

## Curriculum vitae Manuela Aragno

### **Personal details**

Born in Turin

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### **Educations**

1983 Bachelor Degree in Biological Science (108/110)

1985 Research fellow by Piedmont Region

1990 Ph.D. in Experimental Molecular Pathology, University of Turin

1991 Technician Assistant in Dept Experimental Medicine and Oncology, University of Turin.

2001 PhD Researcher, SSD MED/04, Faculty of Medicine and Surgery, University of Turin.

2006 PhD Associated Professor, SSD MED/04, Faculty of Medicine and Surgery University of Turin

2014 National Scientific Qualification as Full Professor of Pathology (06/A2)

### **Professional experiences and current position**

MA has a well-documented expertise in the pre-clinical investigation of the deleterious effects of advanced glycation end products (AGEs) tissue accumulation and the related activation of selective inflammatory pathways due to different dietary regimens. Her team is also a scientific excellence in multidimensional separation techniques for untargeted and targeted metabolite profiling and fingerprinting. She cooperates in several international projects (SALIVAGES Innovative Technological Approaches for validation of Salivary AGEs as novel biomarkers in evaluation of risk factors in diet-related diseases” Programma: Eranet Cofund ERA HDHL Call 2016, HDHL INTIMIC-Knowledge Platform on food, diet, intestinal microbiomics and human health; PROGETTO CARB-Q-4-HEALTH DURATA 36 MESI Progetto ID 1170 – Carb-Q-4-Health: Tailored Carbohydrate Quality for Personalized Weight Management and Metabolic Health. Bando HDHL INTIMIC METADIS 2019 “Impact of Diet, Food Components and Food Processing on Body Weight Regulation and Overweight Related Metabolic Diseases” and as PI units in National PRIN, CRT Foundation and Piedmont Region. International and national scientific collaborations: Prof. Cristoph Thiemermann, Queen Mary University of London, Barts and The London School of Medicine & Dentistry, The William Harvey Research Institute, London, UK; Prof. Florence Wong, Division of Gastroenterology, Dpt. of Medicine, University of Toronto, Dr. Giovanni Sansoè , Gastroenterology Unit, Humanitas Gradenigo Hospital, Torino; Prof Angela Lezza, Department of Biosciences, Biotechnologies, and Environment, University of Bari; Prof Claudio Medana, Department of Molecular Biotechnology and Health Sciences University of Turin; Dott. Francesco Felicetti , SSD Unità di Transizione per Neoplasie Curate in Età Pediatrica, A.O.U. Città della Salute e della Scienza di Torino; Prof. Catalina Ciocan, Dip Dipartimento di Scienze della sanità pubblica e pediatriche Torino; Prof Massimo Collino, Department of Neuroscience, University of Turin.

### **Participation Institutions:**

Secretary of Medicine Degree Course of Turin 20-2013;

Secretary of Nurse Degree Course of Turin 2010-2013;

Member of President Council of Nurse Degree Course of Turin 2010-2015

Member of “Commissione Consultiva Paritetica Permanente and Consiglio di Presidenza” of Nursing Degree Aosta ;

Member of Ph.D School in "Medicine and Experimental Therapy";

Member of Study Committee of Clinical and Biological Science Department;

Coordinator of Pathology and Physiopathology Course in Medicine Degree Course of Turin.

Member Miur in Bachelor Thesis

Dean of Nursing Degree, Aosta, - School of Medicine, University of Turin, 2021.

**Honor:** Paper: Dietary Sugars and Endogenous Formation of Advanced Glycation Endproducts: Emerging Mechanisms of Disease. 2017, *Nutrients* 9 (4); in November/December 2021, Highly cited received enough

citations to place it in the top 1% of the academic field of Agricultural Sciences based on a highly cited threshold for the field and publication year.

**Teaching activity:**

Pathology Tirocinio in Medicine and Surgery University School of Turin since 2002;

School of PhD in Experimental Medicine and Therapy since 2010;

Pathology, Immunology and Physiopathology in Nursing Degree –School of Medicine (located in Turin, Ivrea and Aosta ) since 2000.

