D, Aragno M, Medana C, Collino M, Wouters K, Schalkwijk CG. Altered hepatic sphingolipid metabolism in insulin resistant mice: role of advanced glycation endproducts. *Free Radical Biology and Medicine* 169:425–435, 2021.
 7. Mastrocola R, Collotta D, Gaudio G, Le Berre M, Cento AS, Ferreira Alves G, Chiazza F, Verta R, Bertocchi I, Manig F, Hellwig M, Fava F, Cifani C, Aragno M, Henle T, Joshi L, Tuohy K, Collino M. Effects of Exogenous Dietary Advanced Glycation End Products on the Cross-Talk Mechanisms Linking Microbiota to Metabolic Inflammation. *Nutrients* 12(9):E2497, 2020. doi: 10.3390/nu12092497.
 8. Collotta D, Hull W, Mastrocola R, Chiazza F, Cento AS, Murphy C, Verta R, Alves GF, Gaudio G, Fava F, Yaqoob M, Aragno M, Tuohy K, Thiemermann C, Collino M. Baricitinib counteracts metaflammation, thus protecting against diet-induced metabolic abnormalities in mice. *Mol Metab* 39:101009, 2020. doi: 10.1016/j.molmet.2020.101009.
 9. Felicetti F, Cento AS, Fornengo P, Cassader M, Mastrocola R, D'Ascenzo F, Settanni F, Benso A, Arvat E, Collino M, Fagioli F, Aragno M, Brignardello E. Advanced glycation end products and chronic inflammation in adult survivors of childhood leukemia treated with hematopoietic stem cell transplantation. *Pediatr Blood Cancer* 67(3):e28106, 2020. doi: 10.1002/pbc.28106.
 10. Vieceli Dalla Sega F*, Mastrocola R*, Aquila G, Fortini F, Fornelli C, Zotta A, Cento AS, Perrelli A, Boda E, Pannuti A, Marchi S, Pinton P, Ferrari R, Rizzo P, Retta SF. KRIT1 Deficiency Promotes Aortic Endothelial Dysfunction. *Int J Mol Sci.* 20(19):4930, 2019. pii: E4930. doi: 10.3390/ijms20194930. IF 4.183. *Equally contributing authors.
 11. Purvis GSD, Collino M, Loiola RA, Baragetti A, Chiazza F, Brovelli M, Sheikh MH, Collotta D, Cento A, Mastrocola R, Aragno M, Cutrin JC, Reutelingsperger C, Grigore L, Catapano AL, Yaqoob MM, Norata GD, Solito E, Thiemermann C. Identification of AnnexinA1 as an Endogenous Regulator of RhoA, and Its Role in the Pathophysiology and Experimental Therapy of Type-2 Diabetes. *Front Immunol* 10:571, 2019. doi: 10.3389/fimmu.2019.00571.
 12. Collotta D, Lucarini L, Chiazza F, Cento AS, Durante M, Sgambellone S, Chini J, Baratta F, Aragno M, Mastrocola R, Masini E, Collino M. Reduced Susceptibility to Sugar-Induced Metabolic Derangements and Impairments of Myocardial Redox Signaling in Mice Chronically Fed with D-Tagatose when Compared to Fructose. *Oxid Med Cell Longev* 19;2018:5042428, 2018. doi: 10.1155/2018/5042428.
 13. Barutta F, Bellini S, Mastrocola R, Gambino R, Piscitelli F, di Marzo V, Corbetta B, Vemuri VK, Makriyannis A, Annaratone L, Bruno G, Gruden G. Reversal of albuminuria by combined AM6545 and Perindopril therapy in experimental diabetic nephropathy. *Br J Pharmacol*, 175(23):4371-4385, 2018. doi: 10.1111/bph.14495.
 14. Barutta F, Bellini S, Mastrocola R, Bruno G, Gruden G. The role of cannabinoid signaling in acute and chronic kidney diseases. *Kidney International* 94(2):252-258, 2018. doi: 10.1016/j.kint.2018.01.024.
 15. Barutta F, Bellini S, Mastrocola R, Bruno G and Gruden G. MiRNA and microvascular complications of diabetes. Special Issue on Circulating Noncoding RNAs as Candidate Biomarkers of Endocrine and Metabolic Disease, *Int J Endocrinol* 7;2018:6890501, 2018. doi: 10.1155/2018/6890501.
 16. Mastrocola R, Ferrocino I, Liberto E, Chiazza F, Cento AS, Querio G, Nigro D, Bitonto V, Cutrin JC, Rantsiou K, Durante M, Masini E, Aragno M, Cordero C, Cocolin L, Collino M. Fructose liquid and solid formulations differently affect gut integrity, microbiota composition and related liver toxicity: a comparative in vivo study. *J Nutr Biochem* 55:185-199, 2018. doi: 10.1016/j.jnutbio.2018.02.003.
