

## Scientific Curriculum of **Antonia Lanni**

1982: Master's degree in Biological Science, Faculty of Mathematical, Physical and Natural Sciences, University of Naples "Federico II, Italy

1983-1985 Internship in the Department of General and Environmental Physiology (Supervisor: Prof. F. Goglia)

1985-1988: Phd Course in Physiology at the Faculty of Medicine, University of Naples, Italy

1989: Title of Phd in Physiology discussing a thesis entitled: "Light mitochondria as a pathway of cellular thermogenesis and non-shivering thermogenesis in the processes of acclimatation to low temperatures"

1990: Visiting fellow at Institute de Physiologie, Université Paul Sabatier de Toulouse (France) (Supervisor Prof. L. Ambid)

1991-1998 Reseaecher in Physiology, Department of General and Environmental Physiology, University of Naples "Federico II"

1993: Visiting fellow at Laboratoire de Thermoregulation et Energetique de L'Exercice, Université Claude Bernard, Lyon (France) (Supervisor Prof. A. Geloën)

1998-2005: Associated Professor of Physiology, Department of Life Science, Second University of Naples.

2005 to date: Full Professor of Physiology, Department of Environmental, Biological, and Pharmaceutical Sciences and Technologies, University of Campania "L. Vanvitelli"

2005-2009: President of Council of Study Courses of Biology, University of Campania "L. Vanvitelli"

2012-2013: Member of Commission for National Scientific Qualification for Full and Associate Professor , -sector 05/D1 Physiology

2014: Coordinator of the Phd Program in "Molecular and Cellular Biology", University of Campania "L. Vanvitelli"

2015 to date Member of Academic Board of Phd Program "Biomolecular Sciences", Department of Biological and Pharmaceutical Environmental Sciences and Technologies -University of Campania "L. Vanvitelli"

### **Research activity**

She has been working for many years on cellular mechanisms involved in energy expenditure and specifically on the effects of thyroid hormones at the cellular level and their mechanism of action.

In the last years her attention has been focused on the study of biological activity of both triiodothyronine (T3) and 3,5-diiodothyronine (T2), a derivative of the peripheral metabolism of T3. She demonstrated that T2 is able, similar to T3, to stimulate the resting metabolism but the mechanism of action of T2 is different from that of T3 since T2 acts directly on mitochondria (its cellular target) in a protein synthesis-independent pathway in contrast to T3 that acts through the well known nuclear way. In addition, administration of T2 to rats receiving a hyperlipidic diet prevents adiposity and body weight gain without inducing thyreotoxicosis. T2 strongly increases hepatic fat oxidation leading to an improvement of lipid serum profile and of diet-induced insulin resistance.

These results are of potential clinical importance because recently he showed that the administration of T2 increase resting metabolic rate and reduces body weight in human, without undesirable side effects at cardiac level. These studies have given rise to the application for a national patent (Lanni Antonia, Moreno Maria, Lombardi Assunta, Goglia Fernando. -2007- Composition including 3,5-diiodothyronine and harmacological use of them. N. 0001343549).

She also investigated on the mechanisms through which thyroid hormones are able to induce, at itochondrial level, an uncoupling between the electron transport and ATP synthesis and, thus, regulate heat production at cell level. Her studies contributed to the demonstration that Uncoupling Protein 3 (UCP3) is a molecular determinant of the calorogenic effect of T3. Furtherly, starting from previous results indicating that UCP3-mediated uncoupling in skeletal muscle mitochondria from hyperthyroid rats is associated to a higher fatty acid content and ROS production in comparison with the euthyroid, she showed that UCP3 translocates lipid hydroperoxide and mediates lipid hydroperoxide-dependent mitochondrial uncoupling. These results have contribute to clarify the physiological function of this protein.

Her attention is also focused on knowledge of complexity of adipose tissue biology and its role in metabolism. She studied not only differences between white and brown adipocytes, but also differences in white adipose

tissue at the depot level such as the conversion of subcutaneous white adipose cells into beige adipose cells that promote energy expenditure through heat production.

From her researches it is evident that targeting adipose tissue and its signaling molecules can provide unique opportunities to better understand the pathophysiology and treatment of obesity, insulin resistance, T2D, and metabolic syndrome.

Her scientific activity has produced more than 115 full length papers (citations: 3974, H index: 38) in peer-reviewed journals and several book chapters.