**Research main topics**

The activity has been mainly focused on the role of advanced glycation end products (AGEs) and oxidative stress in the development of chronic degenerative pathologies in experimental models. My study contributed to demonstrate the molecular mechanisms by which AGEs induces oxidative and inflammatory damage in target tissues, in animal models of STZ-induced diabetes and in diet-induced insulin resistance. Research activity has been focused on role of the NLRP3 “inflammasome” leading to produced pro-inflammatory state and on role of the AGE, through their chemical classification, to provide to individuate more details on signalling pathways by AGEs and inflammation play toxic role. AGEs deriving from high diet interfere with glucose metabolism through the induction of the lipogenic transcription factor SREBP, leading to lipid accumulation, mitochondrial dysfunction and oxidative stress. Mitochondrial dysfunctions represent an important aim in my studies. More, recently research involving human acute pediatric lymphoblastic leukemia survivors, with total body irradiation, showed for the first time in plasma and PBMC, the presence of higher oxidative stress, inflammation and AGE levels with respect to controls suggesting a key role of AGEs and of subsequent activation of receptor RAGE. These mechanisms could have an important role in the onset of late complications. Research activities also try to identify innovative strategies to counteract diet-induced tissue damage by anti-inflammatory agents, antioxidants or anti-age product. Future aim of my research will be evaluate molecular pathways affected by AGEs that are responsible for the onset of premature age-related diseases (i.e. epigenetic modifications of genes involved in pro-inflammatory/defensive pathways; mitochondrial dysfunction) in different working classes of populations and lymphoma survivors.

**Bibliometry** ([www.scopus.com](http://www.scopus.com))

Citations: 5354

H index: 42

Documents: 115

**Publications** (last 5 years)

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, Thiernemann C, Dianzani C, Dianzani U, Collino M. ICOS-Fc as innovative immunomodulatory approach to counteract inflammation and organ injury in sepsis. *Front Immunol.* 2022 Sep 2;13:992614 . doi: 10.3389/fimmu.2022.992614. PMID: 36119089; PMCID: PMC9479331.

Alloatti G, Penna C, Comità S, Tullio F, Aragno M, Biasi F, Pagliaro P. Aging, sex and NLRP3 inflammasome in cardiac ischaemic disease. *Vascul Pharmacol.* 2022 Aug;145:107001. doi: 10.1016/j.vph.2022.107001. Epub 2022 May 24. PMID: 35623548.

Alves GF, Aimaretti E, Einaudi G, Mastrocola R, de Oliveira JG, Collotta D, Porchietto E, Aragno M, Cifani C, Sordi R, Thiernemann C, Fernandes D, Collino M. Pharmacological Inhibition of FAK-Pyk2 Pathway Protects Against Organ Damage and Prolongs the Survival of Septic Mice. *Front Immunol.* 2022 Feb 1;13:837180. doi: 10.3389/fimmu.2022.837180. PMID: 35178052; PMCID: PMC8843946.

Felicetti F, Aimaretti E, Dal Bello F, Gatti F, Godono A, Saba F, Einaudi G, Collino M, Fagioli F, Aragno M, Brignardello E. Advanced glycation end products and their related signaling cascades in adult survivors of childhood Hodgkin lymphoma: A possible role in the onset of late complications. *Free Radic Biol Med.* 2022 Jan;178:76-82. doi: 10.1016/j.freeradbiomed.2021.11.036. Epub 2021 Nov 30. PMID: 34856327.

Chimienti G, Orlando A, Russo F, D'Attoma B, Aragno M, Aimaretti E, Lezza AMS, Pesce V. The Mitochondrial Trigger in an Animal Model of Nonalcoholic Fatty Liver Disease. *Genes (Basel).* 2021 Sep 18;12(9):1439. doi: 10.3390/genes12091439. PMID: 34573421; PMCID: PMC8471525.

Wouters K, Cento AS, Gaens KH, Teunissen M, Scheijen JLJM, 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. *Sci Rep*. 2021 Aug 30;11(1):17373. doi: 10.1038/s41598-021-96859-7. PMID: 34462492; PMCID: PMC8405685.

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 Radic Biol Med*. 2021 Jun;169:425-435. doi: 10.1016/j.freeradbiomed.2021.04.028. Epub 2021 Apr 24. PMID: 33905864.

Sansoè G, Aragno M, Wong F. COVID-19 and Liver Cirrhosis: Focus on the Nonclassical Renin-Angiotensin System and Implications for Therapy. *Hepatology*. 2021 Aug;74(2):1074-1080. doi: 10.1002/hep.31728. Epub 2021 Jul 26. PMID: 33524188; PMCID: PMC8013494.