 17. Bressanello D, Liberto E, Collino M, Chiazza F, Mastrocola R, Reichenbach S, Bicchi C, Cordero C. Combined Untargeted and Targeted Fingerprinting by Comprehensive Two-Dimensional Gas Chromatography: Revealing Fructose-Induced Changes in Mice Urinary Metabolic Signatures. *Anal Bioanal Chem* 410(11):2723-2737, 2018. doi: 10.1007/s00216-018-0950-9.
 18. Barutta F, Mastrocola R, Bellini S, Bruno G, Gruden G. Cannabinoid Receptors in Diabetic Kidney Disease. *Curr Diab Rep* 18(2):9, 2018. doi: 10.1007/s11892-018-0975-7.
 19. Benetti, E, Mastrocola R, Chiazza F, Nigro D, D'Antona G, Bordano V, Fantozzi R, Aragno M, Collino M, Minetto MA. Effects of vitamin D on insulin resistance and myosteatosis in diet-induced obese mice. *PlosOne* 13(1):e0189707, 2018. doi: 10.1371/journal.pone.0189707.
 20. Spallotta F, Cencioni C, Atlante S, Garella D, Cocco M, Mori M, Mastrocola R, Künne C, Günther S, Nanni S, Azzimato V, Zukunft S, Kornberger A, Sueruen D, Schnutgen F, von Melchner H, Di Stilo A, Aragno M, Braspenning M, Van Criekinge W, De Blasio MJ, Ritchie RH, Zaccagnini G, Martelli F, Farsetti A, Fleming I, Braun T, Beiras-Fernandez A, Botta B, Collino M, Bertinaria M, Zeiher AM, Gaetano C. Stable Oxidative Cytosine Modifications Accumulate in Cardiac Mesenchymal Cells from Type2 Diabetes Patients: Rescue by Alpha-Ketoglutarate and TET-TDG Functional Reactivation. *Circ Res* 122(1):31-46, 2018. pii: CIRCRESAHA.117.311300.

21. Bellini S, Barutta F, Mastrocola R, Imperatore L, Bruno G, Gruden G. Heat shock proteins in vascular diabetic complications: review and future perspective. *Int J Mol Sci, Special Issue on Molecular Chaperones*, 18(12):2709, 2017. doi:10.3390/ijms181227092017.
22. Chiazza F, Cento AS, Collotta D, Nigro D, Rosa G, Baratta F, Bitonto V, Cutrin JC, Aragno M, Mastrocola R*, Collino M*. Protective effects of pyridoxamine supplementation in the early stages of diet-induced kidney dysfunction. *BioMed Res Int* 2017;2682861, 2017. *Equally contributing authors.
23. Marano F, Frairia R, Rinella L, Argenizano M, Bussolati B, Grange C, Mastrocola R, Castellano I, Berta L, Cavalli R, Catalano MG. Combining doxorubicin-nanobubbles and shockwaves for anaplastic 1 thyroid cancer treatment. *Endocr-Relat Cancer* 24(6):275-286, 2017. doi: 10.1530/ERC-17-0045.
24. Aragno M, Mastrocola R. Dietary sugars and Advanced Glycation Endproducts: emerging mechanisms of disease. *Nutrients. Special Issue on Dietary Fructose and Glucose: The Multifaceted Aspects of their Metabolism and Implication for Human Health* 14;9(4), 2017. pii: E385. doi: 10.3390/nu9040385.
25. Mastrocola R, Aragno M, Alloatti G, Collino M, Penna C, Pagliaro P. Metaflammation: tissue-specific alterations of the NLRP3 inflammasome platform in metabolic syndrome. *Curr Med Chem. Special Issue on Alteration of Redox Equilibrium, Inflammation and Progression of Disease* 25(11):1294-1310, 2018. doi: 10.2174/0929867324666170407123522.
26. Nigro D, Menotti F, Cento A, Serpe L, Chiazza F, Dal Bello F, Romaniello F, Medana C, Collino M, Aragno M, Mastrocola R. Chronic administration of saturated fats and fructose differently affect SREBP activity resulting in different modulation of Nrf2 and Nlrp3 inflammasome pathways in mice liver. *J Nutr Biochem* 42:160-171, 2017. doi: 10.1016/j.jnutbio.2017.01.010.
27. Mastrocola R. AGEs and neurodegeneration: the Nrf2/glyoxalase-1 interaction. *Oncotarget* 8(4):5645-5646, 2017