Member of Editorial Board of Molecular Endocrinology and Metabolism section of International Journal of Molecular Sciences

Associated Editor of Thyroid Research

Reviewer of several International Journals.

Reviewer of scientific projects for foreign Universities and Scientific Agencies.

Member of National and International Scientific Associations.

Invited speaker to National and International Congress.

Member of Organising Committee of 62<sup>o</sup> Meeting of the Italian Physiological Society (SIF) Sorrento • 2011.

### **Project funded**

1990-1994 - CORDIS - EU funded project under FP3 (1990-1994) "Metabolic Integration and energy control (MIEC)"

(PRIN-2002) "Uncoupling proteins: molecular mechanism and physiological role."-

(PRIN-2004) "Cellular and molecular mechanisms underlying the effect of iodothyronines on the metabolism of skeletal muscle and adipose tissue."

2003 - LR (Regional Law) 5/2002 -Year 2003- "Role of 3,5-diiodothyronine and control of metabolic efficiency in skeletal muscle"

(PRIN-2006) "Studies on the uncoupling protein 3 function and on the regulation of its gene expression by T3."

2007 - LR (Regional Law) 5/2002 -Year 2007 - Role of miRNA in T3-dependent regulation of genes involved in lipid metabolism.

(PRIN-2008) "Uncoupling protein 3 (UCP3): mechanisms of activation and its role in energy metabolism."

2014-2020 - POR FESR Campania 2014-2020. O.S. 1.1 - Development and Industrialization of personalized supplements for Senile Maculopathies (SIMS).

2019 - Valere Program - University call for competitive projects - University of Campania L. Vanvitelli "Impact of CB1 gene deletion on mitochondrial activities and molecular pathways".

### **International research collaborations:**

- Laboratoire de Physiologie des Régulations Énergétiques, Cellulaires et Moléculaires, CNRS, Université Claude Bernard Lyon I, Villeurbanne, France.

- Laboratoire des Régulations des Métabolismes et Nutrition Université Paul Sabatier, Toulouse, France.

- Fachbereich Chemie, Philipps-University Marburg, Marburg, Germany.

- Institut für Physiologische Chemie, Universitäts-Krankenhaus Eppendorf, Hamburg, Germany.

- Marion Merrel Dow Research Institute, Henning Berlin R&D, Berlin, Germany

- Departament de Biologia Fonamental i Ciències de la Salut, Universitat de les Illes Balears, Palma de Mallorca, Spain.

- Centre National de la Recherche Scientifique, Centre de Recherche sur l'Endocrinologie Moléculaire et le Développement, Meudon, France

- Department of Medical Biochemistry, Faculty of Medicine, University of Geneva 1, Geneva, Switzerland

- Unité Mixte de Recherches sur le Veau et le Porc, INRA 35590 St-Gilles, France

- Department of Radiology and Nuclear Medicine (G.P.), Benjamin Franklin Medical Center, Free University of Berlin, Berlin, Germany

- Department of Internal Medicine, Erasmus MC, 3000 DR Rotterdam, The Netherlands

- Department of Laboratory Medicine, C1-74 Karolinska University Hospital, Stockholm, Sweden

- Departament de Bioquímica i Biologia Molecular, Universitat de Barcelona, and CIBER Fisiopatologia de la Obesidad y Nutrición, Instituto de Salud Carlos III, Barcelona, Spain

- Clinical Research, Torrent Research Centre, Torrent Pharmaceuticals Ltd., Ahmedabad, Gujarat, India

- Laboratory for Myology, Move Research Institute Amsterdam, Faculty of Behavioral and Movement Sciences, Vrije Universiteit (VU) Amsterdam, Amsterdam, The Netherlands;
- Division of Endocrinology and Division of Pharmacology, Vascular and Metabolic Diseases, Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands
- Institute of Cardiovascular Research and Sport Medicine, Department of Molecular and Cellular Sport Medicine, German Sport University Cologne, Cologne, Germany
- Program of Cardiovascular and Metabolic Disorders, Duke-NUS Medical School, 8 College Road, Singapore, 169857, Singapore
- Baker IDI Heart and Diabetes Institute, Melbourne, Victoria, 3004, Australia

