

## Curriculum vitae GABRIELLA LEONARDUZZI

### **Personal details**

Born in: Ivrea (Turin)

Nationality: Italian

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### **Educations**

- 1987 Degree in Biological Sciences, Faculty of Mathematical, Physical and Natural Sciences, University of Turin, Italy
- 1988 Qualified to practice as a Biologist, University of Turin.
- 1993 PhD degree in “Experimental and Molecular Pathology”, Department of Experimental Medicine and Oncology, University of Turin, Italy

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

- 1985-86 Research scholarship “National Foundation for Cancer Research Inc (U.K.)” in support of the thesis
- 1988 Research scholarship from the company “Industria Chimico Farmaceutica Inverni della Beffa” for the experimental study of the drug IdB 1016 (extracted from *Silybum Marianum*)
- 1988-92 PhD research fellowship for the project “Danno ossidativo, citolisi e fibrogenesi nella cirrosi sperimentale da CCl<sub>4</sub>”, Department of Experimental Medicine and Oncology, Faculty of Medicine and Surgery, University of Turin, Italy
- 1989-90 She attended the Biochemistry laboratory of Prof. T.F. Slater at the Department of Biology and Biochemistry, Brunel University, West London, Uxbridge (U.K.)
- 1993 Collaboration from the company Boehringer Mannheim Italia S.p.A. to develop an experimental protocol for enzymatic parameter dosage
- 1994-96 Post-doc research fellowship, Department of Experimental Medicine and Oncology, Faculty of Medicine and Surgery, University of Turin, Italy
- 1995 She attended the laboratory of Prof. R. Dargel at the Institute of Pathobiochemistry, Friedrich Schiller University of Jena (Germany) to deepen some techniques and studies on hepatocellular damage
- 1997-1998 Adjunct Professor, Faculty of Medicine and Surgery, University of Turin, Italy
- 1998-2001 Research Assistant, Department of Experimental Medicine and Oncology, Faculty of Medicine and Surgery, University of Turin, Italy
- 2001-2007 Assistant Professor (MED/04), Department of Clinical and Biological Sciences, Faculty of Medicine and Surgery, University of Turin, Italy
- 2005-2007 Temporary title of Associate Professor in General Pathology (MED/04), Faculty of Medicine and Surgery, Department of Clinical and Biological Sciences, University of Turin, Italy
- 2007-2020 Associated Professor in General Pathology (MED/04), Department of Clinical and Biological Sciences, School of Medicine, University of Turin, Italy
- 2020-up to now Full Professor in General Pathology (MED/04), Department of Clinical and Biological Sciences, School of Medicine, University of Turin, Italy

### **Participation to Directive Boards of Scientific Societies and/or Institutions:**

- 1-10-2016/30-09-2022 - Head of the Nursing Degree Course of Orbassano (Orbassano and Cuneo), Department of Clinical and Biological Sciences, School of Medicine, University of Turin, Italy
- 2013-up to now - Member of the Academic board of the Doctoral School in Experimental Medicine and Therapy, University of Turin, Italy.
- 2006-2013 - Member of the Academic Board of the PhD in "Immunorheumatology and Clinical and Experimental Oncology, Bioethics and Tumor Epidemiology, University of Foggia, Italy
- Member of the Scientific Societies European Network for Oxysterol Research (ENOR) (group of Experimental and Translational Pathology)
- Member of the Society for Free Radical Research - Europe (SFRR-E)
- Member of the Società Italiana di Patologia (SIP) associated with the American Society for Investigative Pathology (ASIP)

### **Teaching activity**

- Basic Pathology and Immunology - module of General Pathology, MedInTO Medicine and Surgery, School

of Medicine, University of Turin

- Pathology & Pathophysiology, MedInTO Medicine and Surgery, School of Medicine, University of Turin, Italy
- Pathology and Laboratory Diagnostics - module of General Pathology and General Physiopathology, Nursing Degree Course of Orbassano (Orbassano and Cuneo), School of Medicine, University of Turin, Italy
- Pathology and Laboratory Diagnostics - module of General Physiopathology, Immunology and General Pathology, Nursing Degree Course A.O.U. City of Health and Science of Turin, School of Medicine, University of Turin, Italy

### **Research main topics**

#### **Scientific Curriculum**

The recent main research lines focus on molecular and mechanistic studies of age-related human chronic diseases characterized by oxidative stress, inflammation, fibrogenesis, and cell toxicity, such as atherosclerosis and Alzheimer's disease. Experimental studies on several antioxidant molecules and systems regarding cell function and damage have also been performed.