Penna C, Aragno M, Cento AS, Femminò S, Russo I, Bello FD, Chiazza F, Collotta D, Alves GF, Bertinaria M, Zicola E, Mercurio V, Medana C, Collino M, Pagliaro P. Ticagrelor Conditioning Effects Are Not Additive to Cardioprotection Induced by Direct NLRP3 Inflammasome Inhibition: Role of RISK, NLRP3, and Redox Cascades. *Oxid Med Cell Longev*. 2020 Aug 3;2020:9219825. doi: 10.1155/2020/9219825. PMID: 32832010; PMCID: PMC7424511.

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*. 2020 Aug 19;12(9):2497. doi: 10.3390/nu12092497. PMID: 32824970; PMCID: PMC7551182.

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*. 2020 Sep;39:101009. doi: 10.1016/j.molmet.2020.101009. Epub 2020 May 13. PMID: 32413585; PMCID: PMC7267733.

Crisafulli A, Pagliaro P, Roberto S, Cugusi L, Mercurio G, Lazou A, Beauloye C, Bertrand L, Hausenloy DJ, Aragno M, Penna C. Diabetic Cardiomyopathy and Ischemic Heart Disease: Prevention and Therapy by Exercise and Conditioning. *Int J Mol Sci*. 2020 Apr 21;21(8):2896. doi: 10.3390/ijms21082896. PMID: 32326182; PMCID: PMC7215312.

Penna C, Andreadou I, Aragno M, Beauloye C, Bertrand L, Lazou A, Falcão-Pires I, Bell R, Zuurbier CJ, Pagliaro P, Hausenloy DJ. Effect of hyperglycaemia and diabetes on acute myocardial ischaemia-reperfusion injury and cardioprotection by ischaemic conditioning protocols. *Br J Pharmacol*. 2020 Dec;177(23):5312-5335. doi: 10.1111/bph.14993. Epub 2020 Mar 9. PMID: 31985828; PMCID: PMC7680002.

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*. 2020 Mar;67(3):e28106. doi: 10.1002/pbc.28106. Epub 2019 Dec 9. PMID: 31820553.

Sansoè G, Aragno M, Wong F. Pathways of hepatic and renal damage through non-classical activation of the renin-angiotensin system in chronic liver disease. *Liver Int*. 2020 Jan;40(1):18-31. doi: 10.1111/liv.14272. Epub 2019 Nov 4. PMID: 31580514.

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.* 2019 Mar 27;10:571. doi: 10.3389/fimmu.2019.00571. PMID: 30972066; PMCID: PMC6446914.

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.* 2018 Sep 19;2018:5042428. doi: 10.1155/2018/5042428. PMID: 30327714; PMCID: PMC6169220.

Mastrocola R, Ferrocino I, Liberto E, Chiazza F, Cento AS, Collotta D, Querio G, Nigro D, Bitonto V, Cutrin JC, Rantsiou K, Durante M, Masini E, Aragno M, Cordero C, Coccolin 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.* 2018 May;55:185-199. doi: 10.1016/j.jnutbio.2018.02.003. Epub 2018 Feb 13. PMID: 29539590.

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. *PLoS One.* 2018 Jan 17;13(1):e0189707. doi: 10.1371/journal.pone.0189707. PMID: 29342166; PMCID: PMC5771572.

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;2017:2682861. doi: 10.1155/2017/2682861. Epub 2017 Oct 29. PMID: 29214163; PMCID: PMC5682048.

Spallotta F, Cencioni C, Atlante S, Garella D, Cocco M, Mori M, Mastrocola R, Kuenne C, Guenther S, Nanni S, Azzimato V, Zukunft S, Kornberger A, Sürün D, Schnütgen 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.* 2018 Jan 5;122(1):31-46. doi: 10.1161/CIRCRESAHA.117.311300. Epub 2017 Nov 20. PMID: 29158345.

Aragno M, Mastrocola R. Dietary Sugars and Endogenous Formation of Advanced Glycation Endproducts: Emerging Mechanisms of Disease. *Nutrients.* 2017 Apr 14;9(4):385. doi: 10.3390/nu9040385. PMID: 28420091; PMCID: PMC5409724.

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.* 2018;25(11):1294-1310. doi: 10.2174/0929867324666170407123522. PMID: 28403789.