### **Main scientific publications (n. 20)**

1. Giuseppe Petito, Federica Cioffi, Elena Silvestri, Rita De Matteis, Davide Lattanzi, Pieter de Lange, Assunta Lombardi, Maria Moreno, Fernando Goglia, Antonia Lanni and Rosalba Senese. 3,5-Diiodo-L-Thyronine (T2) Administration Affects Visceral Adipose Tissue Inflammatory State in Rats Receiving Long-Lasting High-Fat Diet. *Frontiers in Endocrinology* 2021
2. Silvestri E., Senese R., De Matteis R., Cioffi F., Moreno M., Lanni A., Gentile A., Busiello R. A., Salzano A. M., Scaloni A., de Lange P., Goglia F., Lombardi A. (2020). Absence of uncoupling protein 3 at thermoneutrality influences brown adipose tissue mitochondrial functionality in mice. *THE FASEB JOURNAL* 34(11):15146-15163
3. Antonia Giacco, Giuseppe delli Paoli, Rosalba Senese, Federica Cioffi, Elena Silvestri, Maria Moreno, Margherita Ruoppolo, Marianna Caterino, Michele Costanzo, Assunta Lombardi, Fernando Goglia, Antonia Lanni, Pieter de Lange (2019). The saturation degree of fatty acids and their derived acylcarnitines determines the direct effect of metabolically active thyroid hormones on insulin sensitivity in skeletal muscle cells. *THE FASEB JOURNAL*, vol. 33, p. 1811-1823,
4. Cioffi F., Senese R., Petito G., Lasala P., De Lange P., Silvestri E., Lombardi A., Moreno M., Goglia F., Lanni A. (2019). Both 3,3,5-triiodothyronine and 3,5-diiodo-L-thyronine are able to repair mitochondrial DNA damage but by different mechanisms. *FRONTIERS IN ENDOCRINOLOGY*, vol. 10:216
5. Senese R., Cioffi F., Petito G., de Lange P., Russo A., Goglia F., Lanni A., Potenza N. (2019). miR-22-3p is involved in gluconeogenic pathway modulated by 3,5-diiodo-L-thyronine (T2). *SCIENTIFIC REPORTS*, 12;9(1):16645.
6. Senese, Rosalba, Cioffi, Federica, De Matteis, Rita, Petito, Giuseppe, de Lange, Pieter, Silvestri, Elena, Lombardi, Assunta, Moreno, Maria, Goglia, Fernando, Lanni, Antonia (2019). 3,5-Diiodo-L-Thyronine (T-2) Promotes the Browning of White Adipose Tissue in High Fat Diet-Induced Overweight Male Rats Housed at Thermoneutrality. *CELLS*, 18;8(3):256
7. Silvestri, Elena, Senese, Rosalba, Cioffi, Federica, De Matteis, Rita, Lattanzi, Davide, Lombardi, Assunta, Giacco, Antonia, Salzano, Anna Maria, Scaloni, Andrea, Ceccarelli, Michele, Moreno M, Goglia F, Lanni A, de Lange P. (2019). 3,5-Diiodo-L-Thyronine Exerts Metabolically Favorable Effects on Visceral Adipose Tissue of Rats Receiving a High-Fat Diet. *NUTRIENTS*, vol. 11(2):278
8. Silvestri, Elena, Lombardi, Assunta, COPPOLA, Maria, Gentile, Alessandra, Cioffi, Federica, Senese, Rosalba, Goglia, Fernando, Lanni, Antonia, Moreno, Maria, de Lange, Pieter (2018). Differential effects of 3,5-Diiodo-L-Thyronine and 3,5,3'-Triiodo-L-Thyronine on mitochondrial respiratory pathways in liver from hypothyroid rats. *CELLULAR PHYSIOLOGY AND BIOCHEMISTRY*, 47, p. 2471-2483.
9. Jaspers, Richard T, Zillikens, M. Carola, Friesema, Edith C. H, Paoli, Giuseppe Delli, Bloch, Wilhelm, Uitterlinden, André G, Goglia, Fernando, LANNI, Antonia, DE LANGE, Pieter (2017). Exercise, fasting, and mimetics: Toward beneficial combinations?. *THE FASEB JOURNAL*, vol. 31, p. 14-28.
10. SENESE, Rosalba, Cioffi, Federica, DE LANGE, Pieter, Leanza, Cristina, Iannucci, Liliana F., Silvestri, Elena, MORENO, Maria, LOMBARDI, Assunta, GOGLIA, Fernando, LANNI, Antonia (2017). Both 3,5-Diiodo-L-Thyronine and 3,5,3'-Triiodo-L-Thyronine Prevent Short-term Hepatic Lipid Accumulation via Distinct Mechanisms in Rats Being Fed a High-Fat Diet. *FRONTIERS IN PHYSIOLOGY*, 14;8:706.
11. LANNI, Antonia, Moreno, Maria, Goglia, Fernando (2016). Mitochondrial Actions of Thyroid Hormone. *COMPREHENSIVE PHYSIOLOGY*, vol. 6, p. 1591-1607.
12. Moreno, Maria, LANNI, Antonia (2016). Editorial: Hormonal and neuroendocrine regulation of energy balance. *FRONTIERS IN PHYSIOLOGY*, 5;6:403.