Death and/or survival signaling pathways and target genes modulated by oxidized lipids, mainly cholesterol oxidation products, named oxysterols, and 4-hydroxynonenal, are investigated in vitro, in vivo and ex vivo samples with emphasis on the pathogenesis of Alzheimer's disease. In particular, the role of brain cholesterol metabolism in the pathogenesis of Alzheimer's disease is under investigation with the aim of identifying new biomarkers of neurodegeneration and to develop new therapeutic approaches, based on nanotechnology, to prevent/reduce the disease. The implication of astrocyte reactivity in Alzheimer's disease pathogenesis is also under investigation.

#### **Main projects as PI**

##### **- PRIN**

2004-2006 - Lipids oxidized in the progression of the hepatocarcinogenesis process in susceptible or resistant strains of rats (PI Local Unit)

2006-2008 - Relationship between oxidative damage and inflammatory/fibrogenic response in the stages of hepatocarcinogenesis: new molecular mechanisms and therapeutic targets (PI Local Unit)

2008-2010 - Association between hepatocarcinogenesis and hypercholesterolemia: role of the signal pathways that regulate cholesterol homeostasis and the inflammatory response (PI Local Unit)

##### **- Piedmont Region (Ricerca Scientifica Applicata)**

2004-2006 - Oxidized cholesterol and inflammation in patients with acute coronary syndromes and stabilized coronary artery disease (PI)

##### **- Piedmont Region (Ricerca Sanitaria Finalizzata)**

2006-2008 - Biomarkers of vulnerability of atherosclerotic plaque during the acute coronary event (PI)

2008 II - Role of cholesterol oxidation products in the pathogenesis of Alzheimer's disease. Possible prevention strategies (PI)

2009 - Effect of cholesterol oxidation products on death and survival signals in the progression of neurodegenerative diseases (PI)

##### **- Ricerca Finalizzata**

2023-2026 - In-depth analysis of cholesterol metabolism and related biomarkers in the pathogenesis and progression of the disease in neurodegenerative dementias (Coordinator Unit 2)

#### **Bibliometry (2008-present)** ([www.scopus.com](http://www.scopus.com))

##### **10 best publications**

1. Leonarduzzi G, Gamba P, Gargiulo S, Sottero B, Kadl A, Biasi F, Chiarpotto E, Leitinger N, Vendemiale G, Serviddio G, Poli G. Oxidation as a crucial reaction for cholesterol to induce tissue degeneration: CD36 overexpression in human promonocytic cells treated with a biologically relevant oxysterol mixture. *Aging Cell*, 7:375-382, 2008.
2. Gargiulo S, Gamba P, Sottero B, Biasi F, Chiarpotto E, Serviddio G, Vendemiale G, Poli G, Leonarduzzi G. The core-aldehyde 9-oxononanoyl cholesterol increases the level of transforming growth factor beta1-specific receptors on promonocytic U937 cell membranes. *Aging Cell*, 8:77-87, 2009.
3. Gargiulo S, Sottero B, Gamba P, Chiarpotto E, Poli G, Leonarduzzi G. Plaque oxysterols induce imbalanced upregulation of matrix metalloproteinase-9 in macrophagic cells through redox-sensitive signaling pathways: Implications on the vulnerability of atherosclerotic lesions. *Free Rad Biol Med*, 51:844-855, 2011.
4. Testa G, Gamba P, Di Scipio F, Elio Sprio A, Salamone P, Gargiulo S, Sottero B, Biasi F, Berta GN, Poli G, Leonarduzzi G. Potentiation of amyloid- $\beta$  peptide neurotoxicity in human dental-pulp neuron-

like cells by the membrane lipid peroxidation product 4-hydroxynonenal. *Free Radic Biol Med*, 53:1708-1717, 2012.

- Gamba P, Guglielmotto M, Testa G, Monteleone D, Zerbinati C, Gargiulo S, Biasi F, Iuliano L, Giaccone G, Mauro A, Poli G, Tamagno E, Leonarduzzi G. Up-regulation of  $\beta$ -amyloidogenesis in neuron-like human cells by both 24- and 27-hydroxycholesterol: protective effect of N-acetylcysteine. *Aging Cell*, 13:561-572, 2014.
- Gargiulo S, Gamba P, Testa G, Rossin D, Biasi F, Poli G, Leonarduzzi G. Relation between TLR4/NF- $\kappa$ B signaling pathway activation by 27-hydroxycholesterol and 4-hydroxynonenal, and atherosclerotic plaque instability. *Aging Cell*, 14:569-581, 2015.
- Testa G, Staurengi E, Giannelli S, Gargiulo S, Guglielmotto M, Tabaton M, Tamagno E, Gamba P, Leonarduzzi G. A silver lining for 24-hydroxycholesterol in Alzheimer's disease: The involvement of the neuroprotective enzyme sirtuin 1. *Redox Biol*, 17:423-431, 2018.
- Gargiulo S, Rossin D, Testa G, Gamba P, Staurengi E, Biasi F, Poli G, Leonarduzzi G. Up-regulation of COX-2 and mPGES-1 by 27-hydroxycholesterol and 4-hydroxynonenal: A crucial role in atherosclerotic plaque instability. *Free Radic Biol Med*, 129:354-363, 2018.
- Staurengi E, Cerrato V, Gamba P, Testa G, Giannelli S, Leoni V, Caccia C, Buffo V, Noble W, Gomez Perez-Nievas B, Leonarduzzi G. Oxysterols present in Alzheimer's disease brain induce synaptotoxicity by activating astrocytes: a major role for lipocalin-2, *Redox Biol*, 39:101837, 2021.
- Testa G, Giannelli S, Sottero B, Staurengi E, Giaccone G, Caroppo P, Gamba P, Leonarduzzi G. 24-Hydroxycholesterol Induces Tau Proteasome-Dependent Degradation via the SIRT1/PGC1/Nrf2 Pathway: A Potential Mechanism to Counteract Alzheimer's Disease. *Antioxidants (Basel)* 12:631, 2023.