13. Lombardi A, SENESE, Rosalba, De Matteis R, Busiello RA, Cioffi F, Goglia F, LANNI, Antonia (2015). 3,5-Diiodo-L-Thyronine Activates Brown Adipose Tissue Thermogenesis in Hypothyroid Rats. PLOS ONE, 6;10(2):e0116498.
14. SENESE, Rosalba, Cioffi F, DE LANGE, Pieter, Goglia F, LANNI, Antonia (2014). Thyroid: biological actions of 'nonclassical' thyroid hormones. JOURNAL OF ENDOCRINOLOGY, vol. 221, p. R1-R12.
15. Lombardi A, de Matteis R, Moreno M, Napolitano L, Busiello RA, SENESE, Rosalba, DE LANGE, Pieter, LANNI, Antonia, Goglia F. (2012). Responses of skeletal muscle lipid metabolism in rat gastrocnemius to hypothyroidism and iodothyronine administration: a putative role for FAT/CD36. AMERICAN JOURNAL OF PHYSIOLOGY: ENDOCRINOLOGY AND METABOLISM, vol. 303, p. E1222-E1233.
16. DE LANGE, Pieter, CIOFFI F, SENESE, Rosalba, MORENO M, LOMBARDI A, SILVESTRI E, DE MATTEIS R, LIONETTI L, MOLLICA MP, GOGLIA F, LANNI, Antonia (2011). Nonthyrotoxic Prevention of Diet-Induced Insulin Resistance by 3,5-Diiodo-L-Thyronine in Rats. DIABETES, vol. 60, p. 2730-2739, ISSN: 0012-1797, doi: 10.2337/db11-0207 - **Articolo**
17. MORENO M, SILVESTRI E, DE MATTEIS R, DE LANGE, Pieter, LOMBARDI A, GLINNI D, SENESE, Rosalba, CIOFFI F, SALZANO AM, SCALONI A, LANNI, Antonia, GOGLIA F. (2011). 3,5-Diiodo-L-thyronine prevents high-fat-diet-induced insulin resistance in rat skeletal muscle through metabolic and structural adaptations. THE FASEB JOURNAL, vol. 25, p.3312-3324.
18. SENESE, Rosalba, VALLI V, MORENO M, LOMBARDI A, BUSIELLO RA, CIOFFI F, SILVESTRI E, GOGLIA F, LANNI, Antonia, DE LANGE, Pieter (2011). Uncoupling protein 3 expression levels influence insulin sensitivity, fatty acid oxidation, and related signaling pathways. PFLÜGERS ARCHIV, vol. 461, p. 153-164.
19. LOMBARDI A., DE LANGE, Pieter, SILVESTRI E., BUSIELLO R., LANNI, Antonia, GOGLIA F., MORENO M. (2009). 3,5-Diiodo-L-thyronine rapidly enhances mitochondrial fatty acid oxidation rate and thermogenesis in rat skeletal muscle: AMP-activated protein kinase involvement. AMERICAN JOURNAL OF PHYSIOLOGY: ENDOCRINOLOGY AND METABOLISM, vol. 296, p. E497-E502.
20. DE LANGE, Pieter, SENESE, Rosalba, CIOFFI F., MORENO M., LOMBARDI A., SILVESTRI E., GOGLIA F., LANNI, Antonia (2008). Rapid activation by 3,5,3-L-triiodothyronine of adenosine 5-monophosphate-activated protein kinase/acetyl-coenzyme A carboxylase and Akt/protein kinase B signaling pathways: Relation to changes in fuel metabolism and myosin heavy-chain protein content in rat gastrocnemius muscle in vivo. ENDOCRINOLOGY, vol. 149, p. 6462-6470, ISSN: 0013-7227.