#### ***More relevant publications in the last 5 yrs (2018-2022)***

- Vurusaner B, Gargiulo S, Testa G, Gamba P, Leonarduzzi G, Poli G, Basaga H. The role of autophagy in survival response induced by 27-hydroxycholesterol in human promonocytic cells. *Redox Biol*, 17:400-410, 2018.
- Testa G, Staurengi E, Giannelli S, Gargiulo S, Guglielmotto M, Tabaton M, Tamagno E, Gamba P, Leonarduzzi G. A silver lining for 24-hydroxycholesterol in Alzheimer's disease: The involvement of the neuroprotective enzyme sirtuin 1. *Redox Biol*, 17:423-431, 2018.
- Testa G, Rossin D, Poli G, Biasi F, Leonarduzzi G. Implication of oxysterols in chronic inflammatory human diseases. *Biochimie*, 153:220-231, 2018.
- Gargiulo S, Rossin D, Testa G, Gamba P, Staurengi E, Biasi F, Poli G, Leonarduzzi G. Up-regulation of COX-2 and mPGES-1 by 27-hydroxycholesterol and 4-hydroxynonenal: A crucial role in atherosclerotic plaque instability. *Free Radic Biol Med*, 129:354-363, 2018.
- Gamba P, Staurengi E, Testa G, Giannelli S, Sottero B, Leonarduzzi G. A Crosstalk Between Brain Cholesterol Oxidation and Glucose Metabolism in Alzheimer's Disease. *Front Neurosci*, 13:556, 2019.
- Sottero B, Leonarduzzi G, Testa G, Gargiulo S, Poli G, Biasi F. Lipid Oxidation Derived Aldehydes and Oxysterols Between Health and Disease. *European Journal of Lipid Science and Tecnology*, 121:1-16, 2019.
- Staurengi E, Cerrato V, Gamba P, Testa G, Giannelli S, Leoni V, Caccia C, Buffo V, Noble W, Gomez Perez-Nievas B, Leonarduzzi G. Oxysterols present in Alzheimer's disease brain induce synaptotoxicity by activating astrocytes: a major role for lipocalin-2, *Redox Biol*, 39:101837, 2021.
- Testa G, Staurengi E, Giannelli S, Sottero B, Gargiulo S, Poli G, Gamba P, Leonarduzzi G. Up-regulation of PCSK6 by lipid oxidation products: a possible role in atherosclerosis, *Biochimie*, 181:191-203, 2021.
- Gamba P, Giannelli S, Staurengi E, Testa G, Sottero B, Biasi F, Poli G, Leonarduzzi G. The Controversial Role of 24-S-Hydroxycholesterol in Alzheimer's Disease, *Antioxidants (Basel)*, 10:740, 2021.
- Staurengi E, Giannelli S, Testa G, Sottero B, Leonarduzzi G\*, Gamba P, Cholesterol dysmetabolism in Alzheimer's disease: A starring role for astrocytes? *Antioxidants (Basel)*, 10:1890, 2021 (\* co-Last author).
- Sottero B, Testa G, Gamba P, Staurengi E, Giannelli S, Leonarduzzi G. Macrophage polarization by potential nutraceutical compounds: a strategic approach to counteract inflammation in atherosclerosis, *Free Radic Biol Med*, 181:251-269, 2022.
- Staurengi E, Leoni V, Lo Iacono M, Sottero B, Testa G, Giannelli S, Leonarduzzi G\*, Gamba P. ApoE3 vs. ApoE4 Astrocytes: A Detailed Analysis Provides New Insights into Differences in Cholesterol Homeostasis, *Antioxidants (Basel)*, 11: 2168, 2022 (\* co-Last author).